Cochrane Library

Cochrane Database of Systematic Reviews

Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents (Review)

Marinho VCC, Higgins JPT, Logan S, Sheiham A

Marinho VCC, Higgins JPT, Logan S, Sheiham A.
Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents.
Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD002782.
DOI: 10.1002/14651858.CD002782.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents

Valeria CC Marinho[1], Julian PT Higgins[2], Stuart Logan[3], Aubrey Sheiham[4]

[1]Clinical and Diagnostic Oral Sciences, Institute of Dentistry, Barts and The London School of Medicine and Dentistry, London, UK. [2]MRC Biostatistics Unit, Cambridge, UK. [3]Institute of Health and Social Care Research, Peninsula Medical School, Universities of Exeter & Plymouth, Exeter, UK. [4]Department of Epidemiology and Public Health, University College London Medical School, London, UK

Contact address: Valeria CC Marinho, Clinical and Diagnostic Oral Sciences, Institute of Dentistry, Barts and The London School of Medicine and Dentistry, Queen Mary, University of London, Turner Street, Whitechapel, London, E1 2AD, UK. vcmarinho@yahoo.com, v.marinho@qmul.ac.uk.

Editorial group: Cochrane Oral Health Group
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2010.

Citation: Marinho VCC, Higgins JPT, Logan S, Sheiham A. Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD002782. DOI: 10.1002/14651858.CD002782.

ABSTRACT

Background

Topical fluoride therapy (TFT) in the form of varnish, gel, mouthrinse or toothpaste has been used extensively as a caries-preventive intervention for over 3 decades.

Objectives

To determine the effectiveness and safety of fluoride varnishes, gels, mouthrinses, and toothpastes in the prevention of dental caries in children and to examine factors potentially modifying their effect.

Search methods

We searched the Cochrane Oral Health Group's Trials Register (May 2000), CENTRAL (*The Cochrane Library* 2000, Issue 2), MEDLINE (1966 to January 2000), plus several other databases. We handsearched journals, reference lists of articles and contacted selected authors and manufacturers.

Selection criteria

Randomized or quasi-randomized controlled trials with blind outcome assessment, comparing fluoride varnish, gel, mouthrinse, or toothpaste with placebo or no treatment in children up to 16 years during at least 1 year. The main outcome was caries increment measured by the change in decayed, missing and filled tooth surfaces (D(M)FS).

Data collection and analysis

Inclusion decisions, quality assessment and data extraction were duplicated in a random sample of one third of studies, and consensus achieved by discussion or a third party. Authors were contacted for missing data. The primary measure of effect was the prevented fraction (PF) that is the difference in mean caries increments between the treatment and control groups expressed as a percentage of the mean increment in the control group. Random-effects meta-analyses were performed where data could be pooled. Potential sources of heterogeneity were examined in random-effects metaregression analyses.

Main results

There were 144 studies included. For the 133 that contributed data for meta-analysis (involving 65,169 children) the D(M)FS pooled prevented fraction estimate was 26% (95% CI, 24% to 29%; P < 0.0001). There was substantial heterogeneity, confirmed statistically (P < 0.0001), but the direction of effect was consistent. The effect of topical fluoride varied according to type of control group used, type of TFT used, mode/setting of TFT use, initial caries levels and intensity of TFT application, but was not influenced by exposure to water fluoridation or other fluoride sources. D(M)FS PF was on average 14% (95% CI, 5% to 23%; P = 0.002) higher in non-placebo controlled trials, 14% (95% CI, 2% to 26%; P = 0.25) higher in fluoride varnish trials compared with all others, and 10% (95% CI, -17% to -3%; P = 0.003) lower in trials of unsupervised home use compared with self applied supervised and operator-applied. There was a 0.7% increase in the PF per unit increase in baseline caries (95% CI, 0.2% to 1.2%; P = 0.004).

Authors' conclusions

The benefits of topical fluorides have been firmly established on a sizeable body of evidence from randomized controlled trials. While the formal examination of sources of heterogeneity between studies has been important in the overall conclusions reached, these should be interpreted with caution. We were unable to reach definite conclusions about any adverse effects that might result from the use of topical fluorides, because data reported in the trials are scarce.

PLAIN LANGUAGE SUMMARY

Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents

The use of fluoride toothpastes, mouthrinses, gels or varnishes reduces tooth decay in children and adolescents.
Tooth decay (dental caries) is painful, expensive to treat and can seriously damage teeth. Fluoride is a mineral that prevents tooth decay. The review of trials found that children aged 5 to 16 years who applied fluoride in the form of toothpastes, mouthrinses, gels or varnishes had fewer decayed, missing and filled teeth regardless of whether their drinking water was fluoridated. Supervised use of self applied fluoride increases the benefit. Fluoride varnishes may have a greater effect but more high quality research is needed to be sure of how big a difference these treatments make, and whether they have adverse effects.

BACKGROUND

Dental caries and its consequences pose important and uncomfortable problems in all industrialized societies and in a large number of developing countries. Although the prevalence and severity of dental caries in most industrialized countries have decreased substantially in the past 2 decades, reaching averages as low as 1.1 decayed, missing and filled teeth (DMFT) in 12 year olds, nearly half of those without any tooth decay or fillings (Marthaler 1996), this largely preventable disease is still common, increases significantly with age, and remains a public health problem for a significant proportion of the world population (Burt 1998). In the United Kingdom, 30% of 3.5 to 4.5 year olds (Moynihan 1996), and 50% of 12 year olds (Downer 1995) had experienced caries in 1993. In 2000, the figures were 40% for 5 year olds in Great Britain (Pitts 2001) and 38% for 12 year olds in England and Wales (Pitts 2002). These findings demonstrate the continuing need for effective preventive strategies and treatment services for these age groups in a country that has experienced a substantial caries decline. In general, dental caries levels vary considerably between and within different countries, but children in the lower socio-economic status (SES) groups have higher caries levels than those in the upper SES groups, and these differences are consistent in industrialized and in urbanized developing countries (Chen 1995).

Fluoride therapy has been the cornerstone of caries-preventive strategies since the introduction of water fluoridation schemes over 5 decades ago (Murray 1991). Fluoride controls the initiation and progression of carious lesions. Intensive laboratory and epidemiologic research on the mechanism of action of fluoride in preventing caries indicates that fluoride's predominant effect is topical, which occurs mainly through promotion of remineralization of early caries lesions and by reducing sound tooth enamel demineralization (Featherstone 1988). Various modes of fluoride use have evolved, each with its own recommended concentration, frequency of use, and dosage schedule. The use of topically applied fluorides in particular, which are much more concentrated than the fluoride in drinking water, has increased over recent decades and fluoride containing toothpastes (dentifrices), mouthrinses, gels and varnishes are the modalities most widely used at present, either alone or in different combinations. By definition, the term 'topically applied fluoride' describes those delivery systems which provide fluoride to exposed surfaces of the dentition, at elevated concentrations, for a local protective effect and are therefore not intended for ingestion. Fluoride gels and varnishes are typical methods of professional topical fluoride application and both delivery systems have been used in preventive programs. Fluoride gels have also been used as a self applied intervention in such programs. Fluoride rinses and toothpastes are the main forms of self applied fluoride therapy. The intensive use of fluoride mouthrinsing in school programs has been discontinued in many developed countries because of doubts regarding its cost-effectiveness at a low prevalence of dental caries and are being replaced by selective fluoride therapy directed to high risk children. Such procedures usually involve the combined use of fluoride toothpastes with gels or varnishes. Toothpaste is by far the most widespread form of fluoride usage (Murray 1991a; Ripa 1991) and the decline in the prevalence of dental caries in developed countries has been mainly attributed to its increased use (Glass 1982; Rolla 1991; Marthaler 1994; O' Mullane 1995; Marthaler 1996).

However, there is currently a debate regarding the appropriate use of fluorides. The questions being asked relate to the actual effectiveness and the potential risks (mainly in terms of fluorosis) that may be expected from the various fluoride-based caries preventive measures in an era of decreased caries prevalence and widespread availability of fluoride from multiple sources (Ripa 1991). In this context, even the need for selective professional fluoride applications has been questioned (Seppa 1998). The persistence of this debate and the variations in the use of the main forms of topically applied fluorides suggest the need to search for meaningful ways to summarize the empirical findings on this topic systematically.

Much of the experimental research on the effectiveness of individual fluoride modalities in preventing dental caries was conducted before the 1990s, when dental caries was more common and more severe. Modalities were usually tested separately and with the assumption that the method would provide the main source of fluoride. The studies have been extensively reviewed and synthesized in a number of traditional narrative reviews which often provide very different estimates of effectiveness, probably due to differences in how the literature to be included was selected, and rarely explore the causes of variability in reported effectiveness in a formal way. To date, a few published reviews focusing mainly on the evaluation of specific fluoride active agents within specific delivery systems have used a quantitative meta-analytical approach to synthesize studies' results (Stamm 1984; Clark 1985; Johnson 1993; Helfenstein 1994; Stamm 1995; van Rijkom 1998; Bartizek 2001; Strohmenger 2001; Chaves 2002). However, there has been no systematic investigation evaluating and comparing the overall effectiveness of the main forms of topical fluoride therapy currently used in caries prevention and examining formally the main factors that may influence their effectiveness. Moreover, none of the existing reviews have attempted to identify all relevant experimental research.

OBJECTIVES

The primary objective of this review is to determine the effects of topical fluoride therapy (TFT) in the form of toothpastes, mouthrinses, gels and varnishes in the prevention of dental caries in children and adolescents. The secondary objective is to examine whether the effectiveness of TFT is influenced by the initial level of caries severity, the background exposure to other fluoride sources, the mode/setting of TFT use, and the form of TFT used.

The specific objectives are:
(1) To determine the effectiveness and safety of topical fluoride therapy in the form of toothpastes, mouthrinses, gels and varnishes in preventing dental caries in the child/adolescent population.
(2) To examine whether the effect of TFT is influenced by the level of caries severity.
(3) To examine whether the effect of TFT is influenced by the background exposure to ambient levels of fluoride in water (or salt), or reported fluoride sources other than the study option(s).
(4) To examine whether the effect of TFT is influenced by the mode/setting of use (self applied supervised use of TFT in preventive programmes, self applied 'unsupervised' use of TFT at home, and operator-applied use of TFT), and if this does occur, whether there is a differential effect on caries prevention among the different forms of TFT used in each mode/setting.

(5) To examine whether the effect of TFT is influenced by the form of TFT used.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized or quasi-randomized controlled trials using or indicating blind outcome assessment, in which one form of topical fluoride therapy (TFT) (either as toothpaste, mouthrinse, gel or varnish) is compared concurrently to a placebo or no TFT group during at least 1 year/school year.
Randomized or quasi-randomized controlled trials using within-group paired comparison designs (e.g. split-mouth trials of fluoride varnish, as the effect of the varnish could spread across the mouth leading to contamination of control sites), or with open outcome assessment or no indication of blind assessment, or lasting less than 1 year/school year, or controlled trials where random or quasi-random allocation was not used or indicated were excluded.

Types of participants

Children or adolescents aged 16 or less at the start of the study (irrespective of initial level of dental caries, background exposure to fluorides, dental treatment level, nationality, setting where intervention is received or time when it started).
Studies where participants were selected on the basis of special (general or oral) health conditions were excluded.

Types of interventions

Topical fluoride therapy in the form of toothpastes, mouthrinses, gels or varnishes only, using any fluoride agent (which may be formulated with any compatible abrasive system, in the case of fluoride toothpastes), at any concentration (ppm F), amount or duration of application, and with any technique or method of application, provided the frequency of application was at least once a year. The control group is placebo (for any method of fluoride application) or no treatment (except for brushing or flossing methods of application) resulting in the following comparison: Any single TFT described above compared with a placebo or no TFT.
Studies where the intervention consisted of any caries preventive agent/procedure in addition to any of the forms of TFT described above were excluded (e.g. fluoride-based measures used in combination, anti-plaque or anti-calculus agents, sealants, oral hygiene interventions, xylitol chewing gums, glass ionomers).

Types of outcome measures

The primary outcome measure in this review is caries increment, as measured by change from baseline in the decayed, (missing) and filled surface (D(M)FS) index, in all permanent teeth erupted at start and erupting over the course of the study. For studies in younger children the outcome measure of interest is caries increment in deciduous tooth surfaces, as measured by change in the decayed, (missing/extraction indicated), and filled surface d(e/m)fs index. Dental caries is defined here as being clinically and radiographically recorded at the dentin level of diagnosis. (*See* 'Methods of the review' for the different ways of reporting the decayed, (missing) and filled teeth or surfaces (D(M)FT/S) scores in clinical trials of caries preventives.)
The following outcomes were considered relevant: coronal dental caries and dental fillings, in both the permanent and the deciduous dentitions; tooth loss; proportion of children developing new caries; dental pain/discomfort; specific side effects (fluorosis, tooth staining/discoloration, oral allergic reactions, adverse symptoms such as nausea, vomiting); unacceptability of preventive treatment as measured by drop outs during the trial (in non-placebo controlled studies); use of health service resources (such as visits to dental care units, length of dental treatment time).
Studies reporting only on changes in plaque/calculus formation, plaque regrowth/vitality, plaque/salivary bacterial counts, or gingival bleeding/gingivitis, dentin hypersensitivity or fluoride physiological outcome measures (fluoride uptake by enamel or dentin, salivary secretion levels, etc.) were excluded.

Search methods for identification of studies

With a comprehensive search, we attempted to identify all relevant studies irrespective of language, from 1965 onwards.

Electronic searching

Up to 1998

Relevant studies were identified (for the series of topical fluoride reviews) by searching several databases from date of inception: MEDLINE (1966 to 1997), EMBASE (1980 to 1997), SCISEARCH (1981 to 1997), SSCISEARCH (1981 to 1997), ISTP (1982 to 1997), BIOSIS (1982 to 1997), CINAHL (1982 to 1997), ERIC (1966 to 1996), DISSERTATION ABSTRACTS (1981 to 1997) and LILACS/BBO (1982 to 1997). Two overlapping but complementary subject search phrases (Appendix 1) with low specificity (but high sensitivity), using 'free text 'and 'controlled vocabulary', were formulated within Silverplatter MEDLINE around two main concepts, fluoride and caries, and combined with all three levels of the Cochrane Optimal Search Strategy for Randomized Controlled Trials (RCTs). These subject search phrases were customised for searching EMBASE and the other databases.

RCT filters were also adapted to search EMBASE, BIOSIS, SCISEARCH, DISSERTATION ABSTRACTS, and LILACS/BBO. All the strategies (subject search and methodological filters) developed to search each database are fully described in a report produced for the Systematic Reviews Training Unit (Marinho 1997), and are available on request. These were used for the development of a register of topical fluoride clinical trials for the systematic reviews, as the Cochrane Oral Health Group's Trials Register was not yet developed in 1997/98.

The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 1997, Issue 1), the Community of Science database (1998), which included ongoing trials funded by the National Institute of Dental Research (NIDR), the System for Information on Grey Literature in Europe (SIGLE) database (1980 to 1997), and OLDMEDLINE (1963 to 1965) were searched using the terms 'fluor' and 'carie' truncated. (Grey literature search had also been carried out by searching the Index to Scientific and Technical Proceedings (ISTP) and DISSERTATION ABSTRACTS.)

From 1999 to 2001

The strategy included in Appendix 2 was used to search LILACS/BBO in 1999 (1982 to 1998), where free text subject search terms were combined with a methodological filter for RCTs.

Four supplementary and more specific subject search phrases (including 'free text' and 'controlled vocabulary' terms), refined

exclusively for the reviews on the effects of individual fluoride modalities, formulated around three concepts each (the relevant topical fluoride therapy (TFT), fluoride and caries) were used to search Silverplatter MEDLINE (up to January 2000) without methodological filters (Appendix 3). These strategies were adapted to search the Cochrane Oral Health Group's Trials Register (up to May 2000), and have also been run on CENTRAL (*The Cochrane Library* 2000, Issue 2) to double check.

The *meta*Register of Current Controlled Trials was searched in October 2001 for ongoing RCTs using the terms 'fluoride' and 'caries'.

Reference searching

All eligible trials retrieved from the searches, meta-analyses and review articles located up to January 2000 were checked for relevant references. Reviews had been identified mainly by a MEDLINE search strategy specifically carried out to provide information on available systematic reviews or meta-analyses and on the scope of the literature on the topic, when the *Cochrane Database of Systematic Reviews* (CDSR), and the Database of Abstracts of Reviews of Effects (DARE) and NHS Economic Evaluation Database (NHSEED), were also searched. Reference lists of relevant chapters from preventive dentistry textbooks on topically applied fluoride interventions were also consulted.

Full text searching

Prospective handsearching of the seven journals identified as having the highest yield of eligible RCTs/controlled clinical trials (CCTs) was carried out, from January 1999 until January 2000: *British Dental Journal*, *Caries Research*, *Community Dentistry and Oral Epidemiology*, *Journal of the American Dental Association*, *Journal of Dental Research*, *Journal of Public Health Dentistry* and *European Journal of Oral Sciences*. The handsearch of *Community Dentistry and Oral Epidemiology* was undertaken (1990 to December 1999), as this was the journal with the highest yield of eligible reports.

Personal contact

Searching for unpublished studies (or 'grey' literature such as technical reports and dissertations, or studies published in languages other than English which may not have been indexed to major databases) started by contacting experts in the field of preventive dentistry. A letter was sent to the author(s) of each included study published during the last two decades in order to obtain information on possible unpublished studies eligible for inclusion. All the authors of studies who had been contacted in order to clarify reported information to enable assessment of eligibility or obtain missing data were also asked for unpublished studies.

Based on information extracted mainly from included studies, a list of manufacturers of fluoride toothpastes, mouthrinses, gels and varnishes was created for locating unpublished trials. Letters to manufacturers were sent out by the Cochrane Oral Health Group, in the hope that companies might be more responsive to contact from the editorial base than from individual reviewers. Fourteen manufacturers were contacted (October 2000) and information on any unpublished trials requested: Bristol-Myers Co, Colgate-Palmolive, Davies Rose-Hoyt Pharmaceutical Division, Gaba AG, Ivoclar North America, John O Butler Company, Johnson & Johnson, Oral-B Laboratories, Pharmascience, Procter & Gamble, Smithkline Beecham, Synthelabo, Unilever/Gibbs, Warner-Lambert.

Data collection and analysis

Management of records produced by the searches

Because multiple databases were searched, the downloaded set of records from each database, starting with MEDLINE, was imported to the bibliographic software package Reference Manager and merged into one core database to remove duplicate records and to facilitate retrieval of relevant articles. The records yielded from LILACS, BBO, CENTRAL, SIGLE and NIDR databases were not imported to Reference Manager and were checked without the benefit of eliminating duplicates. The records produced by OLDMEDLINE and by the specific MEDLINE search performed without methodological filter were imported to Reference Manager for inspection, in a database separate from the core database. The records produced by searching the Cochrane Oral Health Group's Trials Register and the *meta*Register of Current Controlled Trials were also checked outside Reference Manager. In order to facilitate importing of all records located from searching other (non-electronic) sources to Reference Manager, we tried to locate these in MEDLINE as well. Those references that could not be downloaded in this way were entered manually. (Reports that might be identified by contacting manufacturers will be obtained to feature in updates of this review.)

Relevance assessment

All records identified by the searches were printed off and checked on the basis of title first, then by abstract (when this was available in English or in languages known by the reviewer) and/or keywords by one reviewer, Valeria Marinho (VM). Records that were obviously irrelevant were discarded and the full text of all remaining records was obtained. Records were considered irrelevant according to study design/duration, participants, or interventions/comparisons (if it could be determined that the article was not a report of a randomized/quasi-randomized controlled trial; or the trial was of less than 6 to 8 months duration; or the trial was exclusively in adults; or the trial did not address one of the four topical fluoride therapies (TFTs); or the trial did not compare a TFT to placebo or no treatment).

Selection of studies for inclusion

With the inclusion criteria form previously prepared and pilot tested, one reviewer (VM) assessed all studies for inclusion in the review, and a second reviewer, Julian Higgins (JH), independently duplicated the process for a sample of those (approximately 30%). In addition, any study that could not be classified by the first reviewer was independently assessed by the second. A third reviewer was consulted, Stuart Logan (SL) or Aubrey Sheiham (AS), to resolve any disagreement. It was decided in advance to exclude any trial where agreement could not be reached (but this did not occur). Trial reports thought to be potentially relevant in languages not known by the reviewers were translated and the reviewer (VM) completed the inclusion form with reference to the translator. Attempts were made to contact authors of trials that could not be classified in order to ascertain whether inclusion criteria were met.

It was considered essential to identify and check all reports related to the same study; in case of any discrepancy, authors were contacted.

Data extraction

Data from all included studies were extracted by one reviewer (VM) using a pilot tested data extraction form. A second reviewer (JH) extracted data from a random sample of approximately one third of included studies. Again, data that could not be coded by the first reviewer were independently coded by the second, any disagreements were discussed and a third reviewer consulted to achieve consensus where necessary. (In future updates all reports will be data extracted and quality assessed in duplicate.) Data presented only in graphs and figures were extracted whenever possible, but were included only if two reviewers independently had the same result. Attempts were made to contact authors through an open-ended request in order to obtain missing information or for clarification whenever necessary. Papers in languages not known by the reviewers were data extracted with help from appropriate translators.

Additional information related to study methodology or quality that was extracted included: study duration (years of follow up); comparability of baseline characteristics: methods used pre-randomization in sizing/balancing (stratification based on relevant variables) or used post-randomization in analysing/adjusting for possible differences in prognostic factors between groups; objectivity/reliability of primary outcome measurement (diagnostic methods and thresholds/definitions used and included, and monitoring of diagnostic errors); any co-intervention and/or contamination. Information on sponsoring institutions and manufacturers involved was also recorded.

Characteristics related to participants that were extracted included: age (range) at start, caries severity at start (average DMFS, DFS, or other measure), background exposure to fluoride sources other than the study option(s) (in water, topical applications, etc.), year study began, place where study was conducted (country), setting where participants were recruited, and dental treatment level (F/DMF). Characteristics of the interventions that were extracted included: fluoride modality(s), mode of application (how the intervention was delivered), methods (technique/device) of application, prior- and post-application, fluoride active agents and concentrations used, frequency and duration of application, and amount applied.

Different ways of assessing/reporting caries increment in the trials (change from baseline as measured by the DMF index) were recorded separately and/or combined according to the components of the index chosen and units of measurement (DMFT/S, or DFT/S, or DT/S, or FT/S), types of tooth/surface considered (permanent/deciduous teeth/surfaces, first molar teeth, approximal surfaces, etc.), state of tooth eruption considered (erupted and/or erupting teeth or surface), diagnostic thresholds used (cavitated/dentin lesions, non-cavitated incipient lesions), methods of examination adopted (clinical and/or radiographical), and approaches to account or not for reversals in caries increment adopted (in a net or observed/crude caries increment respectively). In addition, caries increments have been recorded whenever the authors reported them (various follow ups), and where assessments of caries increments were made during a post-intervention follow-up period, the length of time over which outcomes were measured after the intervention ended was noted.

As we were aware that caries increment could be reported differently in different trials we developed a set of a priori rules to choose the primary outcome data for analysis from each study: data on permanent teeth would be chosen over data on deciduous teeth; data on surface level would be chosen over data on tooth level; DFS data would be chosen over DMFS data, and this would be chosen over DS or FS; data for 'all surface types combined' would be chosen over data for 'specific types' only; data for 'all erupted and erupting teeth combined' would be chosen over data for 'erupted' only, and this over data for 'erupting' only; data from 'clinical and radiological examinations combined' would be chosen over data from 'clinical' only, and this over 'radiological' only; data for dentinal/cavitated caries lesions would be chosen over data for enamel/non-cavitated lesions; net caries increment data would be chosen over crude (observed) increment data; and follow up nearest to 3 years (often the one at the end of the treatment period) would be chosen over all other lengths of follow up, unless otherwise stated. When no specification was provided with regard to the methods of examination adopted, diagnostic thresholds used, groups of teeth and types of tooth eruption recorded, and approaches for reversals adopted, the primary choices described above were assumed.

All other relevant outcomes assessed/reported in the trials were also recorded/listed.

Quality assessment

The methodological quality of the included studies was assessed according to the criteria for concealment of treatment allocation described in the *Cochrane Reviewers' Handbook* (Clarke 2000) used in the Cochrane Review Manager software (RevMan). Allocation concealment for each trial was rated as belonging to one of three categories.
(A) Adequately concealed (an adequate method to conceal allocation is described).
(B) Concealment unclear ('random' allocation stated/indicated but the actual allocation concealment method is not described or an apparently adequate concealment scheme is reported but there is uncertainty about whether allocation is adequately concealed).
(C) Inadequately concealed (an inadequate method of allocation concealment is described).
Excluded: random (or quasi-random) allocation clearly not used in the trial, or 'random' allocation not stated and not implied/possible.

Blinding of main outcome assessment was also rated according to the following three categories defined for the topical fluoride reviews.
(A) Double-blind (blind outcome assessment and use of placebo described).
(B) Single-blind (blind outcome assessment stated and no placebo used).
(C) Blinding indicated (blind outcome assessment not stated but likely in any element/phase of outcome assessment, e.g. clinical and/or radiographic examinations performed independently of previous results, or radiographic examinations performed independently of clinical examinations with results reported separately/added later, or examiners clearly not involved in giving treatment, or use of placebo described) or reported but unclear

(blind outcome assessment reported but there is information that leads to suspicion/uncertainty about whether the examination was blind).
Excluded: clearly open outcome assessment used or blind outcome assessment not reported and unlikely (no description of an examination performed independently of previous results, of x-rays registered independently of clinical examination, of use of a placebo, and of examiners clearly not involved in giving treatment).

One reviewer (VM) assessed the quality of all included studies. A second reviewer (JH) duplicated the process for a random sample of approximately one third. Any disagreement was discussed and where necessary a third reviewer was consulted to achieve consensus. Where uncertainty could not be resolved an effort was made to contact authors directly to clarify the method used to conceal allocation or whether assessment of the main outcome had been carried out blind.

Checking of interobserver reliability was limited to these validity assessments.

Other methodological characteristics of the trials such as completeness of follow up (proportion excluded) and handling of exclusions (extent to which reasons for attrition are explicitly reported, or losses are independent of treatment allocated) were not used as thresholds for inclusion. However, all assessments of study quality are described in the table of included studies, and were coded for possible use in metaregression or sensitivity analyses.

Data analyses

Handling of missing main outcome data

It was decided that missing standard deviations for caries increments that were not revealed by contacting the original researchers would be imputed through linear regression of log standard deviations on log mean caries increments. This is a suitable approach for caries prevention studies since, as they follow an approximate Poisson distribution, caries increments are closely related (similar) to their standard deviations (van Rijkom 1998).

Handling of results of studies (main outcome) with more than one treatment arm

In the studies with more than one relevant intervention group (but of the same modality of TFT) and a common control group, such as those comparing different concentrations of fluoride ions in a mouthrinse for example to a placebo/no treatment group, raw results (the numbers, mean caries increments and standard deviations) from all relevant experimental groups were combined in order to obtain a measure of treatment effect (this enables the inclusion of all relevant data for each form of TFT in the primary meta-analysis, although may slightly compromise any secondary investigations of dose response). In the studies comparing two or more relevant modalities of TFT to a common placebo/no treatment group, we have divided the control group into approximately equally sized smaller groups to provide a pairwise comparison for each modality. Means and standard deviations were unchanged.

Choice of measure of effect and meta-analyses of main outcome

The chosen measure of treatment effect was the prevented fraction (PF), that is (mean increment in the controls minus mean increment in the treated group) divided by mean increment in the controls. For an outcome such as caries increment (where discrete counts are considered to approximate to a continuous scale and are treated as continuous data) this measure was considered more appropriate than the mean difference or standardised mean difference, since it allows combination of different ways of measuring caries increment and a meaningful investigation of heterogeneity between trials. It is also simple to interpret. The meta-analyses were conducted as inverse variance weighted averages. Within-study variances were estimated using the formula presented in Dubey 1965 which was more suitable for use in a weighted average, and for large sample sizes the approximation should be reasonable. Random-effects meta-analyses were performed throughout in RevMan/RevMan Analyses.

Deciduous and permanent teeth were analysed separately throughout.

For illustrative purposes, when overall results were significant, the results were also presented as the number of children needed to treat (NNT) to prevent one carious teeth/surface. These were calculated by combining the overall prevented fraction with an estimate of the caries increment in the control groups of the individual studies.

Assessment of heterogeneity and investigation of reasons for heterogeneity

Heterogeneity in the results of the trials was assessed by inspection of a graphical display of the estimated treatment effects from the trials along with their 95% confidence intervals and by formal tests of homogeneity (Thompson 1999).

In addition to aspects of study quality, four potential sources of heterogeneity were specified a priori as investigations of these formed part of the primary objectives of the review. We hypothesised that: (1) the effect of TFT differs according to the baseline levels of caries severity; (2) the effect of TFT differs according to exposure to other fluoride sources (in water, in toothpastes, etc.); (3) the effect of TFT differs according to mode of use; and (4) forms of TFT used. The association of these factors with estimated effects (D(M)FS PFs) were examined by performing random-effects metaregression analyses in Stata version 6.0 (Stata Corporation, USA) using the program Metareg (Sharp 1998). The random-effects regression model described in detail elsewhere (Thompson 1999) relates treatment effect to study characteristics assuming a normal distribution for the residual errors with both a within- and an additive between-study component of variance. The between-studies variance was estimated by an iterative procedure, using an estimate that is based on a restricted maximum likelihood method.

To allow such investigation, relevant data were dealt with as follows: data on 'baseline levels of caries' were calculated from the study sample analysed (final sample) and in connection with the caries increment index chosen, unless otherwise stated, and were averaged among all relevant study groups.
Data on 'background exposure to other fluoride sources' combined data on the use of fluoride toothpaste or any fluoride other than the study option(s) and the consumption of fluoridated water (or salt) and were grouped into two categories: one for studies which were based on samples provided with non-fluoride toothpaste/reporting no/low use of other fluorides and which were from non-

fluoridated areas (non exposed), and another for studies based on samples using any fluoride other than the study option(s) or studies in fluoridated communities or both. When background exposure to fluoride toothpaste was not clearly indicated in studies carried out in developed countries, it was assumed that fluoride toothpaste was widely used from the middle of the 1970s (Ripa 1989); this information was sought from authors (or obtained from other sources) when missing from studies carried out in other locations. When data on the year a study had begun was not provided this was calculated as a 'probable date' by subtracting the duration of the study (in years) plus one extra year, from the publication date of the study. Background exposure to fluoride rinses, gels, tablets, etc. should be reported to be involving the majority in a study to be considered as such, otherwise it was assumed these had not been used. Exposure to water fluoridation should be above 0.3 ppm F; when information on the fluoridation status of a site was not available/obtainable, no assumptions were made.
Data on the 'fluoride application mode of use and forms of TFT' were classified as self applied unsupervised use (of toothpaste or mouthrinse at home), self applied supervised use (of gel, mouthrinse or toothpaste in school-based programmes), and operator-applied use (of gel or varnish). The four modalities of TFT were categorised as such.

Further potential sources of heterogeneity were investigated by metaregression based on previous investigations of covariates carried out in the individual TFT reviews. These included investigations of the potential influence of fluoride concentration and frequency of use. (Data on 'concentration applied' and 'frequency of use' have not been categorised, but a 'total intensity of application per year' covariate was produced by multiplying frequency of application (per year) by fluoride concentration (in ppm F).) In multiple arm studies we have averaged this intensity score over fluoride treatment groups. These 'post hoc' analyses are clearly identified and the results should be treated with caution. Sensitivity analyses were performed as appropriate.

Investigation of publication and other biases

A funnel plot (plots of effect estimates versus the inverse of their standard errors) was drawn. Asymmetry of the funnel plot may indicate publication bias and other biases related to sample size, though may also represent a true relationship between trial size and effect size. A formal investigation of the degree of asymmetry was performed using the method proposed by Egger et al (Egger 1997).

Measures of effect and meta-analysis of other outcomes

For outcomes other than caries increment, continuous data were to be analysed according to differences in mean treatment effects and their standard deviations. Dichotomous outcome data were to be analysed by calculating risk ratios (RR) or, for adverse effects of fluoride treatment, risk differences (RD). RevMan was used for estimation of overall treatment effects. Again, a random-effects model was used to calculate a pooled estimate of effect. As a general rule only (relevant) outcomes with useable data were shown in the analyses tables.

RESULTS

Description of studies

Search results

Our initial multiple database search (1997/98) produced the following total number of records, according to database searched: MEDLINE, 4599; EMBASE, 5052; BIOSIS, 421; SCISEARCH, 514; SSCISEARCH, 169; ISTP, 66; CINAHL, 133; ERIC, 60; DISSERTATION ABSTRACTS, 95; LILACS, 48; BBO, 47; CENTRAL, 86; SIGLE, 6. Searching OLDMEDLINE produced 545 records, and the Community of Science database, 24 records. In the second stage of searches (1999), searching LILACS and BBO with a modified search strategy produced 210 records (142 and 68 records respectively). The more specific MEDLINE searches (by individual modalities of topical fluoride therapy (TFT)) performed without a randomized controlled trial (RCT) filter produced 2441 records, and the searches performed in the Cochrane Oral Health Group's Trials Register (May 2000) produced 479 records. Searching the *meta*Register of Current Controlled Trials for ongoing studies produced 5 records. Many records retrieved through electronic search were duplicates merged later in the core database, and many appeared more than once in different databases and/or searches performed (overlapped). Searching other non-electronic sources (reference lists of potentially relevant reports, review articles or book chapters, relevant journals, and contacting authors) produced 171 additional records for inspection. (Any search results produced by contacting manufacturers will feature in updates of this review.)

Relevance assessment results

When the records produced from all the above searches were screened, a total of 713 reports were considered potentially eligible and further assessment was sought.

Study selection results

Seven hundred and thirteen reports were sought for detailed assessment for inclusion, of which 19 full text reports could not be obtained (most of these were incomplete references to non-English reports and unpublished studies conducted decades ago by toothpaste manufacturers). Two hundred and ninety-three reports (293) were considered immediately irrelevant for this review, largely as a result of the types of intervention compared with, or used in addition to the relevant topical fluoride treatments (including head to head studies without a placebo or no treatment group), and due to the types of study design described (historical controls or other non-experimental designs).

Thus, 287 studies (401 reports) are considered/cited in this review. These comprise 214 reports relating to 144 included studies, 157 reports relating to 115 excluded studies, two reports relating to two ongoing (fluoride varnish) studies, and 28 reports relating to 26 studies waiting assessment (either because they require translation, because translation and contact with the authors have not ascertained whether all inclusion criteria have been met, or because additional information has not been obtained yet for two studies in abstract form).

Listed either under excluded or included studies are 91 reports (25%) in languages other than English: 39 in German, 14 in Portuguese, seven in Spanish, seven in Russian, five in Japanese, four in French, three in Hungarian, three in Danish, two in Dutch,

two in Italian, two in Polish, one in Czech, one in Bulgarian, one in Norwegian. The reports in Portuguese, Spanish and Italian have been assessed by the contact reviewer, and the others by the reviewer with a translator (some reports have not been translated due to the availability of a full text English report of the same study, or because sufficient information was available in the English abstract to exclude the study).

Excluded studies

See Characteristics of excluded studies table for the description of reasons for rejecting each study.

We have excluded 33 fluoride varnish studies, 11 fluoride gel studies, 38 fluoride mouthrinse studies, and 33 fluoride toothpaste studies.
All 115 studies were excluded for a variety of reasons. Twenty-eight studies had non-fluoride or other fluoride-based interventions, or active agents in addition to the ones considered in this review. In one study a fluoride intervention was associated to the control group, and in two studies the fluoride rinsing solution was supposed to be swallowed. Five studies involved children with specific health problems, and eight studies included participants older than 16 years of age. In two studies, the length of follow up was 6 months (and relevant outcomes were not reported in one of these). Ten (fluoride varnish) studies used the within-subject paired design, or 'split-mouth' design. The remaining studies were excluded for reasons related to random allocation or blind assessment of outcome as described in the Methods section.

Included studies

See Characteristics of included studies table for details of each study.

There are 144 trials included. The studies conducted by Forsman 1974; Hargreaves 1973; Horowitz 1971a; Koch 1967; Koch 1967c; Marthaler 1970; Marthaler 1970b; Zacherl 1970; Held 1968; Marthaler 1965; and Torell 1965 have been treated as two (or more) independent trials each, because the results for the two (or more) age groups, and/or study sites, and/or comparisons involved were reported separately as distinct studies. There were also completely distinct studies published as such in the same year by the same author: Zacherl 1972/Zacherl 1972a; Koch 1967a/Koch 1967b; Koch 1967e/Koch 1967f; and Slack 1967/Slack 1967a. All 214 reports were published between 1955 and 1999. The 144 trials were conducted between 1954 and 1996: three in the 1950s, the great majority in the 1960s and 1970s, 16 in the 1980s, and four in the 1990s. The majority of studies were conducted in industrialized countries, especially USA, UK, European and Scandinavian countries, but there were at least 14 conducted in other countries. Twenty-two studies had at least one report published in languages other than English and 12 studies had only non-English publications (one of these, Treide 1988, reported data for deciduous teeth only).

There are 74 toothpaste trials included, followed by 36 mouthrinse trials, 25 gel trials, and nine varnish trials.
Fifty-eight studies had more than one topical fluoride treatment group compared to a control. Forty-six studies compared different characteristics of the same modality of TFT (e.g. different concentrations of fluoride ions in a mouthrinse) and eight studies (which have been entered as 16 comparisons/studies) compared two or more relevant modalities of TFT to a common control group (in two of these, entered as four studies, different features of each modality were compared concomitantly). One hundred and twenty-five trials used a placebo control group and the remaining 19 used a no treatment control group. Study duration ranged from 1 to 6 years, with the great majority of studies lasting 2 or 3 years. Studies were generally large with only 15 allocating less than 100 children to relevant study groups, nearly all recruited from school settings.

There was substantial variation in the characteristics of participants and interventions in the trials included. While the majority of studies reported on exposure or not to fluoridation, background exposure to fluoride toothpaste (or other fluoride sources) was clearly reported in very few studies. Caries prevalence at baseline was generally reported. All fluoride varnish and gel trials reported whether or not applications were carried out by professionals, and with two exceptions, all fluoride toothpaste, mouthrinse and gel trials (of self applied gel) reported whether or not TFT use was carried out under supervision (by dental personnel, trained non-dental personnel, or by mothers and dental personnel in preventive programmes; or 'unsupervised' at home). Fluoride concentrations and application frequencies varied greatly among TFT modalities and within each modality, and were reported in the great majority of studies.

All but five of the 144 trials reported caries increment data (or data from which these could be derived) at the tooth surface level (D(M)FS was reported in 135 trials, defs in one of these, and d(e/m)fs in the other four trials). Data at the tooth level for the permanent dentition (D(M)FT) were reported in 79 of the 139 trials that reported any caries increment data; only one of the five trials that reported caries increment data for deciduous teeth (dmfs) reported these data at the tooth level (dmft). With regard to the components of the DMFS index used, 92 trials reported DMFS data and 56 trials reported DFS data. Sixty-five trials presented D(M)FS data at more than one follow-up time. Clinical and radiographic examinations provided the definition of different stages or grades of caries lesions. These have been grouped into two basic grades for each method of examination: NCA = non-cavitated incipient enamel lesions clinically visible as white spots or discoloured fissures; CA = lesions showing loss of enamel continuity that can be recorded clinically (undermined enamel, softened floor/walls) or showing frank cavitation; ER = any radiolucency in enamel/enamel-dentin junction; DR = radiolucency into dentin. Many trials presented results using one caries grade only (usually CA/ER or CA/DR), others either did not report the grade, or reported caries increment data at both levels of diagnosis, in which case CA was chosen. Data on the state of tooth eruption considered were not clearly specified in many trials. The seven studies of Marthaler used partial recording as opposed to the full mouth recording used in all others.

The Characteristics of included studies table provides a description of all the main outcome data reported from each study with the primary measure chosen featuring at the top.

Other dental caries data reported in a few trials: caries incidence/attack rate, caries progression, proportion of children developing new caries, proportion of children not remaining caries-free, proportion of teeth developing new caries and failures (carious teeth) over time, proportion of caries-free teeth/surfaces which developed caries.

Data on adverse effects were reported in a few trials (partially reported or unusable data in many of these): stain score, proportion

of children with tooth staining, signs of sensitivity in oral soft tissue, adverse symptoms (nausea/vomiting), etching of enamel. Fluorosis data have not been reported in any of the trials. Data for unacceptability of treatment (as measured by dropouts/exclusions) were reported in 10 non-placebo controlled trials.

Ongoing studies

See Characteristics of ongoing studies table for details of each study.

We have identified two ongoing randomized trials, one from UK and the other from USA, which are described in the table of ongoing studies.

Risk of bias in included studies

Based on 28 studies included in the topical fluoride reviews and randomly selected for assessment of reproducibility and agreement between two reviewers, interrater reliability was excellent (89%) for both allocation concealment and blinding, and agreement was good for allocation (Kappa = 0.61) and very good for blinding (Kappa = 0.73).

As expected, there was a considerable variation in the quality of the studies in this review (using the reported information and additional information obtained from investigators). One hundred and nine trials included in this review were described as randomized but provided no sufficient description on how the 'random' allocation was done, and 21 trials were considered to be quasi-randomized. Double-blinding was described in 118 trials, single-blinding (blind outcome assessment but no placebo used) was described in 14 trials, and blind outcome assessment was indicated in 12 trials.

Seventy-two per cent (72%) of the participants originally enrolled in these studies were included in the final analysis (60,423 analysed out of 85,093 initially randomized). These data exclude 27 of the 144 included studies which provided no information on the number of participants randomized to relevant groups. Drop-out rates were obtained from all but 11 of the 144 included studies and ranged from 4% at 2 years to 66% at 3 years. The most common reason for attrition was that participants were not available for follow-up examination at the end of the study.

Cluster randomization was used in two trials (Bravo 1997; Ruiken 1987) where school classes (in the first trial) and schools (in the second trial) were used as units of randomization and children used as units of analysis. Individuals were allocated to study arms in all other trials, and each participant's caries incidence, over a period of time was used as the unit of analysis.

Effects of interventions

Effect of topical fluorides on dental caries increment

The effects of fluoride toothpaste, mouthrinse, gel and varnish on dental caries increment (as measured by the DMF index) were reported in a variety of ways in the included studies. Where appropriate and possible these have been combined to produce pooled estimates as described in the Methods section. The results are reported separately here for:
(1) Decayed, (Missing) and Filled Surfaces Prevented Fraction (D(M)FS PF), with results from analyses of associations between this and study characteristics;
(2) Decayed, (Missing) and Filled Teeth Prevented Fraction (D(M)FT PF);
(3) decayed, (missing/extraction indicated), and filled surfaces Prevented Fraction (d(m/e)fs PF).
Estimates of the effects of topical fluoride therapy (TFT) are therefore presented for caries increment in the permanent and in the deciduous dentitions.

Five included studies (Brandt 1972; de Liefde 1989; Homan 1969; Powell 1981; Slack 1964) did not contribute (caries increment) data suitable for meta-analysis, although they are retained in the review (characteristics of each are described in the 'Table of included studies' and the basic findings reported or obtained from the authors are described below). Standard deviations (SD) of mean caries increment data in the permanent dentition (new D(M)FS) were (partly) missing in 34 of the 135 studies which contributed data (Abadia 1978; Abrams 1980; Bastos 1989; Bijella 1981; Clark 1985; DePaola 1977; Dolles 1980; Driscoll 1982; Finn 1975; Fogels 1979; Forsman 1974; Forsman 1974a; Gallagher 1974; Hargreaves 1973; Hargreaves 1973a; Hargreaves 1973b; Heidmann 1992; Held 1968; Held 1968a; Held 1968b; James 1977; Kinkel 1972; Laswell 1975; McConchie 1977; Mestrinho 1983; Modeer 1984; Moreira 1972; Muhler 1955; Poulsen 1984; Ran 1991; Ran 1991a; Ruiken 1987; Segal 1967; van Wyk 1986). From the analysis of the 179 available treatment arms for the topical fluoride reviews with complete information (as of October 1999) we derived a regression equation log (SD caries increment) = 0.64 + 0.55 log (mean caries increment), (R^2 = 77%). This equation was used to estimate missing standard deviations from mean D(M)FS increments for the meta-analyses. Similarly, this regression equation was used to estimate missing standard deviation data for 15 of the 79 trials reporting D(M)FT data (Abrams 1980; Bastos 1989; Bijella 1981; Finn 1975; Fogels 1979; Hargreaves 1973; Hargreaves 1973a; Hargreaves 1973b; Held 1968; Held 1968a; Held 1968b; Holm 1984; McConchie 1977; Mestrinho 1983; Muhler 1955). Standard deviation data were missing in four of the five trials reporting mean caries increment data in the deciduous dentition (Clark 1985; Englander 1978; Frostell 1991; Treide 1988). The 'd(e/m)fs' for these trials were also estimated with the regression equation. Only one of the studies reporting d(e/m)fs data is also included in the analysis of D(M)FS PF (Clark 1985).

There were eight included studies that had a common control group and tested two different modalities of TFT (Ashley 1977; Blinkhorn 1983; DePaola 1980; Mainwaring 1978; Marthaler 1970; Marthaler 1970a; Ran 1991, Ringelberg 1979). These have been entered as 16 comparisons/studies (dividing up the control groups into approximately equally sized smaller groups to provide a pairwise comparison for each modality; means and standard deviations were unchanged).

We have decided to exclude the trials of Ran 1991/Ran 1991a (fluoride gel and toothpaste comparisons respectively with a common control group) from all analyses because the control DMFS increment was very small (0.2) in these comparisons, resulting in a poor estimate of PF.

(1) Effect on permanent tooth surfaces: D(M)FS PF

The random-effects meta-analysis of all 133 trials combined suggested a clear benefit from the use of topical fluorides. The D(M)FS PF pooled estimate was 0.26 (95% confidence interval (CI), 0.23 to 0.29; P < 0.00001). However, substantial heterogeneity in results could be observed graphically and statistically (Chi^2 = 745.25

on 132 degrees of freedom, P < 0.00001). The [method of moments-based] estimate of among-trial variance in the random-effects meta-analysis was 0.018, corresponding to a standard deviation of 0.134. Thus, an approximate, though anti-conservative, interval in which at most 95% of underlying PFs might lie is from 0.262 - 1.96*0.134 to 0.262 + 1.96*0.134, that is from 0.00 to 0.53. This provides strong evidence of a generalizable beneficial effect of topical fluoride therapy.

(a) Metaregression, subgroup and sensitivity analyses: D(M)FS PF

Metaregression analyses were performed to examine potential associations between study factors and the estimated treatment effect of topical fluorides. Univariate metaregression suggested a significant association between estimates of D(M)FS PFs and the following pre-specified trial characteristics: baseline caries levels, mode/setting of TFT use (unsupervised self applied home use/supervised self applied use in school-based programmes/ operator-applied use), and type of TFT used (fluoride varnish/ gel/mouthrinse/toothpaste). Further univariate metaregression analyses showed a significant association between estimates of D(M)FS prevented fractions and type of control group (placebo/ no treatment), language of publication (English/other than English only), method of application (paint or tray/brush or rinse), fluoride concentration, and 'total intensity of application', but statistical significance for 'intensity of application' (frequency x concentration) was lost when the trial of Di Maggio 1980, a study with an unusually large PF, and hence of high influence, was excluded, in a sensitivity analysis. Univariate metaregression did not reveal any statistically significant associations between estimates of D(M)FS prevented fractions and the pre-specified factors background exposure to fluoridated water or background exposure to other fluoride sources. In addition, no statistically significant associations were revealed in univariate metaregression between estimates of D(M)FS PFs and allocation concealment (random/quasi-random), blinding of outcome assessment (blind/ blind likely or unclear), drop-out rate, length of follow up, frequency of use, mode of use (operator/self applied) or fluoride agent used (APF/AmF/NaF/SMFP/SnF2).

The difference between TFT types (indirect comparisons) shown in the univariate analysis relates to a greater benefit of TFT with the use of fluoride varnish. This modality has been found to be significantly different (coefficient, 0.20; 95% CI, 0.08 to 0.33; P = 0.001) from the other three types of TFT (fluoride gel/mouthrinse/ toothpaste), while differences among these three modalities were not obvious. The analysis involved all 133 included trials (seven fluoride varnish trials, 22 fluoride gel trials, 34 fluoride rinse trials and 70 toothpaste trials). When the analysis was restricted to 126 trials of fluoride gel, mouthrinse and toothpaste, no significant differences among these or between each and the others were indicated either, although failure to identify such differences may be due to low power. The unadjusted pooled estimate of treatment effects from the seven fluoride varnish trials was 0.46 (95% CI, 0.30 to 0.63; P < 0.0001); from the 22 fluoride gel trials was 0.28 (95% CI, 0.19 to 0.37; P < 0.0001), from the 34 fluoride mouthrinse trials was 0.26 (95% CI, 0.23 to 0.30; P < 0.0001), and from the 70 fluoride toothpaste trials was 0.24 (95% CI, 0.21 to 0.28; P < 0.0001). These results have been reported and examined in detail in separate component reviews in this series focusing on the effectiveness of each TFT modality.

Metaregression results also clearly indicated a greater treatment effect in trials with no treatment rather than placebo control groups (coefficient, 0.16; 95% CI, 0.08 to 0.23; P < 0.0001). The strong evidence on differences in effect estimates by type of control group has been shown in a previous review in this series, which focused on the effectiveness of fluoride gels (Marinho 2002). The pooled estimate of treatment effect on D(M)FS PF from the 17 trials with a no treatment control group was 0.40 (95% CI, 0.31 to 0.49; P < 0.0001), while that from the 116 placebo-controlled trials was 0.24 (95% CI, 0.22 to 0.27; P < 0.0001). However, heterogeneity among the 116 trials with placebo control groups was not substantially less (Q = 575.336 on 115 degrees of freedom, P < 0.0001) than that observed when all trials were included in the meta-analysis.

Statistical significance was not lost when both factors, TFT types and type of control group, were used in the metaregression model; i.e. greater treatment effects were still shown for fluoride varnish trials compared with the other modalities of topical fluorides (coefficient, 0.14; 95% CI, 0.02 to 0.26; p = 0.025) and in trials with no treatment rather than placebo control groups (coefficient, 0.14; 95% CI, 0.05 to 0.23; p = 0.002). In addition, little change could be observed in the metaregression results when all univariate metaregression analyses were performed in the subset of 117 placebo controlled trials. Because both these covariates have been identified as strong predictors of treatment effect, we decided to adjust all metaregression analyses for type of TFT (all four levels) and type of control group. In addition, we have decided to present the results of the D(M)FS PF meta-analyses subgrouped by type of control group and TFT types.

The random-effects meta-analyses of D(M)FS PFs, subgrouped by type of control group and TFT types, are presented in RevMan Analyses. The pooled estimate of treatment effect on D(M)FS PF from the three placebo-controlled fluoride varnish trials was 0.40 (95% CI, 0.09 to 0.72; P = 0.01), from the 13 placebo-controlled fluoride gel trials was 0.21 (95% CI, 0.14 to 0.28; P < 0.00001), from the 30 placebo-controlled fluoride mouthrinse trials was 0.26 (95% CI, 0.22 to 0.29; P < 0.00001), and from the 70 placebo-controlled fluoride toothpaste trials was 0.24 (95% CI, 0.21 to 0.28; P < 0.00001). Pooled estimates from the trials with no treatment control groups were: 0.52 (95% CI, 0.35 to 0.69; P < 0.00001) for fluoride varnish, 0.38 (95% CI, 0.23 to 0.53; P < 0.00001) for fluoride gel, and 0.33 (95% CI, 0.26 to 0.40; P < 0.00001) for fluoride rinse; there were no non-placebo controlled fluoride toothpaste trials. (Differences between the subgroup results from metaregression may differ from differences between the results of separate meta-analyses in separate subgroups due to an assumption of similar residual heterogeneity among PFs made in the metaregression analyses.)

We repeated the metaregression analyses adjusting for type of control group and all four levels of TFT types. The association between baseline caries and D(M)FS PF remained significant (and the regression coefficients almost unchanged) when both factors were included in the model (coefficient, 0.007; 95% CI, 0.002 to 0.01; P = 0.004). Lack of statistically significant associations remained between estimates of D(M)FS prevented fractions and background exposure to fluoridated water (coefficient, 0.03; 95% CI, -0.03 to 0.09; P = 0.36) or background exposure to any fluoride source (coefficient, -0.02; 95% CI, -0.07 to 0.04; P = 0.56). For the three modes/settings of TFT use categories, univariate metaregression analysis had indicated a lower treatment effect with unsupervised home use of TFT (some toothpaste trials only)

(coefficient, -0.08; 95% CI, -0.13 to -0.03; P = 0.002) compared with self applied supervised use or operator-applied use, and no significant differences between these two. This association (unsupervised use of TFT and D(M)FS PF) remained when adjusted first by type of control group (coefficient, -0.06; 95% CI, -0.11 to -0.01; P = 0.025), and then by TFT type (coefficient, -0.10; 95% CI, -0.17 to -0.03; P = 0.003). A higher treatment effect with supervised use of self applied TFT in school programmes (virtually all mouthrinse trials, and some toothpaste and gel trials) compared with unsupervised use and operator-applied TFT, not shown in the univariate analysis, appeared when adjusting for type of control group (coefficient, 0.06; 95% CI, 0.01 to 0.11; P = 0.015) and increased and became highly significant when TFT types were added to the model (coefficient, 0.11; 95% CI, 0.05 to 0.17; P < 0.0001). A lower treatment effect with operator-applied TFT also appeared in the model (coefficient, -0.13; 95% CI, -0.27 to -0.00; P = 0.049). Within each subgroup, statistically significant differences in treatment effect between fluoride varnishes and gels remained in the operator-applied mode of TFT use, and no statistically significant differences were shown among the three TFT types in the self applied supervised mode of use, or between fluoride rinse and toothpaste in the unsupervised mode of use (only two fluoride mouthrinse trials in this subgroup however). Associations between prevented fraction and language of publication remained when adjusting for type of control group and TFT types, where a higher PF was shown for trials reported only in languages other than English (coefficient, 0.11; 95% CI, 0.02 to 0.19; P = 0.02), but associations of D(M)FS PFs with method of application or with fluoride concentration became non-significant when adjusted by type of control group and TFT types. The associations between D(M)FS PFs with frequency of application and intensity of application became significant when type of control group and TFT types were included in the metaregression (with or without the trial of Di Maggio 1980).

The association between type of control group and D(M)FS prevented fraction remained significant when each investigated potential effect modifier was included in all bivariate or multivariate metaregression analyses (with or without the trial of Di Maggio 1980). The associations seen between TFT types (differences in treatment effect between fluoride varnish and that of other TFTs) and D(M)FS prevented fraction also remained significant throughout, except when adjusted by background exposure to fluorides (association between PF and exposure to other fluoride sources remaining non-significant in the model), or by fluoride concentration (association between PF and fluoride concentration becoming non-significant in the model), irrespective of exclusion or not of the trial of Di Maggio 1980. However, associations between language of publication and prevented fraction did not remain after excluding the trial of Di Maggio 1980 from the analyses (in univariate and multivariate metaregression). Further sensitivity analysis removing all but the 12 trials published only in languages other than English produced a D(M)FS pooled estimate of 0.34 (95% CI, 0.20 to 0.48; P < 0.0001), with substantial heterogeneity in results (Q = 122.181 on 11 degrees of freedom, P < 0.0001).

When the effect of each relevant covariate (type of control group, all four levels of TFT types, all three levels of mode/setting of TFT use, background exposure to any fluoride, baseline caries, and intensity of application) was controlled for all others in the metaregression model there remained strong associations between DM(F)S PF and type of control group (0.13 higher PF with no treatment control, 95% CI, 0.05 to 0.21; P = 0.002), baseline caries (0.008 increase in PF per unit increase in caries, 95% CI, 0.004 to 0.012; P < 0.0001), total intensity of application (0.00002 increase in PF per extra equivalent to 100 more applications 1000 ppmF higher, 95% CI, 0.000008 to 0.00004; P = 0.002), mode/setting of TFT use (-0.08 lower PF with unsupervised home use compared with supervised use in preventive programs, 95% CI, -0.15 to -0.02; P = 0.01; and both not significantly different from operator-applied use), and TFT type (-0.20 lower PF with toothpaste compared to fluoride varnish, 95% CI, -0.39 to -0.02; P = 0.033; and both not significantly different from mouthrinse or gel).

All metaregression results, in each case adjusting for type of control group and all four levels of TFT types, are provided in Additional Table 1: Random-effects metaregression analyses of prevented fractions: D(M)FS. The influential study by Di Maggio 1980 is omitted from three analyses: intensity of application and frequency of application with prevented fraction, and language of publication with prevented fraction.

It should be noted that although the number of data points (comparisons) in this review is unusually high, reducing the possibility of spurious claims of association, all metaregression results should be interpreted with a degree of caution given the large number of comparisons made and the observational nature of the comparisons.

The additional uncertainty we should have about the cluster randomized trials by Bravo 1997 and Ruiken 1987 had been taken account of in sensitivity analyses performed in previous component reviews, where the variances of the prevented fraction estimates were inflated (using a conservative value for the intraclass correlation coefficient (ICC)). The adjusted results were virtually identical to the analyses, ignoring the cluster randomized design, since the estimates for the trials were similar to the meta-analyses results and altering their weight had minimal effect.

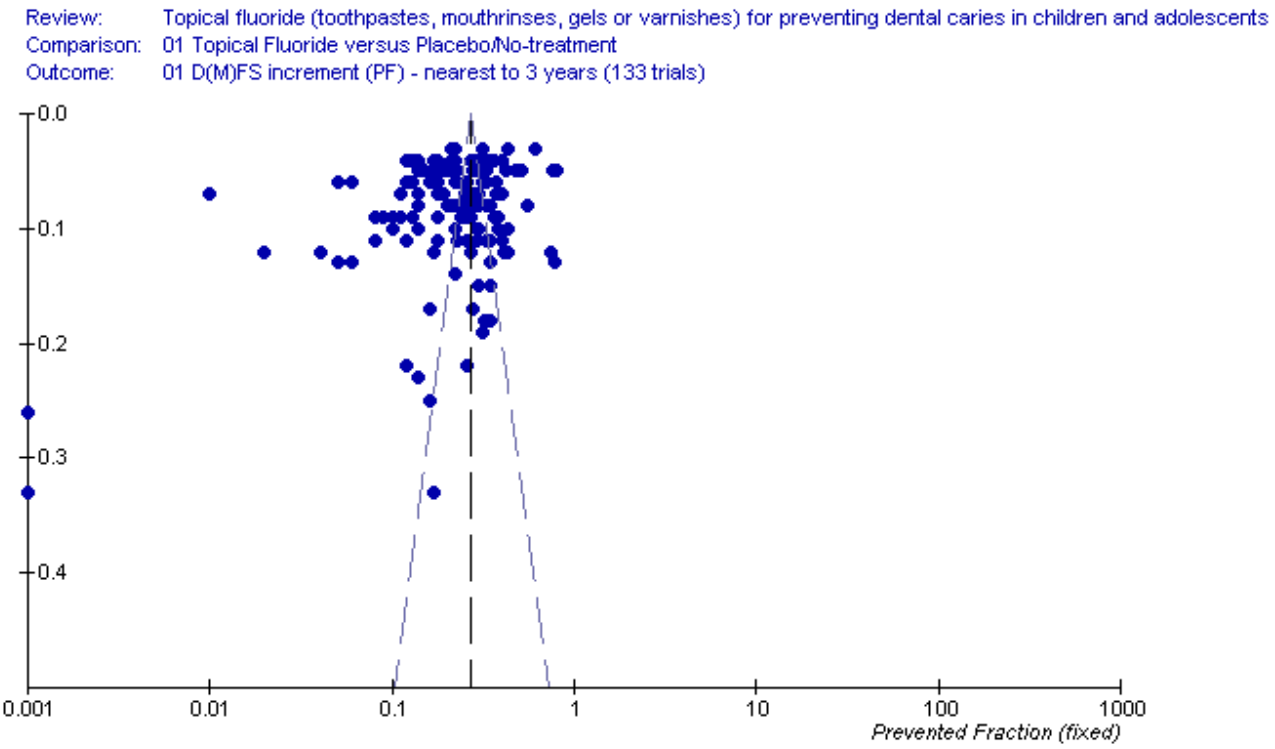
In order to illustrate the magnitude of the overall effect of topical fluorides, numbers of children needed to treat (NNT) to prevent one D(M)FS were calculated based on the pooled D(M)FS PF and on the caries increments in the control groups of the trials that contributed data to the meta-analysis. The overall caries-inhibiting effect (% PF) derived from the pooled results of the 133 trials was 26% (95% CI, 23% to 29%); the caries increments in the included trials ranged from 0.2 to 7.7 D(M)FS per year. In populations with a caries increment of 0.2 D(M)FS per year (at the lowest end of the results seen in the included studies), this implies an absolute caries reduction of 0.052 D(M)FS per year, equivalent to an NNT of 20 (95% CI, 18 to 22): i.e. 20 children need to use topical fluorides to avoid one D(M)FS. In populations with a caries increment of 2.5 D(M)FS per year (at the mid range of the results seen in the included studies), this implies an absolute caries reduction of 0.65 D(M)FS per year, equivalent to an NNT of 2 (95% CI, 2 to 2): i.e. 2 children need to use TFT to avoid one D(M)FS.

(b) Funnel plot and test for funnel plot asymmetry: D(M)FS PF

A funnel plot of the 133 trials reporting D(M)FS PFs may look asymmetrical, but the weighted regression test for asymmetry (Egger 1997) was not statistically significant (asymmetry intercept = -0.41 (95% CI, -1.38 to 0.55; P = 0.4)). There is, therefore, no evidence of bias using this method.

The funnel plot of the 133 trials comparing TFT with placebo/no treatment is available in Figure 1.

Figure 1. Funnel Plot of D(M)FS PFs according to standard errors of the studies included in the meta-analysis



Basic findings from studies which did not contribute data for the D(M)FS PF meta-analysis.

Brandt 1972 - "Preventive effect on the incidence of caries from fluoride mouthrinsing was shown" (compared with placebo).

de Liefde 1989 - "No preventive effect from mouthrinsing was shown" (compared with placebo).

Homan 1969 - "Negative outcome (no significant differences between fluoride toothpastes tested and placebo)".

Powell 1981 - "Inhibitory effect on initial lesion progression was shown for fluoride dentifrice" (compared with non-fluoride dentifrice).

Slack 1964 - "No evidence to support the use of the fluoride dentifrice in the control of caries" (compared with non-fluoride dentifrice).

(2) Effect on permanent teeth: D(M)FT PF

Seventy-nine trials reported data which allowed the calculation of the D(M)FT prevented fraction. All 79 are also included in the analysis of D(M)FS PF. The pooled estimate of D(M)FT prevented fraction was 0.26 (95% CI, 0.21 to 0.30; P < 0.00001). There was substantial heterogeneity between trials (Chi^2 = 845.06 on 78 degrees of freedom, P < 0.00001). The results of this analysis are very similar to those reported in the analysis of D(M)FS PF.

As with the estimates of the effects of TFT on D(M)FS PF, univariate metaregression suggested that the estimates from trials using no treatment as opposed to placebo controls were substantially higher (coefficient, 0.21; 95% CI, 0.09 to 0.34; P = 0.001). The pooled estimate of the D(M)FT prevented fraction from the seven trials with a no treatment control group (fluoride gel and varnish trials only) was 0.45 (95% CI, 0.32 to 0.58; P < 0.0001), while that from the 72 placebo-controlled trials (all four modalities) was 0.24 (95% CI, 0.20 to 0.28; P < 0.0001). When the meta-analysis was confined to those trials with placebo controls, there remained substantial heterogeneity (Q = 591.33 on 71 degrees of freedom, P < 0.0001).

Differences between TFT types (indirect comparisons) shown for D(M)FS PF in metaregression analyses were also suggested for D(M)FT PF. Fluoride varnish has been found to be significantly different from the other types of TFT (coefficient, 0.28; 95% CI, 0.08 to 0.33; P = 0.01); differences among the other three modalities (fluoride gel/mouthrinse/toothpaste) were not obvious. Although no significant differences between fluoride varnish and gel were shown when all TFT types were in the model, these became significant when adjusted for type of control group (in which case, differences between fluoride varnish and mouthrinse became non-significant). The pooled estimate of treatment effect from the three fluoride varnish trials was 0.53 (95% CI, 0.23 to 0.82; P < 0.0001); from the 10 fluoride gel trials was 0.32 (95% CI, 0.19 to 0.46; P < 0.0001), from the 13 fluoride mouthrinse trials was 0.24 (95% CI, 0.18 to 0.30; P < 0.0001), and from the 53 fluoride toothpaste trials was 0.23 (95% CI, 0.19 to 0.28; P < 0.0001). It should be noted that there were only placebo-controlled fluoride toothpaste and mouthrinse trials reporting DMFT data.

The random-effects meta-analyses of D(M)FT prevented fractions are presented in RevMan Analyses, also subgrouped by type of control group and TFT types.

(3) Effect on deciduous tooth surfaces: d(e)fs PF

Five trials reported data which allowed the calculation of the 'd(e/m)fs' prevented fraction. Only one of these (Clark 1985) is also included in the analysis of D(M)FS PF. The pooled estimate of d(m/e)fs prevented fraction was 0.33 (95% CI, 0.22 to 0.44; P < 0.0001), suggesting a substantial benefit of TFT in the deciduous dentition. There was no statistically significant heterogeneity between trials (Chi^2 = 6.13 on 4 degrees of freedom, P = 0.19). These results should be viewed with a degree of caution given the fact that standard deviations (SDs) were imputed (regression equation) in four of the five trials. In addition, the test for heterogeneity has low power to detect excess variability between the results of the trials when only a few trials are included.

Univariate metaregression suggested no significant association between estimates of d(e/m)fs prevented fractions and type of control group (placebo/no treatment). Because the meta-analysis included only five trials (three fluoride varnish trials and two fluoride gel trials), no further exploration of competing explanations for heterogeneity in treatment effects was considered. Metaregression would have had very limited power to detect any association under these circumstances. However, we have decided to present the meta-analysis results stratified by type of control group and TFT type, since there is clear evidence for the influence of these factors on treatment effects. In fact, the pooled estimate of the d(e/m)fs prevented fraction from the two trials with a no treatment control group was 0.41 (95% CI, 0.26 to 0.55; P < 0.0001) while that from the three placebo-controlled trials was 0.27 (95% CI, 0.8 to 0.48; P < 0.004); and the pooled estimate of treatment effect from the three fluoride varnish trials was 0.33 (95% CI, 0.19 to 0.48; P < 0.0001) while that from the two fluoride gel trials was 0.26 (95% CI, -0.11 to 0.63; P = 0.18).

The random-effects meta-analyses of d(e/m)fs prevented fractions are presented in RevMan Analyses, subgrouped by type of control group and TFT types.

Numbers of children needed to treat (NNT) to prevent one defs were calculated based on the pooled d(e/m)fs prevented fraction and on the caries increments in the control groups of the five trials in the meta-analysis. In populations with a caries increment of 0.8 defs per year (at the lowest end of the results seen in the included studies), this implies an absolute caries reduction of 0.26 defs per year, equivalent to an NNT of 3.8 (95% CI, 2.8 to 5.7): i.e. 4 children need to use topical fluorides to avoid one defs. In populations with a caries increment of 1.9 defs per year (at the highest range of the results seen in the included studies), this implies an absolute caries reduction of 0.63 defs per year, equivalent to an NNT of 1.6 (95% CI, 1.2 to 2.4); i.e. 2 children need to use topical fluorides to avoid one defs.

Effect of topical fluorides on other outcomes

Some trials report data for other relevant outcomes (*see* 'Included studies' under Description of studies section). Some of these are simply other measures/indices for dental caries increment in permanent teeth/surfaces and require no further consideration; 12 trials report on the proportion of children developing new caries. Meta-analyses results for the proportion of children developing new caries are presented below.

The few trials that report data on adverse effects either give no useable or incomplete data for analysis, or are so closely related to specific TFT types (already reported in the separate reviews of each) that it would not be meaningful to address these again in this review.

Data for unacceptability of treatment (as measured by drop outs) were reported in 10 of the non-placebo controlled trials that reported drop outs. Meta-analysis results for these are also described below.

Proportion of children developing new caries

Thirteen trials reported results on the proportion of children developing one or more new caries (Dolles 1980; Finn 1975; Forsman 1974; Forsman 1974a; Gisselsson 1999; Hanachowicz 1984; Heidmann 1992; Holm 1979; Holm 1984; Kleber 1996; Marthaler 1974; Torell 1965; Torell 1965a). The pooled estimate (random-effects meta-analysis) of the risk ratio was 0.88, with substantial heterogeneity in the results (95% CI, 0.82 to 0.95; Chi^2 for heterogeneity 53.88 on 12 degrees of freedom, P < 0.00001). (Using alternative measures of effect has not reduced heterogeneity substantially.) This corresponds to an NNT to prevent one child from developing caries of 15 (95% CI, 10 to 34) in a population with a caries risk the same as that found in the control groups in these trials (15 children using TFT for 2 to 3 years will prevent new caries development in one child).

Unacceptability of treatment (drop outs/exclusions)

The pooled estimate of the risk ratio of dropping out from the TFT as opposed to the non-treatment arm in the 10 non-placebo controlled trials that reported drop outs (Abadia 1978; Bryan 1970; Craig 1981; Cobb 1980; Englander 1967; Holm 1979; Horowitz 1971; Ingraham 1970; Modeer 1984; Moreira 1981) was 1.20 (95% CI, 0.85 to 1.70). There was substantial heterogeneity in these results (Chi^2 = 40.85 on 9 degrees of freedom, P < 0.00001).

DISCUSSION

The first question addressed by this review was whether the use of topical fluoride therapy (TFT) in the form of toothpaste, mouthrinse, gel or varnish for the prevention of dental caries in children is overall better than not using a topical fluoride intervention. The review as a whole contains information from over 65,000 children included in the trials comparing a topical fluoride intervention with a placebo or no treatment, and suggests that the use of topical fluorides is associated with a clear reduction in caries increment in both the permanent and the deciduous dentition. For the great majority of children (approximately two thirds) the topical fluoride modality they used was toothpaste, followed by mouthrinse, gel and varnish applications.

There is strong evidence of a generalizable beneficial effect of topical fluoride therapy. The random-effects meta-analysis of 133 trials combined assessing the effect of topical fluorides on the permanent dentition suggests a caries inhibiting effect of 26% on average; an approximate, though anti-conservative, interval in which at most 95% of underlying effects might lie is from 0% to 53%. The average caries reduction of 26% would correspond to a number needed to treat (NNT) of 2 to avoid one decayed, filled or missing

tooth surface (DMFS) per year in a child population with a caries increment of 2.5 D(M)FS per year (in the middle range of control group rates for included studies), or an NNT of 20 for children from a population with a caries increment of 0.2 D(M)FS per year (at the lowest end of the observed range). Only five studies reported the effects of topical fluoride therapy on caries increment in deciduous tooth surfaces, two of these tested self applications of fluoride gel with a toothbrush and three studies tested fluoride varnish applications. The random-effects meta-analysis of the five studies combined suggests that the use of topical fluoride applications is associated on average with a 33% (95% confidence interval (CI), 22% to 44%) reduction in decayed, missing and filled tooth surfaces. This would correspond to an NNT of 2 to avoid one defs per year in a child population with a caries increment of 1.9 defs per year (at the highest end of the control group rates), or an NNT of 4 for children from a population with a caries increment of 0.8 defs per year (at the lowest end of the observed range). It should be noted that although the variation among the results of the 133 studies assessing the effectiveness of topical fluoride on the permanent dentition is substantial, the results of the few studies on the effectiveness of topical fluoride on deciduous tooth surfaces are less heterogeneous. On the other hand, the confidence intervals are relatively wide for the effect on deciduous tooth surfaces, since relatively few trials were included in the meta-analysis (1685 participants).

A secondary objective of this review was to exploit power to look at potential sources of heterogeneity between studies across all four types of topical fluoride interventions and at indirect comparisons of the different TFT types. It was examined extensively whether there was any relationship between the caries-preventive effectiveness of topical fluoride therapy and a number of factors, including initial level of caries, background exposure to extraneous fluoride sources, mode/setting of TFT use and type of topical fluoride intervention used. A significant influence of the pre-specified factors/variables initial level of caries, mode/setting of use, and type of topical fluoride on the prevented fraction (PF) was shown in the metaregression analyses performed. Among the other potential sources of heterogeneity investigated, a significant influence of type of control group was shown.

We have detected a constant relative increase in the PF of 1% on average as trials involved children with higher initial D(M)FS scores (baseline risk of the study population). Although the magnitude of the effect was small, this implies that as the caries levels of a community decline, the percentage caries reductions will decrease. On the other hand, we were unable to detect a clear relationship between background exposure to other fluoride sources and the magnitude of the treatment effect. Although this may have been partly influenced by potential misclassification, especially due to the incomplete reporting of data for exposure to fluorides other than water, the lack of association between background exposure to water fluoridation and treatment effect, based on analysis including 116 trials (20 of which were in fluoridated areas), implies that estimates of treatment effect were similar between trials conducted in fluoridated and non-fluoridated areas i.e. use of topical fluoride may provide additional caries reduction in subjects from fluoridated areas.

There is evidence of a 14% greater caries inhibiting effect with the use of fluoride varnish compared with the other TFT types (gels, mouthrinses and toothpastes), while no significant differences in treatment effects among these or between any one of these and the others were suggested. However, relatively few fluoride varnish trials were included and very few among these were placebo-controlled trials, making it difficult to rule out the possibility of an overestimation of the size of the effect, due to the preponderance of no treatment control studies of lower methodological quality in this subgroup. Further, conclusions about differences in effect due to differences between topical fluoride interventions are on a strongest ground if participants are randomized to one type of TFT or another within a study and a consistent relationship is found across similar studies, but surely such investigations could not be performed in a review including only placebo/no-treatment comparisons. Therefore, these results should be interpreted with caution since the investigation of differences between subgroups is effectively a non-randomized comparison, and is prone to all the difficulties in inferring causality in observational studies. Nevertheless, the adjusted indirect comparisons resulting from the metaregression analyses performed in this review had the advantage that other possible explanations for heterogeneity in different trials, including prognostic factors of participants (such as baseline caries levels and background exposure to fluorides), intervention and actual trial characteristics, could be partially taken into account. Another advantage was that uncertainty could be incorporated in the analyses results by providing wider confidence intervals.

We observed a 10% decrease in the PF with the unsupervised home use of topical fluoride interventions (basically toothpaste) compared with supervised and with operator-applied use in the adjusted metaregression analysis. In addition, the effect of self applied supervised use of TFT appeared to be 11% greater than that of operator-applied and unsupervised home use of TFT. These differences in treatment effect between trials of supervised use and both unsupervised use and operator-applied use are perhaps unsurprising. They are likely to reflect the more intensive use of topical fluoride interventions under supervised schemes. As regards the suggested greater treatment effect with increased frequency and intensity of topical fluoride application in this review, this had been indicated in two other reviews in this series (Marinho 2002; Marinho 2003) and should probably be more relevant in the context of each specific review. It should be pointed out that metaregression analyses including 130 trials should have sufficient power to detect such relationships, but more robust investigations of these aspects of the topical fluoride interventions also require direct, head to head comparisons of different frequencies/intensities of application, which were not within the scope of this review.

Treatment effects estimates from the trials that employed a no-treatment control group were on average 14% more beneficial than from those with a placebo control group. The strong evidence on differences in effect estimates by type of control group shown in this review (which included 116 placebo controlled trials and 17 no-treatment control comparisons in the analysis) was also indicated in a previous systematic review in this series (Marinho 2002). Blind assessment of outcome was an inclusion criterion used across all reviews but clearly participants could not have been blinded in trials with no treatment controls. Although it is unclear why this should have been associated with differences in outcome in these particular circumstances, type of control group can be considered a useful 'proxy' for the use or not of double-blinding in included studies, a key methodological feature that may represent the best

indicator of study quality in these reviews. With regards to the key quality domain of allocation concealment, no association with treatment effect could be demonstrated for this, possibly due to the fact that the randomization process was poorly described in the studies included.

We observed a significantly greater treatment effect in non-English language trials in the post hoc metaregression analyses performed. Although plausible (Juni 2002), this relationship was dependent on the inclusion of one study with particularly powerful effects (Di Maggio 1980). After exclusion of this study in a sensitivity analysis no significant association was seen with this factor. It should be noted however that comprehensive searching and data extraction from as many trials as possible published in any language was an important component of this review in an attempt to reduce biases and imprecision. Although the exclusion of trials published in languages other than English may have little impact on the summary effect estimate of a review that includes so many trials, such studies carried out in a variety of countries should maximise the ability of users of the review to judge its applicability for specific decisions on the appropriate use of topical fluorides.

Although visual inspection of the funnel plot may suggest a degree of asymmetry, the Egger formal test for asymmetry provided no evidence of a significant relationship between trial size and effect estimate. Therefore, there is no evidence that the smaller studies in the meta-analysis of D(M)FS PFs tend to show larger treatment effects in this review.

We found little useful information about the risk of adverse effects in the topical fluoride reviews, and the few results available are discussed in the context of each relevant separate review in this series.

AUTHORS' CONCLUSIONS

Implications for practice

The use of topical fluoride therapy is associated with a clear reduction in caries increment in children. While we found evidence that the relative effect of topical fluoride may be greater in those who have higher baseline levels of decayed, missing and filled tooth surfaces (D(M)FS), we found no evidence that the effect of topical fluoride was dependent on background exposure to fluoridated water or other fluoride sources. In addition, a higher D(M)FS prevented fraction was shown with increased total intensity of fluoride application, with self applied supervised use (where a higher compliance with topical fluoride interventions as recommended should be expected), and with the use of fluoride varnishes compared with the other topical fluoride modalities. Research on the effects of fluoride varnish has been of lower methodological quality however. The effect of topical fluoride also varied according to type of control group used; the D(M)FS prevented fraction was higher with no treatment compared with placebo. Unfortunately, little information is available on the effects of topical fluoride therapy on outcomes such as caries incidence in the deciduous dentition and on the likelihood of adverse effects. The general lack of evidence on outcomes other than caries increment in children's permanent teeth makes it more difficult for policy makers to weigh the benefits of topical fluoride use in preventing caries against potential negative effects.

Implications for research

This systematic review included placebo controlled trials as well as trials with no treatment controls on the effects of topical fluoride therapy (TFT) on dental caries in children. There is sufficient evidence to establish that this factor (type of control group) represents an important source of heterogeneity and a strong indicator of study quality in the topical fluoride reviews. Although many reports lacked important methodological details, the review findings are quite strong, based on a sizeable body of randomized evidence. In this review, the meta-analyses were stratified by both type of control group and type of topical fluoride intervention (all four levels). Here, a test of differences between subgroups in multivariate metaregression analyses was effectively an indirect comparison of the effects of the various topical fluoride interventions. Although such a test can provide indirect evidence of relative treatment effects, it may be less reliable than evidence from randomized controlled trials that compare the interventions directly (head to head comparisons). We need therefore to be cautious about drawing conclusions about the relative efficacy of the TFT interventions based on such evaluation of the magnitude of treatment effects across studies. Fortunately, direct evidence from head to head comparisons is available for the various topical fluoride interventions and this will be the subject of the next systematic review in this series.

ACKNOWLEDGEMENTS

The authors wish to thank the Systematic Reviews Training Unit (UCL) and the Cochrane Oral Health Group for their continuous support. Many thanks are due to the investigators who have kindly provided additional information about their trials or supplied reports of trials, as well as to those who helped with the translations or provided comments and editorial input to this review but are too numerous to be mentioned here.

REFERENCES

References to studies included in this review

Abadia 1978 *{published data only}*

Abadia SMS. Prevenção da cárie dentária através da aplicação tópica de gel de flúor fosfato ácido, utilizando-se isolamento relativo e absoluto [dissertation]. Baurú (SP): Universidade de São Paulo, 1978.

Abrams 1980 *{published data only (unpublished sought but not used)}*

Abrams RG, Chambers DW. Caries-inhibiting effect of a stannous fluoride silica gel dentifrice: a three-year clinical study. *Clinical Preventive Dentistry* 1980;**2**:22-7.

Andlaw 1975 *{published data only}*

* Andlaw RJ, Tucker GJ. A dentifrice containing 0.8 per cent sodium monofluorophosphate in an aluminium oxide trihydrate base. A 3-year clinical trial. *British Dental Journal* 1975;**138**:426-32.

Tucker GJ, Andlaw RJ, Burchell CK. The relationship between oral hygiene and dental caries incidence in 11-year-old children. A 3-year study. *British Dental Journal* 1976;**141**:75-9.

Ashley 1977 *{published data only}*

Ashley FP, Mainwaring PJ, Emslie RD, Naylor MN. Clinical testing of a mouthrinse and a dentifrice containing fluoride. A two-year supervised study in school children. *British Dental Journal* 1977;**143**:333-8.

Ashley 1977a *{published data only}*

Ashley FP, Mainwaring PJ, Emslie RD, Naylor MN. Clinical testing of a mouthrinse and a dentifrice containing fluoride. A two-year supervised study in school children. *British Dental Journal* 1977;**143**:333-8.

Bastos 1989 *{published and unpublished data}*

Bastos JR, Viegas AR, Lopes ES. Comparacao entre o uso de solucoes de fluoreto de sodio a 0,2%, monofluorfosfato de sodio a 0,7% e monofluorfosfato de sodio a 0, 7% em alcool a 4%, em bochechos semanais, na prevencao de carie dentaria. Resultados de 12 meses [Comparison between the use of 0.2% sodium fluoride solutions, 0.7% sodium monofluorophosphate solutions and 0.7% sodium monofluorophosphate solutions in 4% alcohol, in weekly rinsing, in the prevention of dental caries. Results after 12 months]. *Revista da Associacao Paulista de Cirurgioes Dentistas* 1981;**35**:390-5.

* Bastos JRM. Comparação entre uso de soluçoes de fluoreto de sodio a 0.2%, monofluorfosfato de sodio a 0.7% e monofluorfosfato de sodio a 0.7% em alcool a 4%, em bochechos, na prevenção da cárie dentária [dissertation]. São Paulo (SP): Universidade de São Paulo, 1979.

Bastos JRM, Lopes ES. Fluoride mouthwashes: anticaries effectiveness of a weekly mouthrinsing program using sodium fluoride or sodium monofluorphosphate after 32 months in schoolars from 9 to 12 years old [Bochechos com fluoretos: efeito anticariogenico de bochechos semanais com solucoes de fluoreto de sodio ou monofluor fosfato de sodio, apos 32 meses em escolares de 9-12 anos de idade]. *Revista da Associacao Paulista de Cirurgioes Dentistas* 1989;**43**:34-6.

Bastos JRM, Viegas AR, Lopes ES. Weekly mouthwashing in caries prevention using solution of NaF 0.2 percent, 0.7 percent in alcohol 0.4 percent: results after 20 months (comparative study) [Solucoes de fluoreto de sodio a 0,2 por cento, monofluorfosfato de sodio a 0,7 por cento e monofluorfosfato a 0,7 por cento, em alcool a 4 por cento, em bochechos semanais, na prevencao da carie dentaria: resultados de 20 meses]. *Revista da Associacao Paulista de Cirurgioes Dentistas* 1986;**40**:443-5.

Bijella 1981 *{published data only}*

Bijella MF, Bijella VT, Lopes ES, Bastos JR. Comparison of dental prophylaxis and toothbrushing prior to topical fluoride applications. *Community Dentistry and Oral Epidemiology* 1985;**13**:208-11.

* Bijella MFTB. Prevenção da cárie dentária através da aplicação tópica de gel e solução de fuor fosfato acidulado com e sem profilaxia prévia [dissertation]. Bauru (SP): Universidade de São Paulo, 1981.

Blinkhorn 1983 *{published and unpublished data}*

Blinkhorn AS, Holloway PJ, Davies TG. Combined effects of a fluoride dentifrice and mouthrinse on the incidence of dental caries. *Community Dentistry and Oral Epidemiology* 1983;**11**:7-11.

Blinkhorn 1983a *{published and unpublished data}*

Blinkhorn AS, Holloway PJ, Davies TG. Combined effects of a fluoride dentifrice and mouthrinse on the incidence of dental caries. *Community Dentistry and Oral Epidemiology* 1983;**11**:7-11.

Borutta 1991 *{published and unpublished data}*

Borutta A, Kunzel W, Rubsam F. The caries-protective efficacy of 2 fluoride varnishes in a 2-year controlled clinical trial [Kariesprotektive Wirksamkeit zweier Fluoridlacke in einer klinisch kontrollierten Zweijahresstudie]. *Deutsche Zahn Mund und Kieferheilkunde Zentralblatt* 1991;**79**:543-9.

Brandt 1972 *{published data only (unpublished sought but not used)}*

Brandt RS, Slack GL, Waller DF. The use of a sodium fluoride mouthwash in reducing the dental caries increment in eleven year old English school children. *Proceedings of the British Paedodontic Society* 1972;**2**:23-5.

Bravo 1997 *{published and unpublished data}*

* Bravo M, Baca P, Llodra JC, Osorio E. A 24-month study comparing sealant and fluoride varnish in caries reduction on different permanent first molar surfaces. *Journal of Public Health Dentistry* 1997;**57**:184-6.

Bravo M, Garcia Anllo I, Baca P, Llodra JC. A 48-month survival analysis comparing sealant (Delton) with fluoride varnish (Duraphat) in 6- to 8-year-old children. *Community Dentistry and Oral Epidemiology* 1997;**25**:247-50.

Bravo M, Llodra JC, Baca P, Osorio E. Effectiveness of visible light fissure sealant (Delton) versus fluoride varnish (Duraphat): 24-month clinical trial. *Community Dentistry and Oral Epidemiology* 1996;**24**:42-6.

Bravo Perez M, Llodra Calvo JC, Baca Garcia P, Osorio Ruiz E, Junco Lafuente P. Fissure sealants versus fluorine varnish on the first permanent molars: economic assessment [Selladores de fisuras frente a barniz de fluor en primeros molares permanentes: evaluacion economica]. *Atencion Primaria* 1995;**15**:143-7.

Brudevold 1966 *{published data only}*

* Brudevold F, Chilton NW. Comparative study of a fluoride dentifrice containing soluble phosphate and a calcium-free abrasive: second-year report. *Journal of the American Dental Association* 1966;**72**:889-94.

Brudevold F, Chilton NW, Wellock WD. A preliminary comparison of a dentifrice containing fluoride and soluble phosphate and employing a calcium-free abrasive with other types of fluoride dentifrices. First year report of a clinical study. *Journal of Oral Therapeutics and Pharmacology* 1964;**56**:1-6.

Bryan 1970 *{published data only}*

Bryan ET, Williams JE. The cariostatic effectiveness of a phosphate-fluoride gel administered annually to school children. I. The results of the first year. *Journal of Public Health Dentistry* 1968;**28**:182-5.

* Bryan ET, Williams JE. The cariostatic effectiveness of a phosphate-fluoride gel administered annually to school children; final results. *Journal of Public Health Dentistry* 1970;**30**:13-6.

Buhe 1984 *{published data only (unpublished sought but not used)}*

Barlage B, Buhe H, Buttner W. A 3-year clinical dentifrice trial using different fluoride levels: 0.8 and 1.2% sodium monofluorophosphate [abstract]. *Caries Research* 1981;**15**:185.

* Buhe H, Buttner W, Barlage B. 3-year clinical tooth cream test with toothpastes of varying fluoride content: 0.8% and 1.2% sodium monofluorophosphate [Uber einen dreijahrigen klinischen Zahncremetest mit Zahnpasten unterschiedlicher Fluoridkonzentration: 0,8% und 1,2% Natriummonofluorphosphat]. *Quintessenza* 1984;**35**:103-11.

Cahen 1982 *{published data only (unpublished sought but not used)}*

Cahen PM, Frank RM, Turlot JC, Jung MT. Comparative unsupervised clinical trial on caries inhibition effect of monofluorophosphate and amine fluoride dentifrices after 3 years in Strasbourg, France. *Community Dentistry and Oral Epidemiology* 1982;**10**:238-41.

Clark 1985 *{published data only (unpublished sought but not used)}*

Clark DC, Stamm JW, Quee TC, Robert G. Results of the Sherbrooke-Lac Megantic fluoride varnish study after 20 months. *Community Dentistry and Oral Epidemiology* 1985;**13**:61-4.

* Clark DC, Stamm JW, Robert G, Tessier C. Results of a 32-month fluoride varnish study in Sherbrooke and Lac-Megantic, Canada. *Journal of the American Dental Association* 1985;**111**:949-53.

Clark DC, Stamm JW, Tessier C, Robert G. The final results of the Sherbrooke-Lac Megantic fluoride varnish study. *Journal of the Canadian Dental Association* 1987;**53**:919-22.

Cobb 1980 *{published data only (unpublished sought but not used)}*

Cobb BH, Rozier GR, Bawden JW. A clinical study of the caries preventive effects of an APF solution and APF thixotropic gel. *Pediatric Dentistry* 1980;**2**:263-6.

Cons 1970 *{published data only}*

Cons NC, Janerich DT, Senning RS. Albany topical fluoride study. *Journal of the American Dental Association* 1970;**80**:777-81.

Craig 1981 *{published and unpublished data}*

* Craig EW, Suckling GW, Pearce EI. The effect of a preventive programme on dental plaque and caries in school children. *New Zealand Dental Journal* 1981;**77**:89-93.

Pearce EI, Craig EW, Suckling GW. Stability of fluoride levels in surface layer of normal enamel during a 21-month fluoride mouthrinsing program. *Community Dentistry and Oral Epidemiology* 1980;**8**:396-400.

de Liefde 1989 *{published and unpublished data}*

de Liefde B. Identification and preventive care of high caries-risk children: a longitudinal study. *New Zealand Dental Journal* 1989;**85**:112-6.

DePaola 1977 *{published data only}*

DePaola PF, Soparkar P, Foley S, Bookstein F, Bakhos Y. Effect of high-concentration ammonium and sodium fluoride rinses on dental caries in schoolchildren. *Community Dentistry and Oral Epidemiology* 1977;**5**:7-14.

DePaola 1980 *{published data only (unpublished sought but not used)}*

* DePaola PF, Soparkar M, Van Leeuwen M, DeVelis R. The anticaries effect of single and combined topical fluoride systems in school children. *Archives of Oral Biology* 1980;**25**:649-53.

Lu KH, Porter DR, Pickles TH. Separate and combined cariostatic effects of fluoride gel and rinse [abstract No 239]. *Journal of Dental Research* 1980;**59**:947.

DePaola 1980a *{published data only (unpublished sought but not used)}*

* DePaola PF, Soparkar M, Van Leeuwen M, DeVelis R. The anticaries effect of single and combined topical fluoride systems in school children. *Archives of Oral Biology* 1980;**25**:649-53.

Lu KH, Porter DR, Pickles TH. Separate and combined cariostatic effects of fluoride gel and rinse [abstract]. *Journal of Dental Research* 1980;**59**:947.

Di Maggio 1980 *{published data only (unpublished sought but not used)}*

Di Maggio M, Zuccarino L. Cariostatic effect of Fluocaril; controlled clinical research [Effetto cariostatico del Fluocaril; ricerca clinica controllata]. *Minerva Stomatologica* 1980;**29**:45-50.

Dolles 1980 *{published and unpublished data}*

Dolles OK, Eriksen HM, Gjermo P. Tooth stain during 2 years' use of chlorhexidine - and fluoride-containing dentifrices. *Scandinavian Journal of Dental Research* 1979;**87**:268-74.

* Dolles OK, Gjermo P. Caries Increment and gingival status during 2 years' use of chlorhexidine- and fluoride-containing dentifrices. *Scandinavian Journal of Dental Research* 1980;**88**:22-7.

Driscoll 1982 *{published data only (unpublished sought but not used)}*

* Driscoll WS, Swango PA, Horowitz AM, Kingman A. Caries-preventive effects of daily and weekly fluoride mouthrinsing in a fluoridated community: final results after 30 months. *Journal of the American Dental Association* 1982;**105**:1010-3.

Driscoll WS, Swango PA, Horowitz AM, Kingman A. Caries-preventive effects of daily and weekly fluoride mouthrinsing in an optimally fluoridated community: findings after eighteen months. *Pediatric Dentistry* 1981;**3**:316-20.

Duany 1981 *{published data only}*

* Wallenstein S, Fleiss JL, Chilton NW. Confidence intervals for percentage reduction in caries increments [Describes Duany L, Zinner DD, and Chilton, NW: unpublished study]. *Journal of Dental Research* 1982;**61**:828-30.

Englander 1967 *{published data only}*

Englander HR, Carlos JP, Senning RS, Mellberg JR. Residual anticaries effect of repeated topical sodium fluoride applications by mouthpieces. *Journal of the American Dental Association* 1969;**78**:783-7.

* Englander HR, Keyes PH, Gestwicki M, Sultz HA. Clinical anticaries effect of repeated topical sodium fluoride applications by mouthpieces. *Journal of the American Dental Association* 1967;**75**:638-44.

Englander 1971 *{published data only}*

Englander HR, Sherrill LT, Miller BG, Carlos JP, Mellberg JR, Senning RS. Incremental rates of dental caries after repeated topical sodium fluoride applications in children with lifelong consumption of fluoridated water. *Journal of the American Dental Association* 1971;**82**:354-8.

Englander 1978 *{published data only}*

Englander HR, Mellberg JR, Engler WO. Observations on dental caries in primary teeth after frequent fluoride toplications in a program involving other preventives. *Journal of Dental Research* 1978;**57**:855-60.

Fanning 1968 *{published data only}*

Cellier KM, Fanning EA, Gotjamanos T, Vowles NJ. Some statistical aspects of a clinical study on dental caries in children. *Archives of Oral Biology* 1968;**13**:483-508.

Fanning EA, Cellier KM, Gotjamanos T, Vowles NJ. The effect of fluoride dentifrices on the caries incidence of individual tooth surfaces. *Australian Dental Journal* 1971;**16**:287-90.

Fanning EA, Gotjamanos T, Vowles NH, Wielen I. The effects of fluoride dentifrices on the incidence and distribution of stained tooth surfaces in children. *Archives of Oral Biology* 1968;**13**:467-9.

* Fanning EA, Gotjamanos T, Vowles NJ. The use of fluoride dentifrices in the control of dental caries: methodology and results of a clinical trial. *Australian Dental Journal* 1968;**13**:201-6.

Fanning EA, Gotjamanos T, Vowles NJ, Cellier KM, Simmons DW. The use of fluoride dentifrices in the control of dental caries: a preliminary report of a clinical trial. *Medical Journal of Australia* 1967;**1**:383-5.

Finn 1975 *{published data only}*

Finn SB, Moller P, Jamison H, Regattieri L, Manson Hing L. The clinical cariostatic effectiveness of two concentrations of acidulated phosphate-fluoride mouthwash. *Journal of the American Dental Association* 1975;**90**:398-402.

Fogels 1979 *{published data only}*

Fogels HR, Alman JE, Meade JJ, O'Donnell JP. The relative caries-inhibiting effects of a stannous fluoride dentifrice in a silica gel base. *Journal of the American Dental Association* 1979;**99**:456-9.

Forsman 1974 *{published data only}*

Forsman B. Studies on the effect of dentifrices with low fluoride content. *Community Dentistry and Oral Epidemiology* 1974;**2**:166-75.

Forsman 1974a *{published data only}*

Forsman B. Studies on the effect of dentifrices with low fluoride content. *Community Dentistry and Oral Epidemiology* 1974;**2**:166-75.

Frostell 1991 *{published and unpublished data}*

* Frostell G, Birkhed D, Edwardsson S, Goldberg P, Petersson L-G, Priwe C, et al. Effect of partial substitution of invert sugar for sucrose in combination with Duraphat treatment on caries development in preschool children: the Malmo Study. *Caries Research* 1991;**25**:304-10.

Peyron M, Matsson L, Birkhed D. Progression of approximal caries in primary molars and the effect of Duraphat treatment. *Scandinavian Journal of Dental Research* 1992;**100**:314-8.

Gallagher 1974 *{published data only}*

Gallagher SJ, Glassgow I, Caldwell R. Self-application of fluoride by rinsing. *Journal of Public Health Dentistry* 1974;**34**:13-21.

Gish 1966 *{published data only}*

Gish CW, Muhler JC. Effectiveness of a stannous fluoride dentifrice on dental caries. *ASDC Journal of Dentistry for Children* 1971;**38**:211-4.

* Gish CW, Muhler JC. Effectiveness of a stannous fluoride-calcium pyrophosphate (SnF2-Ca2P2O7) dentifrice on dental caries in children whose teeth calcified in a natural fluoride area. II. Results at the end of 24 months. *Journal of the American Dental Association* 1966;**73**:853-5.

Gish CW, Muhler JC, Stookey GK. Effectiveness of a stannous fluoride-calcium pyrophosphate (SnF2-Ca2P2O7) dentifrice on dental caries in children whose teeth calcified in a natural fluoride area. I. Results at the end of 12 months. *Journal of the American Dental Association* 1965;**71**:60-5.

Gisselsson 1999 *{published and unpublished data}*

Gisselsson H, Birkhed D, Emilson CG. Effect of professional flossing with NaF or SnF2 gel on approximal caries in 13-16-year-old schoolchildren. *Acta Odontologica Scandinavica* 1999;**57**:121-5.

Glass 1978 *{published data only (unpublished sought but not used)}*

Glass RL. Caries reduction by a dentifrice containing sodium monofluorophosphate in a calcium carbonate base. Partial explanation for diminishing caries prevalence. *Clinical Preventive Dentistry* 1981;**3**:6-8.

* Glass RL, Shiere FR. A clinical trial of a calcium carbonate base dentifrice containing 0.76% sodium monofluorophosphate. *Caries Research* 1978;**12**:284-9.

Glass 1983 *{published data only (unpublished sought but not used)}*

Glass RL, Peterson JK, Bixler D. The effects of changing caries prevalence and diagnostic criteria on clinical caries trials. *Caries Research* 1983;**17**:145-51.

Hagan 1985 *{published data only (unpublished sought but not used)}*

Hagan PP, Rozier RG, Bawden JW. The caries-preventive effects of full-strength and half-strength topical acidulated phosphate fluoride. *Pediatric Dentistry* 1985;**7**:185-91.

Hanachowicz 1984 *{published data only (unpublished sought but not used)}*

* Hanachowicz L. Caries prevention using a 1.2% sodium monofluorophosphate dentifrice in an aluminium oxide trihydrate base. *Community Dentistry and Oral Epidemiology* 1984;**12**:10-6.

Hanachowicz L. Prevention of caries with a dentifrice containing a 1.2% concentration of sodium monofluorophosphate in an alumina base (a 3- year clinical trial) [Prevention des caries par un dentrifrice contenant du monofluorophosphate de sodium a la concentration de 1.2% dans une base alumine (Test clinique de 3 ans)]. *Chirurgien Dentiste de France* 1984;**54**:59-67.

Hargreaves 1973 *{published data only}*

Hargreaves JA, Chester CG. Clinical trial among Scottish children of an anti-caries dentifrice containing 2 percent sodium monofluorophosphate. *Community Dentistry and Oral Epidemiology* 1973;**1**:47-57.

Hargreaves 1973a *{published data only}*

Hargreaves JA, Chester CG. Clinical trial among Scottish children of an anti-caries dentifrice containing 2 percent sodium monofluorophosphate. *Community Dentistry and Oral Epidemiology* 1973;**1**:47-57.

Hargreaves 1973b *{published data only}*

Hargreaves JA, Chester CG. Clinical trial among Scottish children of an anti-caries dentifrice containing 2 percent sodium monofluorophosphate. *Community Dentistry and Oral Epidemiology* 1973;**1**:47-57.

Heidmann 1992 *{published and unpublished data}*

* Heidmann J, Poulsen S, Arnbjerg D, Kirkegaard E, Laurberg L. Caries development after termination of a fluoride rinsing program. *Community Dentistry and Oral Epidemiology* 1992;**20**:118-21.

Heidmann JM, Arnbjerg D, Poulsen S, Kirkegaard E, Laurbjerg L. Development of caries in a group of Danish school-age children after cessation of systematic fluoride rinsing [Kariesudvikling hos en gruppe danske skoleborn efter ophor af systematiske fluorskylninger]. *Ugeskr Laeger* 1993;**155**:2995-8.

Heifetz 1970 *{published and unpublished data}*

Heifetz SB, Horowitz HS, Driscoll WS. Evaluation of a self-administered procedure for the topical application of acidulated phosphate-fluoride [abstract]. *Journal of Dental Research* 1968;**102**(IADR Abstr. No 257):102.

* Heifetz SB, Horowitz HS, Driscoll WS. Two-year evaluation of a self-administered procedure for the topical application of acidulated phosphate-fluoride; final report. *Journal of Public Health Dentistry* 1970;**30**:7-12.

Heifetz 1973 *{published data only}*

Heifetz SB, Driscoll WS, Creighton WE. The effect on dental caries of weekly rinsing with a neutral sodium fluoride or an acidulated phosphate-fluoride mouthwash. *Journal of the American Dental Association* 1973;**87**:364-8.

Heifetz 1982 *{published and unpublished data}*

Heifetz SB, Meyers R, Kingman A. A comparison of the anticaries effectiveness of daily and weekly rinsing with sodium fluoride solutions: findings after two years. *Pediatric Dentistry* 1981;**3**:17-20.

Heifetz SB, Meyers RJ, Kingman A. A comparison of the anticaries effectiveness of daily and weekly rinsing with sodium fluoride solutions: Final results after 3 years [abstract]. *Journal of Dental Research* 1981;**60**:471.

* Heifetz SB, Meyers RJ, Kingman A. A comparison of the anticaries effectiveness of daily and weekly rinsing with sodium fluoride solutions: final results after three years. *Pediatric Dentistry* 1982;**4**:300-3.

Held 1968 *{published data only}*

Held AJ, Spirgi M. Clinical experimentation with a fluoridated dentifrice [Experimentation clinique d'une pate dentifrice fluoree]. *Revue Francaise d'Odontostomatologie* 1966;**13**:1109-20.

Held AJ, Spirgi M. Clinical experimentation with a fluoridated toothpaste [Experimentation clinique d'une pate dentifrice fluores]. *SSO Schweiz Monatsschrift Fuer Zahnheilkund* 1965;**75**:883-905.

Held AJ, Spirgi M. Clinical experiments with a fluoridated toothpaste [Klinische versuche mit einer mit fluor versetzten zahnpasta]. *DDZ (Das Deutsche Zahnarzteblatt)* 1966;**20**:288-93.

* Held AJ, Spirgi M. Three years of clinical observations with fluoridated tooth-pastes [Trois ans d'observations cliniques avec des pates dentifrices fluorees]. *Bulletin du Groupement International pour la Recherche Scientifique en Stomatologie* 1968;**11**:539-70.

Held 1968a *{published data only}*

Held AJ, Spirgi M. Clinical experimentation with a fluoridated dentifrice [Experimentation clinique d'une pate dentifrice fluoree]. *Revue Francaise d'Odontostomatologie* 1966;**13**:1109-20.

Held AJ, Spirgi M. Clinical experimentation with a fluoridated dentifrice [Experimentation clinique d'une pate dentifrice fluores]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1965;**75**:883-905.

Held AJ, Spirgi M. Clinical experiments with a fluoridated toothpaste [Klinische versuche mit einer mit fluor versetzten zahnpasta]. *DDZ (Das Deutsche Zahnarzteblatt)* 1966;**20**:288-93.

* Held AJ, Spirgi M. Three years of clinical observations with fluoridated tooth-pastes [Trois ans d'observations cliniques avec des pates dentifrices fluorees]. *Bulletin du Groupement International pour la Recherche Scientifique en Stomatologie* 1968;**11**:539-70.

Held 1968b *{published data only}*

Held AJ, Spirgi M. Clinical experimentation with a fluoridated dentifrice [Experimentation clinique d'une pate dentifrice fluoree]. *Revue Francaise d'Odontostomatologie* 1966;**13**:1109-20.

Held AJ, Spirgi M. Clinical experimentation with a fluoridated toothpaste [Experimentation clinique d'une pate dentifrice fluores]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1965;**75**:883-905.

Held AJ, Spirgi M. Clinical experiments with a fluoridated toothpaste [Klinische versuche mit einer mit fluor versetzten zahnpasta]. *DDZ (Das Deutsche Zahnarzteblatt)* 1966;**20**:288-93.

* Held AJ, Spirgi M. Three years of clinical observations with fluoridated tooth-pastes [Trois ans d'observations cliniques avec des pates dentifrices fluorees]. *Bulletin du Groupement International pour la Recherche Scientifique en Stomatologie* 1968;**11**:539-70.

Hodge 1980 *{published data only (unpublished sought but not used)}*

Hodge HC, Holloway PJ, Davies TG, Worthington HV. Caries prevention by dentifrices containing a combination of sodium monofluorophosphate and sodium fluoride. Report of a 3-year clinical trial. *British Dental Journal* 1980;**149**:201-4.

Holm 1979 *{published data only}*

Holm AK. Effect of a fluoride-containing varnish (Duraphat) in preschool children [Abstract No 804]. *Journal of Dental Research* 1978;**57**:275.

* Holm AK. Effect of fluoride varnish (Duraphat) in preschool children. *Community Dentistry and Oral Epidemiology* 1979;**7**:241-5.

Holm 1984 *{published and unpublished data}*

Holm GB, Holst K, Mejare I. The caries-preventive effect of a fluoride varnish in the fissures of the first permanent molar. *Acta Odontologica Scandinavica* 1984;**42**:193-7.

Homan 1969 *{published and unpublished data}*

Homan BT, Messer HH. The comparative effect of three fluoride dentifrices on clinical dental caries in Brisbane schoolchildren. Preliminary report [abstract]. *Journal of Dental Research* 1969;**48**:1094.

Horowitz 1966 *{published data only}*

Horowitz HS, Chamberlin SR. Evaluation of a stannous fluoride dentifrice for use in dental public health programs. II. Operational procedures. *Journal of the American Dental Association* 1966;**73**:1090-4.

* Horowitz HS, Law FE, Thompson MB, Chamberlain SR, Shirley R. Evaluation of a stannous fluoride dentifrice for use in dental public health programs. I. Basic findings. *Journal of the American Dental Association* 1966;**72**:408-21.

Horowitz HS, Thompson MB, Mary B. Evaluation of a stannous fluoride dentifrice for use in dental public health programs. III. Supplementary findings. *Journal of the American Dental Association* 1967;**74**:979-86.

Horowitz 1971 *{published and unpublished data}*

Horowitz HS. Effect of topically applied acidulated phosphate-fluoride on dental caries in Hawaiian school children [abstract]. *Journal of Dental Research* 1967;**105**(IADR Abstr. No 275):105.

Horowitz HS. Effect of topically applied acidulated phosphate-fluoride on dental caries in Hawaiian school children [abstract]. *Journal of Dental Research* 1968;**101**(IADR Abstr. No 256):101.

Horowitz HS. Effect on dental caries of topically applied acidulated phosphate-fluoride: results after two years. *Journal of the American Dental Association* 1969;**78**:568-72.

Horowitz HS. The effect on dental caries of topically applied acidulated phosphate-fluoride: results after one year. *Journal of Oral Therapeutics and Pharmacology* 1968;**4**:286-91.

* Horowitz HS, Doyle J. The effect on dental caries of topically applied acidulated phosphate-fluoride: results after three years. *Journal of the American Dental Association* 1971;**82**:359-65.

Horowitz HS, Kau MC. Retained anticaries protection from topically applied acidulated phosphate-fluoride: 30- and 36-month post-treatment effects. *Journal of Preventative Dentistry* 1974;**1**:22-7.

Horowitz 1971a *{published data only}*

Frandsen AM, McClendon BJ, Chang JJ, Creighton WE. The effect of oral rinsing with sodium fluoride on the gingiva of children. *Scandinavian Journal of Dental Research* 1972;**80**:445-8.

Horowitz HS, Creighton WE, McClendon BJ. The effect on human dental caries of weekly oral rinsing with a sodium fluoride mouthwash: a final report. *Archives of Oral Biology* 1971;**16**:609-16.

Horowitz 1971b *{published data only}*

Frandsen AM, McClendon BJ, Chang JJ, Creighton WE. The effect of oral rinsing with sodium fluoride on the gingiva of children. *Scandinavian Journal of Dental Research* 1972;**80**:445-8.

Horowitz HS, Creighton WE, McClendon BJ. The effect on human dental caries of weekly oral rinsing with a sodium fluoride mouthwash: a final report. *Archives of Oral Biology* 1971;**16**:609-16.

Horowitz 1974 *{published and unpublished data}*

Horowitz HS, Heifetz SB, McClendon BJ, Viegas AR, Guimaraes LO, Lopes ES. Evaluation of self-administered prophylaxis and supervised toothbrushing with acidulated phosphate fluoride. *Caries Research* 1974;**8**:39-51.

Howat 1978 *{published data only}*

Howat AP, Hollaway PJ, Davies TG. Caries prevention by daily supervised use of a MFP gel dentifrice. Report of a 3-year clinical trial. *British Dental Journal* 1978;**145**:233-5.

Ingraham 1970 *{published data only}*

Ingraham RQ, Williams JE. An evaluation of the utility of application and cariostatic effectiveness of phosphate-fluorides in solution and gel states. *Journal of Tennessee State Dental Association* 1970;**50**:5-12.

Jackson 1967 *{published data only}*

Jackson D. Allocation to control and experimental groups in short-term clinical trials designed to test a caries preventive. In: Hardwick JL, Dustin JP, Held HR editor(s). Advances in fluorine research and dental caries prevention. Oxford: Pergamon Press, 1964:17-9.

* Jackson D, Sutcliffe P. Clinical testing of a stannous fluoride-calcium pyrophosphate children in Yorkshire school children. *British Dental Journal* 1967;**123**:40-8.

James 1967 *{published data only}*

* James PM, Anderson RJ. Clinical testing of stannous fluoride-calcium pyrophosphate dentifrices in Buckinghamshire school children. *British Dental Journal* 1967;**123**:33-9.

James PMC. Organization of a clinical trial. In: James PMC, Konig KG, Held HR editor(s). Advances in fluorine research and dental caries prevention. Oxford: Pergamon Press, 1966:33-9.

James 1977 *{published data only}*

James PM, Anderson RJ, Beal JF, Bradnock G. A 3-year clinical trial of the effect on dental caries of a dentifrice containing 2% sodium monoflurophosphate. *Community Dentistry and Oral Epidemiology* 1977;**5**:67-72.

Kinkel 1972 *{published data only}*

Kinkel HJ, Raich R. Caries prevention by means of a Na 2 FPO 3 toothpaste after 3 years of application [Die Karieshemmung einer Na 2 FPO 3 -Zahnpasta nach 3 Jahren Applikation]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1972;**82**:1240-4.

Kinkel HJ, Raich R. Caries-inhibiting properties of Na2FPO3 toothpaste after 5-year evaluation studies [Die Karieshe-mung einer Na2FPO3-Zahnpasta nach 5 Jahren Applikation]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1974;**84**:1245-7.

* Kinkel HJ, Raich R. Effectiveness of a Na2FP03 toothpaste on caries in children [Zur Wirkung einer Na2FPO3-Zahnpasta auf die Karies bei Kindern]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1972;**82**:169-75.

Kinkel HJ, Raich R. The caries-inhibiting property of a Na2FPO3 toothpaste after 4-year use [Die Karieshemmung einer Na2FPO3-Zahnpasta nach 4 Jahren Applikation]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1974;**84**:226-9.

Kinkel HJ, Raich R, Muller M. Caries prevention by means of a Na2FPO3-toothpaste after 7 year's application [Die Karieshemmung durch eine Na2FPO3-Zahnpasta nach 7 Jahren Applikation]. *Deutsche Zahnarztliche Zeitschrift* 1977;**32**:859-60.

Kinkel HJ, Raich R, Muller M. Caries prevention by the use of a Na2FPO3 containing toothpaste, after 7 years [Die Karieshemmung einer Na2FPO3-Zahnpasta nach 7 Jahren Applikation]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1977;**87**:1218-20.

Kleber 1996 *{published data only}*

Kleber CJ, Putt MS, Smith CE, Gish CW. Effect of supervised use of an alum mouthrinse on dental caries incidence in caries-susceptible children: a pilot study. *ASDC Journal of Dentistry for Children* 1996;**63**:393-402.

Koch 1967 *{published data only}*

Bawden JW, Granath L, Holst K, Koch G, Krasse P, Rootzen H. Effect of mouthrinsing with a sodium fluoride solution in children with different caries experience. *Swedish Dental Journal* 1980;**4**:111-7.

Hollender L, Koch G. Influence of topical application of fluoride on rate of progress of carious lesions in children. A long-term roentgenographic follow-up. *Odontologisk Revy* 1969;**20**:37-41.

Koch G. Caries increment in schoolchildren during and two years after end of supervised rinsing of the mouth with sodium fluoride solution. *Odontologisk Revy* 1969;**20**:323-30.

* Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school children. 11. Effect of supervised fortnightly rinsing of the mouth with 0.5 per cent sodium fluoride solution. A 3-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:77-88.

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school-children. *Odontologisk Revy* 1967;**18**(Suppl. 12):1-125.

Koch G, Lindhe J. The effect of supervised oral hygiene on the gingiva of children. The effect of sodium fluoride. *Journal of Periodontal Research* 1967;**2**:64-9.

Koch G, Lindhe J. The state of the gingivae and the caries-increment in school-children during and after withdrawal of various prophylactic measures. In: McHugh WD editor(s). Dental Plaque. A symposium held at the University of Dundee, 22 to 24 September, 1969. Edinburgh and London: E. & S. Livingstone, 1970:271-81.

Koch 1967a *{published data only}*

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school children. 12. Effect of surpervised rinsing of the mouth with 0.5 per cent sodium fluoride solution at the regular visits to the school dentist. A 3-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:89-96.

Koch 1967b *{published data only}*

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school children. 13. Effect of supervised rinsing of the mouth with 0.05 per cent sodium fluoride solution at the regular visits to the school dentist. A 2-year double-blind test. *Odontologisk Revy* 1967;**18**:97-100.

Koch 1967c *{published data only}*

Hollender L, Koch G. Influence of topical application of fluoride on rate of progress of carious lesions in children. A long-term roentgenographic follow-up. *Odontologisk Revy* 1969;**20**:37-41.

* Koch G. Effect of sodium fluoride in dentifrice and mouthwash on dental caries in school children. 8. Effect of daily supervised toothbrushing with a sodium fluoride dentifrice. A 3-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:48-66.

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school-children. *Odontologisk Revy* 1967;**18**(Suppl. 12):1-125.

Koch G. Long-term study of effect of supervised toothbrushing with a sodium fluoride dentifrice. *Caries Research* 1970;**4**:149-57.

Koch G, Lindhe J. The effect of supervised oral hygiene on the gingiva of children. The effect of sodium fluoride. *Journal of Periodontal Research* 1967;**2**:64-9.

Koch G, Lindhe J. The state of the gingivae and the caries-increment in school-children during and after withdrawal of various prophylactic measures. In: McHugh WD editor(s). Dental Plaque. A symposium held at the University of Dundee, 22 to 24 September, 1969. Edinburgh and London: E. & S. Livingstone, 1970:271-81.

Koch 1967d *{published data only}*

Hollender L, Koch G. Influence of topical application of fluoride on rate of progress of carious lesions in children. A long-term roentgenographic follow-up. *Odontologisk Revy* 1969;**20**:37-41.

* Koch G. Effect of sodium fluoride in dentifrice and mouthwash on dental caries in school children. 8. Effect of daily supervised toothbrushing with a sodium fluoride dentifrice. A 3-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:48-66.

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school-children. *Odontologisk Revy* 1967;**18**(Suppl. 12):1-125.

Koch G. Long-term study of effect of supervised toothbrushing with a sodium fluoride dentifrice. *Caries Research* 1970;**4**:149-57.

Koch G, Lindhe J. The effect of supervised oral hygiene on the gingiva of children. The effect of sodium fluoride. *Journal of Periodontal Research* 1967;**2**:64-9.

Koch G, Lindhe J. The state of the gingivae and the caries-increment in school-children during and after withdrawal of various prophylactic measures. In: McHugh WD editor(s). Dental Plaque. A symposium held at the University of Dundee, 22 to 24 September, 1969. Edinburgh and London: E. & S. Livingstone, 1970:271-81.

Koch 1967e *{published data only}*

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school children. 9. Effect of unsupervised toothbrushing at home with sodium fluoride dentifrice. A 2-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:67-71.

Koch 1967f *{published data only}*

Koch G. Effect of sodium fluoride in dentifrice and mouthwash on incidence of dental caries in school children. 10. Effect of supervised toothbrushing with a sodium fluoride dentifrice at the regular visits to the school dentist. A 3-year double-blind clinical test. *Odontologisk Revy* 1967;**18**:72-6.

Koch 1975 *{published data only}*

Koch G, Petersson LG. Caries preventive effect of a fluoride-containing varnish (Duraphat) after 1 year's study. *Community Dentistry and Oral Epidemiology* 1975;**3**:262-6.

Laswell 1975 *{published data only}*

* Laswell HR, Pacher MW, Wiggs JS. Cariostatic effects of fluoride mouthrinses in a fluoridated community. *Journal of the Tennessee Dental Association* 1975;**55**:198-200.

Laswell HR, Packer MW, Wiggs JS. Cariostatic effects of fluoride mouthrinses in a fluoridated community. *Journal of the Kentucky Dental Association* 1975;**27**:21-5.

Lind 1974 *{published data only}*

Lind OP, Larsen MJ, Moller IJ, von der Fehr FR. A 2% sodium monofluorophosphate toothpaste's caries preventive effect in a Danish fluoride area [En 2% natrium monofluorfosfattandpasta's cariesforebyggende effekt i et dansk fluoromrade]. *Tandlaegebladet* 1975;**79**:793-9.

Lind OP, Moller IJ, von der Fehr FR, Larsen MJ. Caries-preventive effect of a dentifrice containing 2 percent sodium monofluorophosphate in a natural fluoride area. Results after 3 years. *Helvetica Odontologica Acta* 1974;**18**:53.

* Lind OP, Moller IJ, von der Fehr FR, Larsen MJ. Caries-preventive effect of dentifrice containing 2 percent sodium monofluorophosphate in a natural fluoride area in Denmark. *Community Dentistry and Oral Epidemiology* 1974;**2**:104-13.

Lind OP, von der Fehr FR, Larsen MJ, Moller IJ. Anti-caries effect of a 2% Na2PO3F-dentifrice in a Danish fluoride area. *Community Dentistry and Oral Epidemiology* 1976;**4**:7-14.

Mainwaring 1978 *{published data only}*

Mainwaring PJ, Naylor MN. A three-year clinical study to determine the separate and combined caries-inhibiting effects of sodium monofluorophosphate toothpaste and an acidulated phosphate-fluoride gel. *Caries Research* 1978;**12**:202-12.

Mainwaring 1978a *{published data only}*

Mainwaring PJ, Naylor MN. A three-year clinical study to determine the separate and combined caries-inhibiting effects of sodium monofluorophosphate toothpaste and an acidulated phosphate-fluoride gel. *Caries Research* 1978;**12**:202-12.

Mainwaring 1983 *{published data only (unpublished sought but not used)}*

* Mainwaring PJ, Naylor MN. A four-year clinical study to determine the caries-inhibiting effect of calcium glycerophosphate and sodium fluoride in calcium carbonate base dentifrices containing sodium monofluorophosphate. *Caries Research* 1983;**17**:267-76.

Mainwaring PJ, Naylor MN. Anti-caries effects of NaMFP/CaCO3 toothpastes containing calcium glycerohosphate (CaGP) or sodium fluoride (NaF) - A 4 year clinical study [abstract]. *Journal of Dental Research* 1981;**60**:1091.

Marthaler 1965 *{published data only}*

Konig KG, Muhlemann HR. Caries inhibiting effect of aminfluoride containing dentifrices tested in an animal experiment and in a clinical study. In: Muhlemann HR, Konig KG editor(s). The present status of caries prevention by fluorine-containing dentifrices. Caries Symposium Zurich. Berne and Stuttgart: Hans Huber, 1961:30.

* Marthaler T. The caries inhibiting effect of amine fluoride dentifrices in children during three years of unsupervised use. *British Dental Journal* 1965;**119**:153-63.

Marthaler TM. Caries inhibition after five years of unsupervised use of a dentifrice containing amine fluoride. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1965;**75**:509-15.

Marthaler TM. Caries inhibiton with amino fluoride toothpastes following a 7-year-long study [Karieshemmung durch Aminfluoridzahnpasten nach 7 jahriger Studiendauer]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1968;**78**:134-47.

Marthaler TM. Caries-inhibition after seven years of unsupervised use of an amine fluoride dentifrice. *British Dental Journal* 1968;**124**:510-5.

Marthaler TM. The cariostatic effect of amine fluoride containing dentifrices in an unsupervised clinical study. In: Muhlemann HR, Konig KG editor(s). The present status of caries prevention by fluorine-containing dentifrices. Caries Symposium Zurich. Berne and Stuttgart: Hans Huber, 1961:14-25.

Marthaler 1965a *{published data only}*

Konig KG, Muhlemann HR. Caries inhibiting effect of aminfluoride containing dentifrices tested in an animal experiment and in a clinical study. In: Muhlemann HR, Konig KG editor(s). The present status of caries prevention by fluorine-containing dentifrices. Caries Symposium Zurich. Berne and Stuttgart: Hans Huber, 1961:30.

* Marthaler T. The caries inhibiting effect of amine fluoride dentifrices in children during three years of unsupervised use. *British Dental Journal* 1965;**119**:153-63.

Marthaler TM. Caries inhibition after five years of unsupervised use of a dentifrice containing amine fluoride. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1965;**75**:509-15.

Marthaler TM. Caries inhibiton with amino fluoride toothpastes following a 7-year-long study [Karieshemmung durch Aminfluoridzahnpasten nach 7 jahriger Studiendauer]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1968;**78**:134-47.

Marthaler TM. Caries-inhibition after seven years of unsupervised use of an amine fluoride dentifrice. *British Dental Journal* 1968;**124**:510-5.

Marthaler TM. The cariostatic effect of amine fluoride containing dentifrices in an unsupervised clinical study. In: Muhlemann HR, Konig KG editor(s). The present status of caries prevention by fluorine-containing dentifrices. Caries Symposium Zurich. Berne and Stuttgart: Hans Huber, 1961:14-25.

Marthaler 1970 *{published data only}*

Marthaler TM, Konig KG, Muhlemann HR. The effect of a fluoride gel used for supervised toothbrushing 15 or 30 times per year. *Helvetica Odontologica Acta* 1970;**14**:67-77.

Marthaler 1970a *{published data only}*

Marthaler TM, Konig KG, Muhlemann HR. The effect of a fluoride gel used for supervised toothbrushing 15 or 30 times per year. *Helvetica Odontologica Acta* 1970;**14**:67-77.

Marthaler 1970b *{published data only}*

Marthaler TM, Konig KG, Muhlemann HR. The effect of a fluoride gel used for supervised toothbrushing 15 or 30 times per year. *Helvetica Odontologica Acta* 1970;**14**:67-77.

Marthaler 1970c *{published data only}*

* Marthaler TM, Konig KG, Muhlemann HR. The effect of a fluoride gel used for supervised toothbrushing 15 or 30 times per year. *Helvetica Odontologica Acta* 1970;**14**:67-77.

Marthaler 1974 *{published data only}*

Marthaler TM. Caries-inhibition by an amine fluoride dentifrice. Results after 6 years in children with low caries activity. *Helvetica Odontologica Acta* 1974;**18(Suppl. VIII)**:35-44.

McConchie 1977 *{published data only}*

McConchie JM, Richardson AS, Hole LW, McCombie F, Kolthammer J. Caries-preventive effect of two concentrations

of stannous fluoride mouthrinse. *Community Dentistry and Oral Epidemiology* 1977;**5**:278-83.

Mergele 1968 *{published data only}*

Mergele M. Report II. An unsupervised brushing study on subjects residing in a community with fluoride in the water. *Bulletin of the New York Academy of Medicine* 1968;**14**:251-5.

Mestrinho 1983 *{published and unpublished data}*

Mestrinho HD, Bijella MFTB, Bijella VT, Lopes ES. Prevention of dental caries through topical application of APF gel with plastic trays [Prevenção da cárie dental pela aplicação tópica de gel de flúor fosfato acidulado, através de moldeiras plásticas]. *Odontologo Moderno* 1983;**10**:29-32.

Modeer 1984 *{published and unpublished data}*

Modeer T, Twetman S, Bergstrand F. Three-year study of the effect of fluoride varnish (Duraphat) on proximal caries progression in teenagers. *Scandinavian Journal of Dental Research* 1984;**92**:400-7.

Molina 1987 *{published data only (unpublished sought but not used)}*

Molina MX, Rodriguez FG, Urbina T, Vargas S. Effect of weekly mouthrinses with 0.2% neutral NaF solution on caries incidence in first permanent molars [Efecto de enjuagatorios semanales con una solucion neutra de NaF al 0.2% en la incidencia de caries en primeros molares definitivos]. *Odontologia Chilena* 1989;**37**:176-82.

* Molina MX, Rodriguez GP, Sepulveda MM, Urbina TR, Vargas SJ. Increase of caries in a school children group that participated in a weekly mouth wash program with sodium fluoride 0.2 [Efecto en la incidencia de caries dentarias, de enjuagatorios semanales con solucion neutra de fluoruro de sodio al 0,2 en escolares de enseganza basica fiscal]. *Revista de la Facultad de Odontologia de la Universidad de Chile* 1987;**5**:18-27.

Moreira 1972 *{published and unpublished data}*

Moreira BH, Tumang AJ. Mouthwashes with 1 per cent sodium fluoride solutions in the prevention of dental caries [Bochechos com solucoes de fluoreto de sodio a 0,1% na prevencao da carie dental]. *Revista Brasileira de Odontologia* 1971;**28**:11-9.

* Moreira BH, Tumang AJ. Prevention of dental caries by means of mouthwashes with 0.1 solutions of sodium fluoride. Results of a 2 year study [Prevencao da carie dentaria atraves de bochechos com solucoes de fluoreto de sodio a 0.1%. Resultados apos dois anos de estudos]. *Revista Brasileira de Odontologia* 1972;**29**:37-42.

Moreira 1981 *{published and unpublished data}*

Moreira BH, Guimaraes LO, Vieira S, Piedade EF. Fluoride mouthwashes in combination with fluoridation of the public water supply for the prevention of dental caries [Bochecho com fluor associado a fluoretacao da agua de abastecimento publico, na prevencao da carie dentaria]. *Revista da Associacao Paulista de Cirurgioes Dentistas* 1981;**35**:296-301.

Muhler 1955 *{published data only}*

Muhler JC, Radike AW, Nebergall WH, Day HG. A comparison between the anticariogenic effects of dentifrices containing stannous fluoride and sodium fluoride. *Journal of the American Dental Association* 1955;**51**:556-9.

Muhler 1970 *{published data only}*

Muhler JC. A clinical comparison of a fluoride and antienzyme dentifrices [abstract]. *Journal of Dental Research* 1967;**105**(IADR Abstr. No 273):105.

* Muhler JC. A clinical comparison of fluoride and antienzyme dentifrices. *ASDC Journal of Dentistry for Children* 1970;**37**:501.

Murray 1980 *{published and unpublished data}*

Murray JJ, Shaw L. A 3-year clinical trial into the effect of fluoride content and toothpaste abrasivity on the caries inhibitory properties of a dentifrice. *Community Dentistry and Oral Epidemiology* 1980;**8**:46-51.

Naylor 1967 *{published data only (unpublished sought but not used)}*

Ashley FP, Naylor MN, Emslie RD. Stannous fluoride and sodium monofluorophosphate dentifrices. Clinical testing in London school children-radiological findings. *British Dental Journal* 1969;**127**:125-8.

* Naylor MN, Emslie RD. Clinical testing of stannous fluoride and sodium monofluorophosphate dentifrices in London school children. *British Dental Journal* 1967;**123**:17-23.

Naylor 1979 *{published data only (unpublished sought but not used)}*

Naylor MN, Glass RL. A 3-year clinical trial of calcium carbonate dentifrice containing calcium glycerophosphate and sodium monofluorophosphate. *Caries Research* 1979;**13**:39-46.

Olivier 1992 *{published and unpublished data}*

Olivier M, Brodeur JM, Simard PL. Efficacy of APF treatments without prior toothcleaning targeted to high-risk children. *Community Dentistry and Oral Epidemiology* 1992;**20**:38-42.

Packer 1975 *{published data only}*

Packer MW, Laswell HR, Doyle J, Naff HH, Brown F. Cariostatic effects of fluoride mouthrinses in a non-fluoridated community. *Journal of the Tennessee Dental Association* 1975;**55**:22-6.

Peterson 1967 *{published data only}*

Peterson JK, Williamson L. Comparative effectiveness of a sodium fluoride-acid orthophosphate-insoluble metaphosphate dentifrice on caries reduction in children [abstract]. *Journal of Dental Research* 1966;**IADR Abstr. No 249**:100.

* Peterson JK, Williamson L. Field test of a sodium fluoride dentifrice containing acid orthophosphate and an insoluble metaphosphate abrasive-second year report. *Journal of Oral Therapeutics and Pharmacology* 1967;**4**:1-4.

Peterson JK, Williamson L. Three-years caries inhibition of a sodium fluoride acid orthophosphate dentifrice compared with a stannous fluoride dentifrice and a non-fluoride dentifrice [abstract]. *Journal of Dental Research* 1968;**IADR Abstr. No 255**:101.

Peterson 1979 *{published data only}*

* Peterson JK. A supervised brushing trial of sodium monofluorophosphate dentifrices in a fluoridated area. *Caries Research* 1979;**13**:68-72.

Peterson JK, Williamson L, Casad R. Caries inhibition with MFP-calcium carbonate dentifrice in fluoridated area [abstract]. *Journal of Dental Research* 1975;**54**:L85.

Petersson 1998a *{published data only (unpublished sought but not used)}*

Petersson LG, Svanholm I, Andersson H, Magnusson K. Approximal caries development following intensive fluoride mouthrinsing in teenagers. A 3-year radiographic study. *European Journal of Oral Sciences* 1998;**106**:1048-51.

Poulsen 1984 *{published and unpublished data}*

Kirkegaard E, Poulsen S, Bangsbo G, Bro K. A clinical-trial of fluoride rinses in a danish public child dental service [abstract]. *Caries Research* 1984;**18**:183-4.

* Poulsen S, Kirkegaard E, Bangsbo G, Bro K. Caries clinical trial of fluoride rinses in a Danish Public Child Dental Service. *Community Dentistry and Oral Epidemiology* 1984;**12**:283-7.

Powell 1981 *{published data only (unpublished sought but not used)}*

Powell KR, Barnard PD, Craig GG. Effect of stannous fluoride treatments on the progression of initial lesions in approximal surfaces of permanent posterior teeth. *Journal of Dental Research* 1981;**60**:1648-54.

Radike 1973 *{published data only}*

Radike AW, Gish CW, Peterson JK, King JD, Segreto VA. Clinical evaluation of stannous fluoride as an anticaries mouthrinse. *Journal of the American Dental Association* 1973;**86**:404-8.

Ran 1991 *{published data only (unpublished sought but not used)}*

Ran F, Gedalia I, Fried M, Hadani P, Tved A. Effectiveness of fortnightly tooth brushing with amine fluorides in caries-prone subjects. *Journal of Oral Rehabilitation* 1991;**18**:311-6.

Ran 1991a *{published data only (unpublished sought but not used)}*

Ran F, Gedalia I, Fried M, Hadani P, Tved A. Effectiveness of fortnightly tooth brushing with amine fluorides in caries-prone subjects. *Journal of Oral Rehabilitation* 1991;**18**:311-6.

Reed 1973 *{published data only}*

Reed MW. Clinical evaluation of three concentrations of sodium fluoride in dentifrices. *Journal of the American Dental Association* 1973;**87**:1401-3.

Reed 1975 *{published data only}*

* Reed MW, King JD. A clinical evaluation of a sodium fluoride dentifrice. *Pharmacology and Therapeutics in Dentistry* 1975;**2**:77-82.

Reed MW, King JD. A clinical evaluation of a sodium fluoride dentifrice [abstract]. *Journal of Dental Research* 1970;**IADR Abstr. No 340**:133.

Ringelberg 1979 *{published data only}*

Ringelberg ML, Webster DB. Effects of an amine fluoride mouthrinse and dentifrice on the gingival health and the extent of plaque of school children. *Journal of Periodontology* 1977;**48**:350-3.

Ringelberg ML, Webster DB, Dixon DO. Effects of an amine fluoride dentifrice and mouthrinse on the dental caries of school children after 18 months. *Journal of Preventive Dentistry* 1978;**5**:26-30.

Ringelberg ML, Webster DB, Dixon DO, Fairchild S, Driscoll WS. Results of gingival, plaque, and stain assessments after 30 months use of amine fluorides and their inorganic counterparts. *Pharmacology and Therapeutics in Dentistry* 1979;**4**:27-31.

* Ringelberg ML, Webster DB, Dixon DO, LeZotte DC. The caries-preventive effect of amine fluorides and inorganic fluorides in a mouthrinse or dentifrice after 30 months of use. *Journal of the American Dental Association* 1979;**98**:202-8.

Ringelberg 1979a *{published data only (unpublished sought but not used)}*

Ringelberg ML, Webster DB. Effects of an amine fluoride mouthrinse and dentifrice on the gingival health and the extent of plaque of school children. *Journal of Periodontology* 1977;**48**:350-3.

Ringelberg ML, Webster DB, Dixon DO. Effects of an amine fluoride dentifrice and mouthrinse on the dental caries of school children after 18 months. *Journal of Preventive Dentistry* 1978;**5**:26-30.

Ringelberg ML, Webster DB, Dixon DO, Fairchild S, Driscoll WS. Results of gingival, plaque, and stain assessments after 30 months use of amine fluorides and their inorganic counterparts. *Pharmacology and Therapeutics in Dentistry* 1979;**4**:27-31.

* Ringelberg ML, Webster DB, Dixon DO, LeZotte DC. The caries-preventive effect of amine fluorides and inorganic fluorides in a mouthrinse or dentifrice after 30 months of use. *Journal of the American Dental Association* 1979;**98**:202-8.

Ringelberg 1982 *{published data only (unpublished sought but not used)}*

Ringelberg ML, Conti AJ, Ward CB, Clark B, Lotzkar S. Effectiveness of different concentrations and frequencies of sodium fluoride mouthrinse. *Pediatric Dentistry* 1982;**4**:305-8.

Rugg-Gunn 1973 *{published data only}*

Rugg-Gunn AJ, Holloway PJ, Davies TG. Caries prevention by daily fluoride mouthrinsing. Report of a three-year clinical trial. *British Dental Journal* 1973;**135**:353-60.

Ruiken 1987 *{published data only (unpublished sought but not used)}*

Ruiken HM, Truin GJ, Konig DG, Vogels AL, van't Hof MA. Cariostatic effect of fluoride mouth rinsing in children with low socioeconomic status [Cariesreducerend effect van fluoridespoelingen bij kinderen met een lage sociaal-economische status]. *Nederlands Tijdschrift voor Tandheelkunde* 1987;**94**:429-32.

* Ruiken R, Truin GJ, Konig K, Vogels A, van't Hof M. Clinical cariostatic effectiveness of a NaF rinse in a low prevalence child population. *Community Dentistry and Oral Epidemiology* 1987;**15**:57-9.

Rule 1984 *{published data only (unpublished sought but not used)}*

Rule J, Smith M, Truelove R, Macko D, Castaldi C. Anticaries properties of a 0.78% sodium monofluorophosphate-silica base dentifrice [abstract]. *Journal of Dental Research* 1982;**61**:281.

* Rule JT, Smith MR, Truelove RB, Macko DJ, Castaldi CR. Caries inhibition of a dentifrice containing 0.78% sodium monofluorophosphate in a silica base. *Community Dentistry and Oral Epidemiology* 1984;**12**:213-7.

Segal 1967 *{published data only}*

Segal AH, Stiff RH, George WA. Caries inhibiting effectiveness of a stannous fluoride-insoluble sodium metaphosphate (IMP) dentifrice in children. Two year results. *Journal of Dental Research* 1966;**IADR Abstr. No 250**:101.

* Segal AH, Stiff RH, George WA, Picozzi A. Cariostatic effect of a stannous fluoride-containing dentifrice on children: two-year report of a supervised toothbrushing study. *Journal of Oral Therapeutics and Pharmacology* 1967;**4**:175-80.

Shern 1976 *{published data only}*

Shern RJ, Duany LF, Senning RS, Zinner DD. Clinical study of an amine fluoride gel and acidulated phosphate fluoride gel. *Community Dentistry and Oral Epidemiology* 1976;**4**:133-6.

Slack 1964 *{published data only}*

Slack GL, Martin WJ. The use of a dentifrice containing stannous fluoride in the control of dental caries. Report of an unsupervised clinical trial. *British Dental Journal* 1964;**117**:275-80.

Slack 1967 *{published data only}*

Slack GL, Berman DS, Martin WJ, Young J. Clinical testing of stannous fluoride-insoluble metaphosphate dentifrice in Kent girls. *British Dental Journal* 1967;**123**:9-16.

Slack 1967a *{published data only}*

Slack GL, Berman DS, Martin WJ, Hardie JM. Clinical testing of a stannous fluoride-calcium pyrophosphate dentifrice in Essex school girls. *British Dental Journal* 1967;**123**:26-33.

Slack 1971 *{published data only}*

Slack GL, Bulman JS, Osborn JF. Clinical testing of fluoride and non-fluoride containing dentifrices in Hounslow school children. *British Dental Journal* 1971;**130**:154-8.

Spets-Happonen 1991 *{published data only (unpublished sought but not used)}*

Spets-Happonen S, Luoma H, Forss H, Kentala J, Alaluusua S. Effects of a chlorhexidine-fluoride-strontium rinsing program on caries, gingivitis and some salivary bacteria among Finnish schoolchildren. *Scandinavian Journal of Dental Research* 1991;**99**:130-8.

Szwejda 1972 *{published data only}*

Szwejda LF. Fluorides in community programs; a study of four years of various fluorides applied topically to the teeth of children in fluoridated communities. *Journal of Public Health Dentistry* 1972;**32**:25-33.

Tewari 1990 *{published data only (unpublished sought but not used)}*

Tewari A, Chawla HS, Utreja A. Caries preventive effect of three topical fluorides (1 1/2 years clinical trial in Chandigarh school children of North India). *Journal of the International Association of Dentistry for Children* 1984;**15**:71-81.

* Tewari A, Chawla HS, Utreja A. Comparative evaluation of the role of NaF, APF & Duraphat topical fluoride applications in the prevention of dental caries-a 2 1/2 years study. *Journal of the Indian Society of Pedodontics and Preventative Dentistry* 1990;**8**:28-35.

Thomas 1966 *{published data only}*

Thomas AE, Jamison HC. Effect of SnF2 dentrifices on caries in children: two-year clinical study of supervised brushing in children's homes. *Journal of the American Dental Association* 1966;**73**:844-52.

Torell 1965 *{published data only}*

Torell P. The Goteborg studies of methods of applying fluorides topically. In: Hardwick JL, Held HR, Konig KG editor(s). Advances in fluorine research and dental caries prevention. Vol. **3**, Oxford: Pergamon Press, 1965:255-8.

* Torell P, Ericsson Y. Two year clinical tests with different methods of local caries-preventive fluorine application in Swedish school-children (Part I: The Goteborg study). *Acta Odontologica Scandinavica* 1965;**23**:287-312.

Torell 1965a *{published data only}*

Torell P. The Goteborg studies of methods of applying fluorides topically. In: Hardwick JL, Held HR, Konig KG editor(s). Advances in fluorine research and dental caries prevention. Vol. **3**, Oxford: Pergamon Press, 1965:255-8.

* Torell P, Ericsson Y. Two year clinical tests with different methods of local caries-preventive fluorine application in Swedish school-children (Part I: The Goteborg study). *Acta Odontologica Scandinavica* 1965;**23**:287-312.

Torell 1965b *{published data only}*

Torell P, Ericsson Y. Two-year clinical tests with different methods of local caries-preventive fluorine application in Swedish school-children (Part II: The Sodertalje study). *Acta Odontologica Scandinavica* 1965;**23**:313-22.

Torell 1965c *{published data only}*

Torell P, Ericsson Y. Two-year clinical tests with different methods of local caries-preventive fluorine application in Swedish school-children (Part II: The Sodertalje study). *Acta Odontologica Scandinavica* 1965;**23**:313-22.

Treide 1988 *{published and unpublished data}*

Treide A, Treide B. The anticaries effectiveness of newly developed fluoride-containing gels following 3 years of

clinical use in preschool children [Die karieshemmend effektivitat neuentwickelter fluoridhaltiger gele nach deijahriger klinischer Anwendung im vorschulalter]. *Stomatologie der DDR* 1988;**38**:708-12.

Trubman 1973 *{published data only}*

Trubman A, Crellin JA. Effect on dental caries of self-application of acidulated phosphate fluoride paste and gel. *Journal of the American Dental Association* 1973;**86**:153-7.

van Wyk 1986 *{published and unpublished data}*

van Wyk I, van Wyk CW. The effectiveness of a 0.2 percent and a 0.05 percent neutral NaF mouthrinsing programme. *Journal of the Dental Association of South Africa* 1986;**41**:35-40.

Weisenstein 1972 *{published data only}*

Weisenstein PR, Zacherl WA. A multiple-examiner clinical evaluation of a sodium fluoride dentifrice. *Journal of the American Dental Association* 1972;**84**:621-3.

Zacherl 1970 *{published data only (unpublished sought but not used)}*

Zacherl WA, McPhail CW. Evaluation of a stannous fluoride-calcium pyrophosphate dentifrice. *Journal of the Canadian Dental Association* 1965;**31**:174-80.

* Zacherl WA, McPhail CW. Final report on the efficacy of a stannous fluoride-calcium pyrophosphate dentifrice. *Journal of the Canadian Dental Association* 1970;**36**:262-4.

Zacherl 1970a *{published data only (unpublished sought but not used)}*

Zacherl WA, McPhail CW. Evaluation of a stannous fluoride-calcium pyrophosphate dentifrice. *Journal of the Canadian Dental Association* 1965;**31**:174-80.

* Zacherl WA, McPhail CW. Final report on the efficacy of a stannous fluoride-calcium pyrophosphate dentifrice. *Journal of the Canadian Dental Association* 1970;**36**:262-4.

Zacherl 1972 *{published data only (unpublished sought but not used)}*

Zacherl WA. Clinical evaluation of an aged stannous fluoride-calcium pyrophosphate dentifrice. *Journal of the Canadian Dental Association* 1972;**38**:155-7.

Zacherl 1972a *{published data only (unpublished sought but not used)}*

Zacherl WA. A clinical evaluation of a sodium fluoride and stannous fluoride dentifrices [abstract]. *Journal of Dental Research* 1968;**IADR Abstr. No 253**:101.

* Zacherl WA. Clinical evaluation of neutral sodium fluoride, stannous fluoride, sodium monofluorophosphate and acidulated fluoride-phosphate denifrices. *Journal of the Canadian Dental Association* 1972;**38**:35-8.

Zacherl 1973 *{published data only (unpublished sought but not used)}*

* Zacherl WA. A clinical evaluation of a stannous fluoride and a sarcosinate dentifrice. *ASDC Journal of Dentistry for Children* 1973;**40**:451-3.

Zacherl WA. Clinical evaluation of a sarcosinate dentifrice [abstract]. *Journal of Dental Research* 1970;**IADR Abstr. No 339**:133.

Zacherl 1981 *{published data only (unpublished sought but not used)}*

Biesbrock AR, Faller RV, Bartizek RD, Court LK, McClanahan SF. Reversal of incipient and radiographic caries through the use of sodium and stannous fluoride dentifrices in a clinical trial. *Journal of Clinical Dentistry* 1998;**9**:5-10.

Caplan DJ, Slade GD, Biesbrock AR, Bartizek RD, McClanahan SF, Beck JD. A comparison of increment and incidence density analyses in evaluating the anticaries effects of two dentifrices. *Caries Research* 1999;**33**:16-22.

* Zacherl WA. A three-year clinical caries evaluation of the effect of a sodium fluoride-silica abrasive dentifrice. *Pharmacology and Therapeutics in Dentistry* 1981;**6**:1-7.

Zacherl WA. Clinical evaluation of a sodium fluoride-silica abrasive dentifrice [abstract]. *Journal of Dental Research* 1981;**60**:577.

References to studies excluded from this review

Aasenden 1972 *{published data only}*

Aasenden R, DePaola PF, Brudevold F. Effects of daily rinsing and ingestion of fluoride solutions upon dental caries and enamel fluoride. *Archives of Oral Biology* 1972;**17**:1705-14.

Antia 1974 *{published data only (unpublished sought but not used)}*

Antia FE, Shahani DR, Kapadia JD. A clinical study of sodium monofluorophosphate dentifrice in institutionalized children in the city of Bombay. *Journal of the Indian Dental Association* 1974;**46**:165-70.

Arcieri 1981 *{published data only}*

Arcieri RM, Saliba NA, Saliba O. Appraisal of the reduction of the incidence of dental caries, due to mouthwashes with a 0.2% sodium fluoride solution [Avaliacao da reducao na incidencia da carie dentaria, devida a bochechos com solucao de fluoreto de sodio a 0.2%]. *Revista da Associacao Paulista de Cirurgioes Dentistas* 1981;**35**:126-31.

Axelsson 1976 *{published data only}*

Axelsson P, Lindhe J, Waseby J. The effect of various plaque control measures on gingivitis and caries in schoolchildren. *Community Dentistry and Oral Epidemiology* 1976;**4**:232-9.

Badersten 1975 *{published data only}*

Badersten A, Egelberg J, Koch G. Effect of monthly prophylaxis on caries and gingivitis in schoolchildren. *Community Dentistry and Oral Epidemiology* 1975;**3**:1-4.

Bellini 1981 *{published data only}*

Bellini HT, Campi R, Denardi JL. Four years of monthly professional toothcleaning and topical fluoride application in Brazilian schoolchildren. I. Effect on gingivitis. *Journal of Clinical Periodontology* 1981;**8**:231-8.

Bibby 1945 *{published data only}*

Bibby BG. A test of the effect of fluoride containing-dentifrices on dental caries. *Journal of Dental Research* 1945;**24**:297-303.

Billy-Pryga 1983 *{published data only}*

* Billy-Pryga Z, Ilewicz L, Zakrzewska-Pysz E. Clinical evaluation of Duraphat and Fluor-Protector preparations in caries prevention [Ocena kliniczna preparatow Duraphat i Fluor-Protector w profilaktyce prochnicowej]. *Czasopismo Stomatologiczne* 1983;**36**:109-15.

Bily-Pryga Z, Zakrzewka-Pysz E, Ilewicz L. Klinische untersuchung der schutzwirkung des Fluor-Protector-Lackes in der kariesprophylaxe. *Dental Revue* 1980;**10**:16-8.

Birkeland 1973 *{published data only}*

Birkeland JM, Jorkjend L, von der Fehr FR. The influence of fluoride mouthrinsing on the incidence of gingivitis in Norwegian children. *Community Dentistry and Oral Epidemiology* 1973;**1**:17-21.

Bixler 1962 *{published data only}*

Bixler D, Muhler JC. Experimental clinical human caries test design and interpretation. *Journal of the American Dental Association* 1962;**65**:482-8.

Bixler 1966 *{published data only}*

Bixler D, Muhler JC. Effectiveness of a stannous fluoride-containing dentifrice in reducing dental caries in children in a boarding school environment. *Journal of the American Dental Association* 1966;**72**:653-8.

Bixler 1966a *{published data only}*

Bixler D, Muhler JC. Combined use of three agents containing stannous fluoride: a prophylactic paste a solution and a dentifrice. *Journal of the American Dental Association* 1964;**68**:792-800.

* Bixler D, Muhler JC. Effect on dental caries in children in a nonfluoride area of combined use of three agents containing stannous fluoride: a prophylactic paste, a solution, and a dentifrice. II. Results at the end of 24 and 36 months. *Journal of the American Dental Association* 1966;**72**:392-6.

Bohannan 1985a *{published data only}*

Preventing tooth decay: results from a four-year national study. Princetown (NJ): The Robert Wood Johnson Foundation; 1983. Special Report No. 2.

Bell RM, Klein SP, Bohannan HM, Disney JA, Graves RC, Madson R. Treatment effects in the national preventive dentistry demonstration program. Santa Monica (CA): The Rand Corporation; 1984. Report No. R-3072-RWJ.

* Bohannan HM, Klein SP, Disney JA, Bell RM, Graves RC, Foch CB. A summary of the results of the National Preventive Dentistry Demonstration Program. *Journal of the Canadian Dental Association* 1985;**51**:435-41.

Klein SP, Bohannan HM, Bell RM, Disney JA, Foch CB, Graves RC. The cost and effectiveness of school-based preventive dental care. *American Journal of Public Health* 1985;**75**:382-91.

Boyd 1985 *{published data only}*

Boyd CH, Boyd CM, Gallien GS Jr. A preliminary report: the effectiveness of 0.4% stannous fluoride on controlling dental caries. *Arkhiv Dental Journal* 1985;**56**:14-5.

Bristow 1975 *{published data only}*

* Bristow PD. Notes on a fluoride mouth-rinsing scheme in Portsmouth. *British Dental Jounal* 1975;**139**:329-30.

Taylor GO, Dowell TB. A field trial in preventive dentistry [letter]. *British Dental Journal* 1976;**140**:39-40.

Brodeur 1989 *{published data only}*

* Brodeur JM, Simard PL, Demers M, Contandriopoulos A-P, Tessier G, Lepage Y, et al. Comparative effects of FMR programs in fluoridated and unfluoridated communities. *Journal of the Canadian Dental Association* 1988;**54**:761-5.

Brodeur JM, Simard PL, Demers M, Contandriopoulos A-P, Tessier G, Lepage Y, et al. Recruitment and compliance in school-based FMR programs. *Journal of the Canadian Dental Association* 1990;**56**:53-6.

Brodeur JM, Simard PL, Tessier C, Lepage Y, Contandriopoulos AP, Lachapelle D. Effectiveness of a fluoride mouthrinsing program in Quebec, Canada [abstract]. *Journal of Dental Research* 1986;**65**:198.

Castellanos 1983 *{published and unpublished data}*

Castellanos RA. Comparative study of the effect of a .5% NaF solution by mouthwash, toothbrushing or both, in the prevention of dental caries [Estudo comparativo do efeito de solucao de NaF a 0,5%, atraves de bochecho, escovacao e ambos, na prevencao da carie dental]. *Revista de Saude Publica* 1983;**17**:461-75.

Chikte 1996 *{published data only}*

Chikte UM, Lewis HA, Rudolph MJ. The effectiveness of a school-based fluoride mouth rinse programme. *Journal of the Dental Association of South Africa* 1996;**51**:697-700.

Clark 1985a *{published data only}*

Clark DC, Robert G, Tessier C, Frechette N, Le Blanc G, Boucher L, et al. The results after 20 months of a study testing the efficacy of a weekly fluoride mouthrinsing program. *Journal of Public Health Dentistry* 1985;**45**:252-6.

Corpus 1973 *{published data only}*

Corpus BT. The effect of 0.2 percent sodium fluoride mouthrinse in the prevention of dental caries in school children born and reared in a non-fluoridated community. *Journal of the Philippine Dental Association* 1973;**25**:5-12.

de Canton 1983 *{published data only}*

de Canton LP, Basso ML, Ishikawa I, Kaufman A, Marcantoni M, Sveile R, et al. Supragingival plaque and smooth surface caries in children undergoing preventive measures [Placa supragingival y caries de superficies lisas en ninos con medidas preventivas]. *Revista de la Asociacion Odontologica Argentina* 1983;**71**:153-6.

DePaola 1967 *{published data only}*

DePaola PF. Combined use of a sodium fluoride prophylaxis paste and a spray containing acidulated sodium fluoride solution. *Journal of the American Dental Association* 1967;**75**:1407-11.

Disney 1989 *{published data only}*

Disney JA, Graves RC, Stamm JW, Bohannan HM, Abernathy JR. Comparative effects of a 4-year fluoride mouthrinse program on high and low caries forming grade 1 children. *Community Dentistry and Oral Epidemiology* 1989;**17**:139-43.

Downer 1976 *{published data only}*

* Downer MC, Holloway PJ, Davies TG. Clinical testing of a topical fluoride caries preventive programme. *British Dental Journal* 1976;**141**:242-7.

Downer MC, Spencer SJ. Evaluating a dental caries preventive programme. *Royal Society Health Journal* 1973;**93**:129-32.

Ennever 1980 *{published data only (unpublished sought but not used)}*

Ennever J, Peterson JK, Hester WR, Segreto VA, Radike AW. Influence of alkaline pH on the effectiveness of sodium fluoride dentifrices. *Journal of Dental Research* 1980;**59**:658-61.

Esteva Canto 1991 *{published data only}*

Esteva Canto M, March Cerda JC, Abraham Paris C, Quintana Torres L, Botey Ornedal A, Ferrer Riera J, et al. Community trial for the evaluation of the fluoride mouthwash program among students in Palma de Mallorca [Ensayo comunitario de evaluacion del programa de enjuagues con fluor en los escolares de Palma de Mallorca]. *Atencion Primaria* 1991;**8**:928-31.

Fernandez 1979 *{published data only}*

Fernandez RAC. Estudo comparativo do efeito de solucao de NaF a 0.5% atraves de bochecho, escovacao e ambos, na prevencao da carie dental [dissertation]. Sao Paulo (SP): Universidade de Sao Paulo, 1979.

Finn 1963 *{published data only}*

Finn SB, Jamison HC. A comparative clinical study of three dentifrices. *ASDC Journal of Dentistry for Children* 1963;**30**:17-25.

Frankl 1972 *{published data only}*

Frankl SN, Fleisch S, Diodati RR. The topical anticariogenic effect of daily rinsing with an acidulated phosphate fluoride solution. *Journal of the American Dental Association* 1972;**85**:882-6.

Gish 1965 *{published data only}*

Gish CW, Muhler JC. Effect on dental caries in children in a natural fluoride area of combined use of three agents containing stannous fluoride: a prophylactic paste, a solution and a dentifrice. *Journal of the American Dental Association* 1965;**70**:914-20.

Gray 1980 *{published data only}*

Gray AS, Gunther DM, Munns PM. Fluoride paste and rinse in a school dental program. *Journal of the Canadian Dental Association* 1980;**46**:651-4.

Grodzka 1982 *{published and unpublished data}*

Grodzka K, Augustyniak L, Budny J, Czarnocka K, Janicha J, Mlosek K, et al. Caries increment in primary teeth after application of Duraphat fluoride varnish. *Community Dentistry and Oral Epidemiology* 1982;**10**:55-9.

Gutherz 1968 *{published data only}*

Gutherz M. Clinical demonstration of the inhibitory effect on caries of a metaphosphate containing fluoride toothpaste [Klinischer Nachweis der Karieshemmwirkung einer metaphosphathaligen Fluorzahnpaste]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkund* 1968;**78**:235-47.

Halikis 1966 *{published data only (unpublished sought but not used)}*

Halikis SE. A pilot study on the effectiveness of a stannous fluoride dentifrice on dental caries in children. *Australian Dental Journal* 1966;**11**:336-7.

Heifetz 1979 *{published data only}*

Heifetz SB, Franchi GJ, Mosley GW, MacDougall O, Brunelle J. Combined anti-cariogenic effect of fluoride gel-trays and fluoride mouthrinsing in a fluoridated community [abstract No 811]. *Journal of Dental Research* 1978;**57**:277.

* Heifetz SB, Franchi GJ, Mosley GW, MacDougall O, Brunelle J. Combined anticariogenic effect of fluoride gel-trays and fluoride mouthrinsing in an optimally fluoridated community. *Clinical Preventative Dentistry* 1979;**1**:21-8.

Hetzer 1973 *{published data only}*

Hetzer G, Irmisch B. Caries prevention using fluoride varnish (Duraphat)-clinical results and experiences [Kariesprotektion durch Fluorlack (Duraphat)-Klinische Ergebnisse und Erfahrungen]. *Deutsche Stomatologie* 1973;**23**:917-22.

Heuser 1968 *{published data only}*

* Heuser H, Schmidt HF. Dental caries prophylaxis by deep impregnation of the dental enamel with fluorine lac [Zahnkariesprophylaxe durch Tiefenimpragnierung des Zahnschmelzes mit Fluor-Lack]. *Stoma Heidelb* 1968;**21**:91-100.

Schmidt H. Caries prevention by means of deep impregnation of the dental enamel with fluoride lacquer Kariesprophylaxe durch Tiefenimpragnierung des Zahnschmelzes mit Fluorlack [Effekten av fluorlakkering pa tannbehandlings-behovet hos en gruppe ungdomsskoleelever]. *Deutsche Stomatologie* 1971;**21**:139-42.

Hill 1959 *{published data only}*

Hill TJ. Fluoride dentifrices. *Journal of the American Dental Association* 1959;**59**:1121-7.

Hochstein 1975 *{published data only}*

Hochstein HJ, Hochstein U, Breitung L. Experience with the fluoride lacker Duraphat [Erfahrungen mit dem Fluorlack Duraphat]. *ZWR* 1975;**84**:26-30.

Irmisch 1974 *{published data only}*

Hetzer G, Irmisch B, Passler J, Pilz W, Voigt I. Results and experiences in controlled toothbrushing with various caries protective solutions [Ergebnisse und Erfahrungen beim kontrollierten Zahnebursten mit verschiedenen kariesprotektiv wirksamen Losungen]. *Deutsche Stomatologie* 1971;**21**:135-9.

* Irmisch B, Hetzer G, Passler J, Voigt I. Caries prevention by controlled mouth rinsing. Results following a 4-year control period. [Kariesprophylaxe durch uberwachte Mundspulaktionen. Ergebnisse nach 4ja hriger Kontrollzeit]. *Zahn Mund und Kieferheilkunde mit Zentralblatt* 1974;**62**:690-3.

Ivanova 1990 *{published data only (unpublished sought but not used)}*

Ivanova EN. The comparative efficacy of local anticaries agents [Sravnitel'naia effektivnost' mestnykh protivokarioznykh sredtsv]. *Stomatologiia Mosk* 1990;**69**:60-1.

Jiraskova 1965 *{published data only}*

Jiraskova M, Bures H, Hoskova M, Kotrba V, Thorova J, Mrklas L. Effect of Czechoslovakian-made toothpaste containing sodium fluoride [Ucinek cs. zubni pasty s pridavkem fluoridu sodneho]. *Ceskoslovenske Stomatologie* 1965;**65**:433-6.

Jordan 1959 *{published data only}*

* Jordan WA, Peterson JK. Caries-inhibiting value of a dentifrice containing stannous fluoride: final report of a two year study. *Journal of the American Dental Association* 1959;**58**:42-4.

Jordan WA, Peterson JK. Caries-inhibiting value of a dentifrice containing stannous fluoride: first year report of a supervised toothbrushing study. *Journal of the American Dental Association* 1957;**54**:589-94.

Kani 1973 *{published data only}*

Kani M, Fujioka M, Nagamine Y, Fuji K, Kani T. The effect of acidulated sodium fluoride mouthwash on dental caries during a three-year period. *Koku Eisei Gakkai Zasshi* 1973;**23**:244-50.

Kasakura 1966 *{published data only}*

Kasakura T. Dental observation on school feeding. 3. Effect of the dental caries prevention by oral rinsing with sodium fluoride solution in school feeding. *Odontology (Tokyo)-Shigaku* 1966;**54**:22-32.

Kitsugi 1978 *{published data only}*

Kitsugi E. Control of dental caries among 6 to 14 year old school children by the application of preventive treatment and incremental care. *Koku Eisei Gakkai Zasshi* 1978;**28**:244-65.

Kolehmainen 1979 *{published data only}*

Kolehmainen L, Kerosuo E. The clinical effect of application of a urethane lacquer containing silane fluorine. A one-year study. *Proceedings of the Finnish Dental Society* 1979;**75**:69-71.

Kolehmainen 1981 *{published data only}*

Kolehmainen L. Evaluation of a fluoride-containing varnish in children with low caries incidence. *Scandinavian Journal of Dental Research* 1981;**89**:228-34.

Kukleva 1983 *{published and unpublished data}*

Kukleva M, Palabikjan V, Stoilova R, Skuleva V, Nenkovsca J. Prevention of dental caries using Kerr fluoride gel (preliminary communication) [Profilaktika na zubniia karies s floren gel "Kerr" (predvaritelno sobshchenie)]. *Stomatologiia Sofiia* 1983;**65**:5-7.

Kukleva 1998 *{published and unpublished data}*

* Kukleva M. Prevention of dental caries on the first permanent molars with fluoride gel in the first year after eruption. *Folia Medica Plovdiv* 1998;**40**:60-4.

Kukleva M, Kondeva V, Kotsikas M. Group caries prophylactic with fluoride gel. 3rd Balkan Congress of Medicine and Dentistry for Students and Young Doctors; 1999 Nov 5-7;Bursa (Turkey).

Kunin 1991 *{published data only}*

Kunin AA, Kharin OV. The use of a fluoride varnish and helium-neon laser light in preventing caries of the deciduous teeth [Ispol'zovanie ftoristogo laka i sveta gelii-neonovogo lazera v profilaktike kariesa vremennykh zubov]. *Stomatologiia Mosk* 1991;**4**:71-2.

Kunzel 1977 *{published data only}*

Franke W, Kunzel W, Treide A, Bluthner K. Caries prevention by means of aminofluoride after 7 years of collectively conducted oral hygiene [Karieshemmung durch Aminfluorid nach 7 Jahren kollektiv angeleiteter Mundhygiene]. *Stomatologie der DDR* 1977;**27**:13-6.

Franke W, Kunzel W, Treide A, Bluthner K. Longitudinal studies on the inhibition of caries by amine fluoride within the framework of guided and supervised oral hygiene actions [Langsschnittstudien zur Karieshemmung durch Aminfluorid im Rahmen angeleiteter und uberwachter Mundhygiene-Aktionen]. *Stomatologie der DDR* 1976;**26**:532-7.

Franke W, Kunzel W, Treide A, Bluthner K. Wirkungsweise und effwktivitat lokal applizierter aminofluoride zur kariespravention. *Medicamentum* 1975;**16**:362.

Geiger L, Kunzel W, Treide A. Comparative clinical-radiological studies on the increase of caries after controlled mouth hygiene with aminofluoride [Vergleichende klinisch-rontgenologische Untersuchungen uber den Karieszuwachs nach kontrollierter Mundhygiene mit Aminfluorid]. *Deutsch Stomatologie* 1971;**21**:132-5.

Kunzel W. Comparative clinical and x-ray study of the cariostatic effectiveness of aminofluorides [Sravnitel'noe kliniko-rentgenologicheskoe issledovanie protivokarioznoi effektivnosti aminoftoridov]. *Stomatologiia Mosk* 1980;**59**:67-70.

* Kunzel W, Franke W, Treide A. Clinical-radiological parallel control of a longitudinal study of the anti-caries effect of aminofluoride applied locally for 7 years in a double-blind test [Klinisch-rontgenologische Paralleluberwachung einer

Langsschnittstudie zum Nachweis der Karieshemmenden Effektivitat 7 Jahre lokal angewandten Aminfluorids im Doppelblindtest]. *Zahn Mund und Kieferheilkund mit Zentralblatt* 1977;**65**:626-37.

Kunzel 1978 *{published data only}*

Kunzel W, Georgi C. Added caries prevention by means of topical fluoride application in children of a district with fluoridation [Additive Karieshemmung durch lokale Fluoridapplikation bei Kindern eines Wohngebietes mit fluoridangereichertem Trinkwasser]. *Stomatologie der DDR* 1978;**28**:465-9.

Lagutina 1978 *{published data only}*

Lagutina NJ, Vorobjev VS, Grabetskij AA, Stepanov AV. Clinical evaluation of home fluoride-containing varnish. *Quintessence International* 1978;**9**:63-6.

Lehnhoff 1966 *{published data only}*

Lehnhoff RW. Clinical measurement of the effect of an anticaries dentifrice by three examiners [abstract]. *Journal of Dental Research* 1966;**IADR Abstr No 246**:100.

Lieser 1978 *{published data only}*

Lieser O, Schmidt HF. Caries preventive effect of fluoride lacquer after several year's use in children [Kariesprophylaktische Wirkung von Fluorlack nach mehrjahriger Anwendung in der Jugendzahnpflege]. *Deutsche Zahnarztliche Zeitschrift* 1978;**33**:176-8.

Lindquist 1989 *{published data only}*

Lindquist B, Edward S, Torell P, Krasse B. Effect of different carriers preventive measures in children highly infected with mutans streptococci. *Scandinavian Journal of Dental Research* 1989;**97**:330-7.

Louw 1995 *{published data only}*

Louw AJ, Carstens IL, Hartshorne JE, Blignaut RJ. Effectiveness of two school-based caries preventive programmes. *Journal of the Dental Association of South Africa* 1995;**50**:43-9.

Lu 1985 *{published data only}*

Lu KH, Yen DJ, Zacherl WA, Ruhlman CD, Sturzenberger OP, Lehnhoff RW. The effect of a fluoride dentifrice containing an anticalculus agent on dental caries in children. *ASDC Journal of Dentistry for Children* 1985;**52**:449-51.

Luoma 1978 *{published data only}*

Luoma H, Murtomaa H, Nuuja T, Nyman A, Nummikoski P, Ainamo J, et al. A simultaneous reduction of caries and gingivitis in a group of schoolchildren receiving chlorhexidine-fluoride applications. Results after 2 years. *Caries Research* 1978;**12**:290-8.

Maiwald 1973 *{published data only (unpublished sought but not used)}*

* Maiwald HJ. Topical application of fluoride varnish for dental caries prevention in collectives following a 3-year testing period [Lokalapplikation von Fluorschulzlack zur Kariespravention in Kollektiven nach dreij''ahriger Kontrollzeit]. *Stomatologie der DDR* 1974;**24**:123-5.

Maiwald HJ, Geiger L. Local application of fluorine protective varnish for caries prevention in collectivities [Lokalapplikation von Fluorschutzlack zur Kariesprophylaxe in Kollektiven]. *Deutsche Stomatologie* 1973;**23**:56-63.

Maiwald 1978 *{published data only}*

Maiwald HJ, Kunzel W, Weatherell J. The use of a fluoride varnish in caries prevention. *Journal of the International Association of Dentistry for Children* 1978;**9**:31-5.

Mari 1988 *{published data only}*

Mari A, Toth K, Kiss Z, Szita V. The effect of Fluor Protector lacquer on the deciduous and permanent teeth in children consuming fluoridated table salt [A Fluor Protector lakk hatasa fluorozott sot fogyaszto gyermekek tej- es maradofogazatanak allapotara]. *Fogorvosi Szemle* 1988;**81**:225-30.

Mari 1988a *{published data only}*

Mari A, Toth K, Kiss Z, Savay G. The effect of Duraphat lacquer on the condition of the permanent teeth in children consuming fluoridated table salt [A Duraphat lakk hatasa fluorozott sot fogyaszto gyermek maradofogazatanak allapotara]. *Fogorvosi Szemle* 1988;**81**:169-74.

McCormick 1970 *{published data only}*

McCormick J, Manson Hing L, Wolff AE, Koulourides T. Remineralizing mouthwash rationale and a pilot clinical study. *Alabama Journal of Medical Sciences* 1970;**7**:92-7.

Mellberg 1978 *{published data only (unpublished sought but not used)}*

Mellberg JR, Franchi GJ, Englander HR, Mosley GW, Nicholson CR. Short intensive topical APF applications and dental caries in a fluoridated area. *Community Dentistry and Oral Epidemiology* 1978;**6**:117-20.

Mendonca 1995 *{published and unpublished data}*

Bohning D, Dietz E, Schlattmann P, Mendonca L, Kirchner U. The zero-inflated poisson model and the decayed, missing and filled teeth index in dental epidemiology. *Journal of the Royal Statist Society* 1999;**162**:195-209.

* Mendonca L. Longitudinalstudie zu kariespraventiven Methoden, durchgefuhrt bei 7- bis 10-jahrigen urbanen kindern in Belo Horizonte (Brasilien) [dissertation]. Berlin: Free University of Berlin, 1995.

Mergele 1968a *{published data only}*

Mergele M. A supervised brushing study in state institution schools. *Bulletin of the New York Academy of Medicine* 1968;**14**:247-50.

Moller 1968 *{published data only}*

Bay I, Moller IJ. The effect of a sodium monofluorophosphate dentifrice on the gingiva. *Journal of Periodontal Research* 1969;**4**:103-8.

* Moller IJ, Holst JJ, Sorensen E. Caries reducing effect of a sodium monofluorophosphate dentifrice. *British Dental Journal* 1968;**124**:209-13.

Moller IJ, Holst JJ, Sorensen E. Effect of a toothpaste containing sodium monofluorophosphate with controlled toothbrushing [Effekten af en natriummonofluorfosfatholdig tandpasta ved kontrolleret tandborstning]. *Tandlaegebladet* 1968;**72**:705-17.

Morgan 1998 *{published data only}*

* Morgan MV, Campain AC, Adams GG, Crowley SJ, Wright FA. The efficacy and effectiveness of a primary preventive dental programme in non-fluoridated areas of Victoria, Australia. *Community Dental Health* 1998;**15**:263-71.

Morgan MV, Campain AC, Crowley SJ, Wright FA. An evaluation of a primary preventive dental programme in non-fluoridated areas of Victoria, Australia. *Australian Dental Journal* 1997;**42**:381-8.

Morgan MV, Crowley SJ, Wright C. Economic evaluation of a pit and fissure dental sealant and fluoride mouthrinsing program in two nonfluoridated regions of Victoria, Australia. *Journal of Public Health Dentistry* 1998;**58**:19-27.

Morozova 1983 *{published data only}*

Morozova NV, Blekher GA, Shchekleina TA, Dobriakova NS. Effectiveness of caries prevention in children with stage-III activity of the carious process [Effektivnost' profilaktiki kariesa u detei s III stepen'iu aktivnosti karioznogo protsessa]. *Stomatologiia Mosk* 1983;**62**:63-5.

Muhler 1955a *{published data only}*

* Muhler JC, Radike AW, Nebergall WH, Day HG. Effect of a stannous fluoride-containing dentifrice on caries reduction in children II. Caries experience after one year. *Journal of the American Dental Association* 1955;**50**:163-6.

Muhler JC, Radike AW, Nebergall WH, Day HG. The effect of a stannous fluoride-containing dentifrice on caries reduction in children. *Journal of Dental Research* 1954;**33**:606-12.

Muhler 1957 *{published data only}*

Muhler JC. Effect on dental caries of a dentifrice containing stannous fluoride and dicalcium phosphate. *Journal of Dental Research* 1957;**36**:399-402.

Muhler 1958 *{published data only}*

Muhler JC. The effect of a modified stannous fluoride-calcium pyrophosphate dentifrice on dental caries in children. *Journal of Dental Research* 1958;**37**:448-50.

Muhler 1960 *{published data only}*

* Muhler JC. Combined anticariogenic effect of a single stannous fluoride solution and the unsupervised use of a stannous fluoride-containing dentifrice. II. Results at the end of three years. *Journal of Dental Research* 1960;**39**:955-8.

Muhler JC. The combined anticariogenic effect of a single stannous fluoride treatment and the unsupervised use of a stannous fluoride-containing dentifrice. *Journal of Dental Research* 1959;**38**:994-7.

Muhler 1962 *{published data only}*

* Muhler JC. Effect of a stannous fluoride dentifrice on caries reduction in children during a three year study period. *Journal of the Americal Dental Association* 1962;**64**:216-24.

Muhler JC. The effect of a stannous fluoride dentifrice on caries reduction in children during a three-year study period (Summary). In: Muhlemann HR, Konig KG editor(s). Caries Symposium Zurich. Berne and Stuttgart: Hans Huber, 1961:9-13.

Murray 1977 *{published data only}*

Murray JJ, Winter GB, Hurst CP. Duraphat fluoride varnish. A 2-year clinical trial in 5-year-old children. *British Dental Journal* 1977;**143**:11-7.

Niwa 1975 *{published data only}*

Niwa T, Baba K, Niwa M. A study on caries prevention effects of dentifrices containing sodium monofluorophosphate, sodium monofluorophosphate plus dextranase, and sodium monofluorophosphate plus sodium phosphate. *Koku Eisei Gakkai Zasshi* 1975;**25**:172-94.

Onisi 1970 *{published data only}*

Onisi M, Tani H. Clinical trial on the reduction of caries incidence by use of two different fluoride dentifrices. *Koku Eisei Gakkai Zasshi* 1970;**20**:105-11.

Onisi 1974 *{published data only}*

Onisi M, Kitamura T, Tokumasu A, Murakami Y, Makino S. Cariostatic effect of a new fluoride dentifrice. *Koku Eisei Gakkai Zasshi* 1974;**24**:1-5.

Pashaev 1977 *{published data only}*

Pashaev KP. Comparative assessment of the caries prevention effectiveness of different fluorine preparations [Sravnitel'naia otsenka kariesprofilakticheskoi effektivnosti razlichnykh preparatov ftora]. *Stomatologiia Mosk* 1977;**56**:82-4.

Patz 1970 *{published data only}*

Patz J, Naujoks R. The caries prophylactic effect of an aminofluoride containing toothpaste in adolescents after 3 years of controlled use [Die kariesprophylaktische Wirkung einer aminfluoridhaltigen Zahnpaste bei Jugendlichen nach dreijahrigem unuberwachten Gebrauch]. *Deutsche Zahnarztliche Zeitschrift* 1970;**25**:617-25.

Peffley 1960 *{published data only}*

Peffley GE, Muhler JC. Effect of a commercial stannous fluoride dentifrice under controlled brushing habits on dental caries incidence in children: preliminary report. *Journal of Dental Research* 1960;**39**:871-4.

Petersson 1998 *{published data only}*

Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: a two-year clinical study in preschool children. *Journal of Public Health Dentistry* 1998;**58**:57-60.

Piccione 1979 *{published data only (unpublished sought but not used)}*

Piccione N. Controlled clinical study of the caries prophylactic activity of a new bifluoride toothpaste (sodium monofluorophosphate + sodium fluoride) [Studio clinico controllato sull'attivita carioprofilattica di una nuova pasta dentifricia bifluorurata (monofluorofosfato di sodio + fluoruro di sodio)]. *Minerva Stomatologica* 1979;**28**:325-7.

Pinto 1993 *{published data only (unpublished sought but not used)}*

Pinto IL. Dental caries prevention through APF Gel-Tray applications each six months [Prevenção da cárie dental com aplicaçõe tópicas semestrais de fluor fosfato]. *Revista de Saude Publica* 1993;**27**:277-90.

Ramos 1995 *{published data only}*

Ramos SB. Efeito de bochechos fluoretados (NaF - 0,2 por cento) e da aplicacao do verniz com fluor (NaF - 5 por cento) na prevencao da carie dentaria: estudo comparativo em escolares da Regiao Norte da cidade de Sao Paulo, 1992-1993 [Effect of fortnightly rinsing with a 0.2 percent NaF solution and a fluoride varnish with 5 percent NaF in dental caries prevention: comparative study in students of the northern region of Sao Paulo city, Brazil, 1992- 1993] [dissertation]. Sao Paulo: Universidade de Sao Paulo (SP), 1995.

Riethe 1975 *{published data only (unpublished sought but not used)}*

Riethe P, Schubring G. Clinical studies on a sodium monofluorophosphate toothpaste in school children [Klinische Prufung einer Natriummonofluorphosphat-Zahnpaste an Schulkindern]. *Deutsche Zahnarztliche Zeitschrift* 1975;**30**:513-7.

Riethe 1977 *{published data only}*

Riethe P, Streib W, Schubring G. Clinical studies of Nuva Seal, Epoxylite 9070 and Fluor-Protector [Klinische Untersuchungen mit Nuva Seal, Epoxylite 9070 und Fluor-Protector]. *Deutsche Zahnarztliche Zeitschrift* 1977;**32**:853-5.

Roberts 1948 *{published data only}*

Roberts JF, Bibby BG, Wellock WD. The effect of an acidulated fluoride mouthwash on dental caries. *Journal of Dental Research* 1948;**27**:497-500.

Rodriguez Miro 1983 *{published data only}*

Rodriguez Miro MJ, Guerra Deben J, Wasersztejn M, Depres PA. Clinical trial of a caries preventive treatment based on the remineralization of the enamel: a preliminary study [Ensayo clinico del tratamiento preventivo de caries basado en la remineralizacion del esmalte: estudio preliminar]. *Revista Cubana de Estomatologia* 1983;**20**:74-85.

Rodriguez Miro 1988 *{published data only}*

Rodriguez Miro MJ, Vega Valdes D. Evaluation of semiannual combined-treatment with fluoride-chlorhexidine varnish and toothbrushing with chlorhexidine toothpaste for 15 days every 3 months in hypercariogenic children [Valoracion del tratamiento combinado de aplicaciones semestrales de barniz-fluor-clorhexidine y del cepillado dental por 15 dias cada tres meses con la crema dental con clorhexidine en ninos hipercariogenicos]. *Revista Cubana de Estomatologia* 1988;**25**:28-35.

Ruszynska 1978 *{published data only}*

Ruszynska H, George B, Anholcer H, Haber Milewska T. Clinical evaluation of fluor-protector varnish in dental caries prevention [Badania kliniczne nad skutecznoscia stosowania lakieru fluor-protektor w zapobieganiu prochnicy]. *Czasopismo Stomatologiczne* 1978;**31**:1021-5.

Salem 1979 *{published data only}*

Salem LV, Raschio AJ, Montoya VC. Klinisch untersuchung uber die karieshemmend langseitwirkung des Fluor-Protector-Lackes. *Kariesprophylaxe* 1979;**1**:145-8.

Schmidt 1970 *{published data only}*

Schmidt HF. Caries prophylaxis by means of local application of sodium fluoride with special reference to long term fluoridation [Untersuchungen zur Prophylaxe der Zahnkaries durch ortliche Applikation von Natriumfluorid unter besonderer Berucksichtigung der Langzeitfluoridierung]. *Stoma Heidelb* 1970;**23**:5-40.

Seppa 1982 *{published data only}*

Birkeland JM. Trials - results - conclusions. Duraphat - Fluor Protector [Forsok - funn - konklusjon. Duraphat - Fluor Protector]. *Norske Tannlaegeforenings Tidende* 1981;**91**:368-9.

Seppa L, Hausen H, Luoma H. Relationship between caries and fluoride uptake by enamel from two fluoride varnishes in a community with fluoridated water. *Caries Research* 1982;**16**:404-12.

Seppa L, Hausen H, Tuutti H, Luoma H. Effect of a sodium fluoride varnish on the progress of initial caries lesions. *Scandinavian Journal of Dental Research* 1983;**91**:96-8.

Seppa L, Tuutti H, Luoma H. A 2-year report on caries prevention by fluoride varnishes in a community with fluoridated water. *Scandinavian Journal of Dental Research* 1981;**89**:143-8.

Seppa L, Tuutti H, Luoma H. Post-treatment effect of fluoride varnishes in children with a high prevalence of dental caries in a community with fluoridated water. *Journal of Dental Research* 1984;**63**:1221-2.

* Seppa L, Tuutti H, Luoma H. Three-year report on caries prevention of using fluoride varnishes for caries risk children in a community with fluoridated water. *Scandinavian Journal of Dental Research* 1982;**90**:89-94.

Shobha 1987 *{published data only (unpublished sought but not used)}*

Shobha T, Nandlal B, Prabhakar AR, Sudha P. Fluoride varnish versus acidulated phosphate fluoride for schoolchildren in Manipal. *Journal of the Indian Dental Association* 1987;**59**:157-60.

Spears 1978 *{published data only}*

Spears ND, Goldstein C, Gordinier N, Crysler C. Effects of a thrice yearly application of fluoride gel. *Dental Hygiene (Chicago)* 1978;**52**:569-72.

Stadtler 1982 *{published data only}*

Busse H, Stadtler P. A statistical model for caries incidence from a double-blind NaF-gel study. *Caries Research* 1990;**24**:427(Abstract).

* Stadtler P. Results of a 3-year clinical, experimental double-blind study of weekly supervised brushing with a sodium fluoride gel [Ergebnisse einer dreijahrigen klinisch experimentellen Doppelblindstudie mit wochentlichem uberwachtem Einbursten eines natriumfluoridhaltigen Gels]. *Osterreichische Zeitschrift fur Stomatologie* 1982;**79**:83-99.

Stadtler P. Results of a 3-year clinical, experimental double-blind study of weekly supervised brushing with a sodium fluoride gel [Ergebnisse einer dreijahrigen klinisch-experimentellen Doppelblindstudie mit wochentlichem uberwachtem Einbursten eines natriumfluoridhaltigen Gels]. *Osterreichische Zeitschrift fur Stomatologie* 1982;**79**:132-54.

Stookey 1975 *{published data only (unpublished sought but not used)}*

Stookey GK, Beiswanger BB. Influence of an experimental sodium fluoride dentifrice on dental caries incidence in children. *Journal of Dental Research* 1975;**54**:53-8.

Suntsov 1991 *{published data only}*

Suntsov VG, Distel' VA, Zhorova TN, Buiankina RG, Toropov VN, Bulanova EL, et al. The trace efficacy of dental caries prevention in children [Sledovaia effektivnost' profilaktiki kariesa zubov u detei]. *Stomatologiia Moskva* 1991;**2**:69-71.

Swerdloff 1969 *{published data only}*

Swerdloff G, Shannon IL. A feasibility study of the use of a stannous fluoride mouthwash in a school preventive dentistry program. USAF School of Aerospace Medicine; 1967. Report No. SAM-TR-67-52 1-10.

* Swerdloff G, Shannon IL. Feasibility of the use of stannous fluoride mouthwash in a school system. *ASDC Journal of Dentistry for Children* 1969;**36**:363-8.

Szoke 1989 *{published data only}*

* Szoke J, Kozma M. Results of 3-year study of toothbrushing with a fluoride amine gel [Ergebnisse einer dreijahrigen Untersuchung uber Zahneputzen mit einem Aminfluorid-Gelee]. *Oral-prophylaxe* 1989;**11**:137-43.

Szoke J, Kozma M. Results of a three-year group test of the use of Elmex gel [Csoportosan vegzett Elmex zsele bedorzsoles harom eves eredmenyei]. *Fogorvosi Szenile* 1988;**81**:161-7.

Szwejda 1971 *{published data only}*

* Szwejda LF. Fluorides in community programs: results after two years from a fluoride gel applied topically. *Journal of Public Health Dentistry* 1971;**31**:241-2.

Szwejda LF, Tossy CV, Below DM. Fluorides in community programs; results from a fluoride gel applied topically. *Bulletin of Michigan Dental Hygienists Association* 1968;**14**:13-5.

Szwejda LF, Tossy CV, Below DM. Fluorides in community programs; results from a fluoride gel applied topically. *Journal of Public Health Dentistry* 1967;**27**:192-4.

Todorashko 1983 *{published data only}*

Todorashko OV. Results of the combined use of remodent and fluorine lacquer for dental caries prevention in preschoolers [Rezul'taty sochetannogo primeneniia remodenta i ftorlaka dlia profilaktiki kariesa zubov u doshkol'nikov]. *Stomatologiia Mosk* 1983;**62**:12-3.

van Eck 1984 *{published data only (unpublished sought but not used)}*

Groeneveld A, Theuns HM, Kwant GW. Effect of a fluoride-containing lacquer on dental caries. *Journal of Dental Research* 1982;**61**:569.

Theuns HM, Groeneveld A, van Eck AA. Clinical experimental field studies of the caries-preventive effect of a fluoride lacquer [Een klinisch experimenteel veldonderzoek naar het caries-preventieve effect van een fluoridelak]. *Netherlands Tijdschrift voor Tandheelkunde* 1985;**92**:66-9.

* van Eck AA, Theuns HM, Groeneveld A. Effect of annual application of polyurethane lacquer containing silane-fluoride. *Community Dentistry and Oral Epidemiology* 1984;**12**:230-2.

Wegner 1976 *{published data only}*

Wegner H. The clinical effect of application of fluoride varnish. *Caries Research* 1976;**10**:318-20.

Weisz 1960 *{published data only}*

Weisz WS. Reduction of dental caries through use of a sodium fluoride mouthwash. *Journal of the American Dental Association* 1960;**60**:438-46.

Widenheim 1989 *{published data only}*

Widenheim J, Birkhed D, Hase JC, Olavi G. Effect on approximal caries in teenagers of interrupting a school-based weekly NaF mouthrinse program for 3 years. *Community Dentistry and Oral Epidemiology* 1989;**17**:83-6.

Wilson 1978 *{published data only (unpublished sought but not used)}*

Wilson CJ, Triol CW, Volpe AR. The clinical anticaries effect of a fluoride dentifrice and mouthrinse [abstract]. *Journal of Dental Research* 1978;**57**:276.

Winter 1975 *{published data only}*

Winter K. Caries prophylaxis by local application of sodium fluoride lacquer [Kariesprophylaxe durch Lokalapplikation von Natriumfluorid-Lack]. *Zahnarztlicher Gesundheitsdienst* 1975;**3**:1-2.

* Winter K. Caries prophylaxis by means of local application of sodium fluoride lacquer [Kariesprophylaxe durch Lokalapplikation von Natriumfluorid-Lack]. *Zahnarztliche Mitteilungren* 1975;**65**:215-21.

Wrinkler 1953 *{published data only}*

Wrinkler KC, Backer-Dirks O, van Amerongen J. A reproducible method for caries evaluation. Test in a therapeutic experiment with a fluorinated dentifrice. *British Dental Journal* 1953;**95**:119-24.

Wycoff 1991 *{published data only}*

Wycoff S, Elisson J. School based fluoride rinse caries prevention demonstration project [abstract]. *Journal of Dental Research* 1991;**70**:359.

Zickert 1982 *{published data only}*

Zickert I, Lindvall AM, Axelsson P. Effect on caries and gingivitis of a preventive program based on oral hygiene measures and fluoride application. *Community Dentistry and Oral Epidemiology* 1982;**10**:289-95.

Zimmer 1999 *{published data only}*

Zimmer S, Robke FJ, Roulet JF. Caries prevention with fluoride varnish in a socially deprived community. *Community Dentistry and Oral Epidemiology* 1999;**27**:103-8.

References to studies awaiting assessment

Ainamo 1981 *{published data only}*

Ainamo J, Tiainen L. The effect of supervised toothbrushing and fluoride rinsing every other week among schoolchildren in Vanda, Finland [Effekten av overvakad tandborstning och fluorskaoljning varannan vecka bland skolelever i Vanda, Finland]. *Tandlaegebladet* 1981;**85**:175-9.

Bodnar 1984 *{published data only}*

Bodnar Z, Tarjan I, Keri I. Clinical experience with the use of Duraphat lacquer [A "Duraphat" lakk alkalmazasaval kapcsolatos klinikai tapasztalatok]. *Fogorvosi Szenile* 1984;**77**:279-82.

Cichocka 1981 *{published data only}*

Cichocka E. Economic evaluation of selected methods of contact fluoridation of the teeth [Ocena ekonomiczna wybranych metod kontaktowego fluorkowania zebow]. *Czasopismo Stomatologiczne* 1981;**34**:245-50.

* Cichocka E. Oral hygiene and the efficacy of selected methods of contact tooth fluoridation [Higiena jamy ustnej a skutecznosc wybranych metod kontaktowego fluorkowania zebow]. *Czasopismo Stomatologiczne* 1981;**34**:145-53.

Forsman 1965 *{published data only}*

Forsman B. Effect of mouth rinses with sodium fluoride in schools at Vaxjo [Effekten av munskoljningar med natriumfluorid-losning vid skolor i Vaxjo]. *Sver Tandlakarforb Tidningen* 1965;**57**:705-9.

Hall 1964 *{published data only}*

Hall B, Lind V. A clinical experiment with daily fluoride mouth-wash under supervision [Ett praktiskt forsok med overvakade dagliga fluoridmunskoljningar]. *Sver Tandlakarforb Tidningen* 1964;**56**:710-4.

Hansson 1965 *{published data only}*

Hansson N. Barntandvarden 1954-1964 i Jonkoping lan. *Sver Tandlakarforb Tidningen* 1965;**57**:388.

Kawall 1981 *{published data only}*

Kawall K, Lewis DW, Hargreaves JA. The effect of a fluoride mouthrinse in an optimally fluoridated community; final two year results [abstract]. *Journal of Dental Research* 1981;**60**:471.

Kinkel 1968 *{published data only}*

Kinkel HJ, Stolte G. On the effect of a sodium monofluorophosphate-bromochlorophenol containing toothpaste in a chronic animal experiment and on caries in children during a 2-year long unsupervised use [Zur Wirkung einer natriummonofluorphosphat- und bromchlorophenhaltigen Zahnpasta im chronischen Tierexperiment und auf die Karies bei Kindern wahrend eines zqei Jahre langen, unuberwachten Gebrauches]. *DDZ (Deutsche Zahnarzteblatt)* 1968;**22**:455-60.

Kinkel 1974 *{published data only}*

* Kinkel HJ, Stolte G, Weststrate J. The effectiveness of a fluorophosphate toothpaste on children's teeth [Etude de l'efficacite d'une pate dentifrice au fluorophosphate sur la denture des enfants]. *SSO Schweizerische Monatsschrift Fuer Zahnheilkunde* 1974;**84**:577-89.

Rijnbeek PLC, Weststrate J. Development and study of the efficacy of a fluoridated dentifrice [Ontwikkeling en effectiviteitsonderzoek van een gefluorideerde tandpasta]. *Nederlands Tijdschrift voor Tandheelkunde* 1976;**83**:123-8.

Kobylanska 1975 *{published data only}*

Kobylanska M. [Evaluation of caries-inhibiting effects of fluoride-containing dentifrices of Polish production] Ocena profilaktycznego dzialania krajowych past do zebow zawierajacych niektore zwiazki fluoru. *Czasopismo Stomatologie* 1975;**28**:247-51.

Mitrega 1981 *{published data only}*

Mitrega J, Opalko K, Lisiecka K. Usefulness of the preparation Flura-Gel in the prevention of dental caries in school children [Przydatnosc preparatu Flura-Gel w profilaktyce prochnicy zebow u dzieci szkolnych]. *Czasopismo Stomatologiczne* 1981;**34**:859-63.

Moungtin 1975 *{published data only}*

Moungtin S, Thavarnton T, Poshakrishna S, Kridakorn O. The caries preventing effect of mouthrinsing with 0.2% sodium fluoride solution in schoolchildren. *Journal of the Dental Association of Thailand* 1975;**25**:259-66.

Nenyei 1971 *{published data only}*

Nenyei J. The use and effect of fluoridated mouthwash in elementary school children [Fluoros szajviz hasznalata es eredmenyei altalanos iskolasokon]. *Fogorvosi Szemle* 1971;**64**:140-5.

Nystrom 1961 *{published data only}*

Nystrom S, Bramstang S, Torell P. Mouthwashes with zirconium fluoride or ferric fluoride complexes [Munskoljning med

zirconiumfluorid- eller jarnfluoridlosningar]. *Svensk Tandlakare Tidskrift* 1961;**54**:217-20.

Ollinen 1963 *{published data only}*

Ollinen P. [Kariesprofylax genom applikation av fluorlosning med ferrosulfat]. *Sver Tandlakarforb Tidningen* 1963;**55**:743-7.

Onishi 1967 *{published data only}*

Onishi E, Okada S, Hinoide M, Akada H, Kon K, Sugano N, et al. Effect of stannous fluoride dentifrice on the reduction of dental caries in schoolchildren. *Koku Eisei Gakkai Zasshi* 1967;**17**:68-74.

Schioth 1981 *{published data only}*

Schioth JT. Effect of fluoride lacquering on the need of dental care in a group of adolescent school pupils [Effekten av fluorlakkering pa tannbehandlings-behovet hos en gruppe ungdomsskoleelever]. *Norske Tannlaegeforenings Tidende* 1981;**91**:123-6.

Shimada 1978 *{published data only}*

Shimada Y, Takagi O, Inoue H. The caries reducing effect of mouth rinsing with a dilute NaF solution. *Koku Eisei Gakkai Zasshi* 1978;**28**:1-9.

Takeuchi 1968 *{published data only}*

Takeuchi M, Shimizu T, Kawasaki T, Kizu T. A field study on effect of a dentifrice containing sodium monofluorophosphate in caries prevention. *Koku Eisei Gakkai Zasshi* 1968;**18**:26-38.

Torell 1963 *{published data only}*

Torell P. Fluorskoljningen i Goteborg lasaren 1960-61 och 1961-62. *Sver Tandlakarforb Tidningen* 1963;**55**:255-8.

Torell 1969 *{published data only}*

Torell P. Influence of fluoride mouthwash on dental caries [Fluorskoljningens inverkan pa kariesbilden]. *Sver Tandlakarforb Tidningen* 1969;**61**:619-22.

Treide 1980 *{published and unpublished data}*

Treide A, Hebenstreit W, Gunther A. Collective preschool caries prevention using a fluoride-containing varnish [Kollektive Kariespravention im Vorschulalter unter Verwendung eines fluoridhaltigen Lackes]. *Stomatologie der DDR* 1980;**30**:734-9.

Ulvestad 1978 *{published data only}*

Ulvestad H. Applisering av Duraphat Fluorlakk. *Norwegian Dental Journal* 1978;**88**:207.

Wacinska 1987 *{published data only}*

Wacinska Drabinska M. Effect of Fluor-Protector varnish on the inhibition of the carious process in milk teeth [Wplyw lakieru Fluor-Protector na zahamowanie procesu prochnicowego w zebach mlecznych]. *Czasopismo Stomatologiczne* 1987;**40**:528-32.

Weisenstein 1967 *{published data only}*

Weisenstein PR, Lehnhoff RW. A clinical evaluation of an anticaries dentifrice comparing conventional and radiographic measures [abstract]. *Journal of Dental Research* 1967;**IADR Abstr. No 425**:143.

Wojtowicz 1986 *{published data only}*

Wojtowicz D, Banach J. Clinical evaluation of Duraphat varnish in the prevention of dental caries in children and in the control of cervical hypersensitivity in adults [Ocena kliniczna laku Duraphat w profilaktyce prochnicy zebow u dzieci oraz w zwalczaniu wrazliwosci szyjek zebow u doroslych]. *Czasopismo Stomatologiczne* 1986;**39**:213-8.

References to ongoing studies

Mancunian *{unpublished data only}*

Davies G. The Mancunian Fluoride Varnish Project. Ongoing trial.

PECC *{unpublished data only}*

Weintraub JA. Prevention of Early Childhood Caries. Ongoing Trial.

Additional references

Bartizek 2001

Bartizek RD, Gerlach RW, Faller RV, Jacobs SA, Bollmer BW, Biesbrock AR. Reduction in dental caries with four concentrations of sodium fluoride in a dentifrice: a meta-analysis evaluation. *Journal of Clinical Dentistry* 2001;**12**:57-62.

Burt 1998

Burt BA. Prevention policies in the light of the changed distribution of dental caries. *Acta Odontologica Scandinavica* 1998;**56**:179-86.

Chaves 2002

Chaves SV, Vieira-da-Silva LM. Anticaries effectiveness of fluoride toothapaste: a meta-analysis. *Revista de Saude Publica* 2002;**36**:598-606.

Chen 1995

Chen MS. Oral health of disadvantaged populations. In: Cohen LK, Gift CH editor(s). Disease Prevention and Oral Health Promotion. Copenhagen: Munksgaard, 1995:152-212.

Clark 1985

Clark DC, Hanley JA, Stamm JW, Weinstein PL. An empirically based system to estimate the effectiveness of caries-preventive agents. A comparison of the effectiveness estimates of APF gels and solutions, and fluoride varnishes. *Caries Research* 1985;**19**:83-95.

Clarke 2000

Clarke M, Oxman AD (editors). Assessment of study quality. Cochrane Reviewers' Handbook version 4.1 [updated June 2000]; Section 6. The Cochrane Collaboration, 2000.

Downer 1995

Downer MC. The 1993 national survey of children's dental health. *British Dental Journal* 1995;**178**:407-12.

Dubey 1965

Dubey SD, Lehnhoff RW, Radike AW. A statistical confidence interval for true per cent reduction in caries-incidence studies. *Journal of Dental Research* 1965;**44**:921-3.

Egger 1997

Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple graphical test. *BMJ* 1997;**315**(7109):629-34.

Featherstone 1988

Featherstone JDB, Ten Cate JM. Physicochemical aspects of fluoride-enamel interactions. In: Ekstrand J, Fejerskov O, Silverstone LM editor(s). Fluoride in Dentistry. Copenhagen: Munksgaard, 1988:125-49.

Glass 1982

Glass RL. The first international conference on the declining prevalence of dental caries. *Journal of Dental Research* 1982;**61**:1301-83.

Helfenstein 1994

Helfenstein U, Steiner M. Fluoride varnishes (Duraphat): a meta-analysis. *Community Dentistry and Oral Epidemiology* 1994;**22**:1-5.

Johnson 1993

Johnson MF. Comparative efficacy of NaF and SMFP dentifrices in caries prevention: a meta-analytic overview. *Caries Research* 1993;**27**:328-36.

Juni 2002

Juni P, Holenstein F, Sterne J, Bartlett C, Egger M. Direction and impact of language bias in meta-analyses of controlled trials: empirical study. *International Journal of Epidemiology* 2002;**31**:115-23.

Marinho 1997

Marinho VC. A systematic review of the effectiveness of topical fluoride therapy in the prevention of dental caries in children and adolescents [dissertation]. London: University of London 1997.

Marinho 2002

Marinho VCC, Higgins J, Logan S, Sheiham A. Fluoride gels for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews* 2002, Issue 2. [Art. No.: CD002280. DOI: 10.1002/14651858.CD002280]

Marinho 2003

Marinho VCC, Higgins J, Logan S, Sheiham A. Fluoride toothpastes for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews* 2003, Issue 1. [Art. No.: CD002278. DOI: 10.1002/14651858.CD002278]

Marthaler 1994

Marthaler TM, Steiner M, Menghini G, Bandi A. Caries prevalence in Switzerland. *International Dental Journal* 1994;**44**:393-401.

Marthaler 1996

Marthaler TM, O'Mullane DM, Vrbic V. The prevalence of dental caries in Europe 1990-1995. ORCA Saturday afternoon symposium 1995. *Caries Research* 1996;**30**:237-55.

Moynihan 1996

Moynihan PJ, Holt RD. The National Diet and Nutrition Survey of 1.5 to 4.5 year old children: summary of the findings of the dental survey. *British Dental Journal* 1996;**181**:328-32.

Murray 1991

Murray JJ, Rugg-Gunn AJ, Jenkins GN. A history of water fluoridation. In: Murray JJ, Rugg-Gunn AJ, Jenkins GN editor(s). Fluorides in Caries Prevention. Oxford: Wright, 1991:7-37.

Murray 1991a

Murray JJ, Rugg-Gunn AJ, Jenkins GN. Fluoride toothpastes and dental caries. In: Murray JJ, Rugg-Gunn AJ, Jenkins GN editor(s). Fluorides in caries prevention. Oxford: Wright, 1991:127-60.

O' Mullane 1995

O'Mullane DM. Contribution of fluoride toothpastes to oral health. In: Bowen WH editor(s). Relative efficacy of sodium fluoride and sodium monofluorophosphate as anti-caries agents in dentifrices. The Royal Society Of Medicine Press Limited, 1995:3-7.

Pitts 2001

Pitts NB, Evans DJ, Nugent ZJ. The dental caries experience of 5-year-old children in Great Britain. Surveys coordinated by the British Association for the Study of Community Dentistry in 1999/2000. *Community Dental Health* 2001;**18**(1):49-55.

Pitts 2002

Pitts NB, Evans DJ, Nugent ZJ, Pine CM. The dental caries experience of 12-year-old children in England and Wales. Surveys coordinated by the British Association for the Study of Community Dentistry in 2000/2001. *Community Dental Health* 2002;**19**(1):46-53.

Ripa 1989

Ripa LW. Review of the anticaries effectiveness of professionally applied and self-applied topical fluoride gels. *Journal of Public Health Dentistry* 1989;**49**:297-309.

Ripa 1991

Ripa LW. A critique of topical fluoride methods (dentifrices, mouthrinses, operator-applied, and self-applied gels) in an era of decreased caries and increased fluorosis prevalence. *Journal Of Public Health Dentistry* 1991;**1**:23-41.

Rolla 1991

Rolla G, Ogaard B, Cruz R-d-A. Clinical effect and mechanism of cariostatic action of fluoride-containing toothpastes: a review. *International Dental Journal* 1991;**41**:171-4.

Seppa 1998

Seppa L, Karkkainen S, Hausen H. Caries frequency in permanent teeth before and after discontinuation of water fluoridation in Kuopio, Finland. *Community Dentistry and Oral Epidemiology* 1998;**26**:256-62.

Sharp 1998

Sharp S. Meta-analysis regression: statistics, biostatistics, and epidemiology 23 (sbe23). Stata Technical Bulletin 1998; Vol. 42:16-22.

Stamm 1984

Stamm JW, Bohannan HM, Graves RC, Disney JA. The efficiency of caries prevention with weekly fluoride mouthrinses. *Journal of Dental Education* 1984;**48**:617-26.

Stamm 1995

Stamm JW. Clinical studies of neutral sodium fluoride and sodium monofluorophosphate dentifrices. In: Bowen WH editor(s). Relative efficacy of sodium fluoride and sodium monofluorophosphate as anti-caries agents in dentifrices. London: The Royal Society of Medicine Press Limited, 1995:43-58.

Strohmenger 2001

Strohmenger L, Brambilla E. The use of fluoride varnishes in the prevention of dental caries: a short review. *Oral Diseases* 2001;**7**:71-80.

Thompson 1999

Thompson SG, Sharp SJ. Explaining heterogeneity in meta-analysis: a comparison of methods. *Statistics in Medicine* 1999;**18**(20):2693-708.

van Rijkom 1998

van Rijkom HM, Truin GJ, van 't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. *Caries Research* 1998;**32**:83-92.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abadia 1978

Methods	Stratified quasi-random allocation; blind caries assessment stated but unclear (C); non-placebo-controlled; 13% drop out after 1 year (study duration = 1 year). Natural losses only; no differential losses among groups.
Participants	254 children analysed at 1 year (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 12.2 DMFS. Exposure to other fluoride: none assumed. Year study began: 1977. Location: Brazil.
Interventions	FG +ptc (2 groups)** versus NT (APF group 1 = 12,300 ppm F, APF group 2 = 12,300 ppm F). Operator-applied, with cotton-paint, once a year, applied for 4 minutes.
Outcomes	1yNetDMFS increment - (CA)(E). Reported at 1 year follow up. O-DMFS. MD-DMFS. BL-DMFS. Drop out.
Notes	Participants randomized (N = 291). Baseline characteristics (dental age, DMFS, gender) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E; diagnostic errors NR. **Prior prophylaxis with non-fluoride paste carried out in FG groups only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Abrams 1980

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 48% drop out after 3 years (study duration = 3 years). Reasons for high drop out described: change of residence, absenteeism, non-adherence to study protocol; no differential group losses.
Participants	1141 children analysed at 3 years (available at final examination). Age range at start: 5-12 years. Surfaces affected at start: 3.2 DFS. Background exposure to fluoride: none reported. Year study began: in/before 1976. Location: USA.
Interventions	FT (2 groups) versus PL (both SnF2 groups = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: silica gel in one SnF2 and placebo toothpaste, Ca pyrophosphate in the other SnF2 toothpaste.
Outcomes	3yNetDFS increment - (E+U) (CA)cl+(ER)xr. Reported at 1, 2 and 3 years follow ups. DMFT. DMFS. DFT. MD-DFS. DFT rate. DFS rate.
Notes	Participants randomized (N = 2210). Baseline characteristics (DFS) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. Radiographic assessment (postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Intra- and inter-examiner reproducibility of clinical caries diagnosis (DFS) assessed annually by duplicate examination of 10% random sample (% of times diagnosis replicated in all 3 examinations ranged 42-97% and 77-92% for both examiners and for each respectively).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Andlaw 1975

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 13% drop out after 3 years (study duration = 3 years). Main reasons for attrition described: moved away, absent at final examination; no differential group losses.
Participants	740 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 6.9 DFS. Background exposure to fluoride: none reported. Year study began: 1970.

Andlaw 1975 *(Continued)*

	Location: UK.
Interventions	FT versus PL (SMFP group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yNetDFS increment - (E+U)(CA)cl+(ER)xr. Reported at 3 years follow up. DMFS. DFT. DMFT. PF-DMFS. MD-BL-DMFS. MD-DMFS. O-DMFS. ECSI.
Notes	Participants randomized (N = 846). Baseline characteristics (age, dental age, TAR, DFS, DMFS, DFT, DMFT, ECSI) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Reproducibility ratio was less than 0.22 for intra-examiner reproducibility of clinical and radiographic caries diagnosis; "significant differences between examiners could not have affected caries increment figures since each examined same children annually".

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ashley 1977

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 12% drop out (for all study groups combined) after 2 years (study duration = 2 years). Natural losses; any differential group losses not assessable.
Participants	488 children analysed at 2 years (available at final examination). Average age at start: 12 years. Surfaces affected at start: 9.1 DFS. Exposure to other fluoride: no. Year study began: 1973. Location: UK.
Interventions	FR+ptc versus PL+ptc** (NaF group = 100 ppm F). School use/supervised, daily, 20 ml applied for 1 min.
Outcomes	2yNetDFS increment - (E+U)(NCA)cl+(ER)xr. Reported at 2 years follow up. PF-DFS. MD-BL-DFS. MD-DFS.

Ashley 1977 *(Continued)*

	DFS (U).
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DFS, DMFS, DMFT) 'balanced'. Clinical (V) caries assessment by one examiner (FOTI used); diagnostic threshold = NCA. Radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = E/U. Intra-examiner reproducibility checks for incremental caries data (icc for clinical 0.95, for radiographic 0.8); reversal rate beween 12% and 7% of observed DFS increment in study groups. ** Prior toothbrushing with non-fluoride toothpaste in both groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ashley 1977a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 12% drop out (for all study groups combined) after 2 years (study duration = 2 years). Natural losses; any differential group losses not assessable.
Participants	489 children analysed at 2 years (available at final examination). Average age at start: 12 years. Surfaces affected at start: 9.1 DFS. Background exposure to fluoride: none. Year study began: 1973. Location: UK.
Interventions	FT versus PL (SMFP group = 1000 ppm F). School use/supervised, daily, 1 g applied for 1 min, post-brushing water rinse done (non-fluoride toothpaste provided to all for home use). Abrasive system: IMP (main abrasive).
Outcomes	2yNetDFS increment - (E+U)(NCA)cl+(ER)xr. Reported at 2 years follow up. PF-DFS. MD-BL-DFS. MD-DFS. DFS (U).
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DFS, DMFS, DMFT) 'balanced'. Clinical (V) caries assessment by one examiner (FOTI used); diagnostic threshold = NCA. Radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = E/U. Intra-examiner reproducibility checks for incremental caries data (icc for clinical 0.95, for radiographic 0.8); reversal rate beween 12% and 7% of observed DFS increment in study groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Bastos 1989

Methods	Stratified quasi-random allocation; double-blind (A); placebo-controlled; 45% drop out after 2.5 years (study duration = 2.5 years). Reasons for high drop-out rate NR; exclusions based on 'statistical reasons' (made 'at random' to keep groups of equal sizes).
Participants	420 children analysed at 2.5 years (after exclusions, available at final examination). Age range at start: 9-12 years (average = 10). Surfaces affected at start: 10 DMFS (from sample randomized). Exposure to other fluoride: none assumed. Year study began: 1977. Location: Brazil.
Interventions	FR (2 groups)** versus PL (SMFP group = 900 ppm F, NaF group = 900 ppm F). School use/supervised, weekly, 10 ml applied for 1 min.
Outcomes	2.5yDMFS increment - (CA)(E). Reported at 1, 1.5 and 2.5 year follow ups. DMFT (E/U). O-DFS. BL-DFS. MD-DFS. DMFS (U). antDMFS. postDMFS. Side effects (incomplete data).
Notes	Participants randomized (N = 766). Baseline characteristics (DMFS, DMFT, dental age) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. State of tooth eruption included = E/U. Consistency of diagnosis assessed by duplicate examinations annually. Reversals were less than 5% of DMFS increments in all groups and equally common. ** Study group of sodium monofluorphosphate solution containing 4% of ethanol not considered.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Bijella 1981

Methods	Stratified quasi-random allocation; blind caries assessment stated but unclear (C); non-placebo-controlled; 20% drop out after 1.5 years (study duration = 1.5 years). Exclusions based on 'statistical reasons' (made at random to keep groups of equal sizes, after 11% natural loss).
Participants	320 children analysed at 1.5 years (after exclusions, available at final examination). Age range at start: 7-10 years. Surfaces affected at start: 6.6 DMFS. Exposure to other fluoride: none assumed.

Bijella 1981 *(Continued)*

	Year study began: 1979. Location: Brazil.
Interventions	FG+ptc** versus NT (APF group = 12,300 ppm F). Operator-applied, with cotton-paint, once a year, 2 ml applied for 4 minutes.
Outcomes	1.5yDMFS increment - (CA)(E). Reported at 1.5 years follow up. O-DMFS. BL-DMFS. MD-DMFS. DMFT(CA)(E). Drop out (no data by group).
Notes	Participants randomized (N = 401); numbers (natural drop out) by group NR. Baseline characteristics (dental age, DMFS, DMFT, gender) 'balanced'. Clinical (VT) caries assessment by four examiners; diagnostic threshold = CA; state of tooth eruption included = E; reversal rate = 2.2% and 0.7% of observed DMFS increment in FG and control groups respectively. **Prior prophylaxis with non-fluoride paste carried out in FG group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Blinkhorn 1983

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 10% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers: 57 left school, 12 withdrawn by parents, 6 absent at final examination; no differential group losses.
Participants	374 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 8.2 DMFS. Exposure to other fluoride: no. Year study began: 1972. Location: UK.
Interventions	FR+ptc versus PL+ptc** (NaF group = 230 ppm F). School use/supervised, daily, for half min.
Outcomes	3yNetDFS increment - (E+U)(CA)cl+(DR)xr. Reported at 3 years follow up. PF-DFS. MD-BL-DFS. MD-DFS. postMD-DFS. DMFT (E/U).

Blinkhorn 1983 *(Continued)*

	anterior DMFT. posterior DMFT. DFS (U).
Notes	Participants randomized (N = 414). Baseline characteristics (DMFS, DMFT, SAR) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by one examiner, diagnostic threshold = CA. Radiographic assessment (1 postBW) by one examiner; diagnostic threshold = DR. State of tooth eruption included = E/U. Intra-examiner reproducibility checks for incremental clinical and radiographic caries data in 10% sample (icc score 0.9). ** Prior toothbrushing with non-fluoride toothpaste in both groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Blinkhorn 1983a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 10% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers: 57 left school, 12 withdrawn by parents, 6 absent at final examination; no differential group losses.
Participants	368 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 8.2 DMFS. Background exposure to fluoride: none reported. Year study began: 1972. Location: UK.
Interventions	FT versus PL (SMFP group = 1000 ppm F). School use/supervised, daily, for 1 min, post-brushing water rinse done (appropriate toothpastes also provided for home use). Abrasive system: IMP (main abrasive).
Outcomes	3yNetDFS increment - (E+U)(CA)cl+(DR)xr. Reported at 3 years follow up. PF-DFS. MD-BL-DFS. MD-DFS. postMD-DFS. DFS (U). DMFT. anterior DMFT. posterior DMFT. DMFT (U).
Notes	Participants randomized (N = 410). Baseline characteristics (DMFS, DMFT, SAR) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by one examiner, diagnostic threshold = CA. Radiographic assessment (1 postBW) by one examiner; diagnostic threshold = DR. State of tooth eruption included = E/U. Intra-examiner reproducibility checks for incremental clinical and radiographic caries data in 10% sample (icc score 0.9).

Blinkhorn 1983a *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Borutta 1991

Methods	Random allocation; double-blind (A); placebo-controlled; 10% drop out after 2 years (study duration = 2 years). "Groups (arms in the trial) kept at equal sizes for statistical reasons".
Participants	360 children analysed at 2 years (available at final examination). Age range at start: 12-14 years. Surfaces affected at start: 5.25 DMFS. Exposure to other fluoride: no. Year study began: in/before 1988. Location: GDR.
Interventions	FV(3 groups)+ptc versus PL+ptc. Group 1 (Bifluorid 12®): NaF+CaF (27,100+29,200 ppm F) applied twice a year. Group 2 (Bifluorid 12®): NaF+CaF (27,100+29,200 ppm F) applied 4 times a year. Group 3 (Lawefluor®): NaF (22,600 ppm F) applied 4 times a year. Placebo group: applied 4 times a year.
Outcomes	2yDMFS increment - (CA)cl. Reported at 2 years follow up. O-DMFS. MD-DMFS. BL-DMFS. DMFT(CA).
Notes	Participants randomized (N = 400). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical caries assessment by two examiners; diagnostic threshold = CA (FOTI assessment - loss of translucency on transillumination - for approximal surfaces.) State of tooth eruption included NR; inter-examiner reproducibility checked for DMFS. Results presented separately by examiner (one chosen by coin flip).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Brandt 1972

Methods	Random allocation; double-blind (A); placebo-controlled; 22% drop out after 2 years (study duration = 2 years). Reasons for attrition described with numbers by group: change of residence (18, 12), absent at final examination (5, 7); plus exclusions based on compliance, presence in all examinations, and for statistical analysis; no differential group losses.
Participants	246 children analysed at 2 years (after exclusions based on compliance, present for all examinations).

Brandt 1972 *(Continued)*

	Average age at start: 11.5 years. Surfaces affected at start: 7.9 DMFS (for sample present at all examinations). Exposure to other fluoride: none assumed. Year study began: 1969. Location: UK.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, twice a week, 10ml applied for 1 min.
Outcomes	2yDFS scores* - (E+U). Reported at 2 years follow up. DMFS. DMFT. postMD-DMFS. CFS. CFT.
Notes	Participants randomized (N = 314). Baseline characteristic (DMFS) with some imbalance. Clinical caries assessment, diagnostic threshold NR. Radiographic assessment; diagnostic threshold = NR. State of tooth eruption included = E/U. Diagnostic errors NR. * Only retrospective matched pair analyses results reported (results for unadjusted analyses not available, data not suitable).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Bravo 1997

Methods	Cluster quasi-random allocation; single-blind (B); non-placebo-controlled; 13% drop out (for all study groups combined) after 2 years (study duration = 4 years). Natural losses (moved to other schools); any differential group losses not assessable.
Participants	214 children analysed at 2* years (present for all examinations). Age range at start: 6-8 years (average = 7). Surfaces affected at start: 0.61 DMFS. Exposure to other fluoride: data not obtained for dentifrice. Year study began: 1990. Location: Spain. Dental treatment level (F/DMF): 4.3%.
Interventions	FV versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied twice a year, with Q-tip, about 0.1 ml applied per tooth (1 stm) or 0.4 ml per child, left to dry for 15 seconds.
Outcomes	2y*Net1stmDMFS increment - (CA)(E+U). Reported at 2 years follow up. 1stmPF-DMFS. 1stmMD-BL-DMFS.

Bravo 1997 *(Continued)*

	1st molar occlusal CIR, molar failures over time (for molars healthy and fully erupted). Drop out (no data by group).
Notes	School classes randomized (15) and children taken as units for caries increment analyses, molars as units for caries incidence and survival analyses; number of children by group NR. Baseline characteristics (age, gender, SES, dft, 1stmF/DM, 1stmM; 1stmDMFS) described as 'balanced' (results NR). Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E+U; examiner reproducibility checks (Kappa coefficient) in 10% sample greater than 0.71 in all 1stmDFT measurements. *Only survival analysis (molar failures over time) reported at 4 years, when results were not available for DMFS increment.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Brudevold 1966

Methods	Stratified random allocation; double-blind ('A'); placebo-controlled; 25% drop out (for all study groups combined) after 2 years (study duration = 2 years). Reasons for attrition NR; any differential group losses not assessable.
Participants	1278 children analysed at 2 years (present for the entire trial period). Average age at start: 7-16 years (average = 12). Surfaces affected at start: 15.7 DFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1961. Location: USA.
Interventions	FT (3 groups)** versus 'PL' (both SnF2 groups = 1000 ppm F, APF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in one SnF2 toothpaste, IMP in the other SnF2 and in the APF toothpaste, control toothpaste abrasive NR.
Outcomes	2yDFS increment - cl+xr. Reported at 2 years follow up. DMFS. DMFT. DFT.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (dental age, DFS, DFT, DMFS, DMFT, gender) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA. Radiographic assessment (10 BW) by one examiner; diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR. **NaF-secondary Ca phosphate toothpaste group not considered (abrasive system known to be incompatible with NaF).

Risk of bias

Brudevold 1966 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Bryan 1970

Methods	Random allocation; single-blind (B); non-placebo-controlled; 28% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses.
Participants	208 children analysed at 2 years (available at final examination). Age range at start: 8-12 years (average = 9.5). Surfaces affected at start: 8.3 DMFS. Exposure to other fluoride: none assumed. Year study began: in/before 1966. Location: USA.
Interventions	FG+ptc versus NT+ptc (APF, concentration NR). Operator-applied, with tray, once a year, applied for 4 min.
Outcomes	2yNetDMFS increment - (CA). Reported at 1 and 2 years follow ups. DMFT(CA). Drop out.
Notes	Participants randomized (N = 287). Baseline characteristics (gender, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Buhe 1984

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 18% drop out after 3 years (study duration = 3 years). No differential group losses.
Participants	1286 children analysed at 3 years (available at final examination). Age range at start: 11-13 years (average = 12). Surfaces affected at start: 17.4 DMFS. Background exposure to fluoride: data not obtained for fluoridation status of site. Year study began: 1976. Location: FRG.

Buhe 1984 *(Continued)*

Interventions	FT (2 groups) versus PL (SMFP groups = 1000 ppm F and 1500 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP.
Outcomes	3yNetDFS increment - cl+xr. Reported at 3 years follow up. DMFS. DMFS (U). DMFT.
Notes	Participants randomized (N = 1562). Baseline characteristics (age, TAR, DMFS) 'balanced' (DFS baseline data NR). Clinical (VT) caries assessment; diagnostic threshold NR; state of tooth eruption included E/U. Radiographic caries assessment; diagnostic threshold NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Cahen 1982

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 20% drop out after 3 years (study duration = 3 years). Natural losses and exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	2008 children analysed at 3 years (present for all examinations). Age range at start: 6-8 years (average = 7). Surfaces affected at start: 1.4 DMFS (control group only). Background exposure to fluoride: data not obtained for fluoridation status of site. Year study began: 1977. Location: France.
Interventions	FT (2 groups) versus PL (SMFP group = 1500 ppm F, AmF group = 1500 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP in the SMFP and placebo toothpaste, Ca carbonate/Na and Al silicates in the AmF toothpaste.
Outcomes	3yDMFS increment - cl+xr. Reported at 3 years follow up. DMFT. df-rate.
Notes	Participants randomized (N = 2500); numbers by group NR. Baseline characteristics (age, gender) 'balanced'. Clinical (V) caries assessment by six examiners; diagnostic threshold = NR; state of tooth eruption included NR. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold NR; partial

Cahen 1982 *(Continued)*

	recording. Inter- and intra-examiner reproducibility of clinical and radiographic caries diagnosis assessed in 10% sample ("good reproducibility, NS difference between or within examiners").

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Clark 1985

Methods	Stratified random allocation; double-blind ('A'); placebo-controlled ('PL'); 14% drop out after 2.5 years (study duration = 4.5 years). Reasons for attrition NR; no differential group losses.
Participants	676 children analysed at 2.5* years (available at 2nd examination, present in at least 5 of 6 treatments). Age range at start: 6-7 years. Surfaces affected at start: 0.39 DMFS. Exposure to other fluoride: toothpaste + others. Year study began: 1981. Location: Canada. Dental treatment level (F/DMF): 83%.
Interventions	FV(2 groups)+ptc versus 'PL'+ptc. Group 1 (Fluor Protector®): Difluorsilane (7000 ppm F). Group 2 (Duraphat®): NaF (22,600 ppm F). Applied twice a year, about 0.5 ml applied per child.
Outcomes	2.5y*DMFS increment - (CA)(E+U). 1st&2ndmolars dfs (CA)(E). Reported at 1.5, 2.5 and 4.5 years follow ups**. O-DMFS. MD-DMFS. BL-DMFS.
Notes	Participants randomized (N = 787). Baseline characteristics (dental age, DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included = E+U/E; duplicate examination of 10% sample between examiners done (mean difference of 0.86 DMFS), "results of integrated analysis of treatment and examiner effects remained the same (significant)". Results presented separately by examiner and combined (integrated results chosen). * Results closest to 3 years chosen.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Cobb 1980

Methods	Random allocation; single-blind (B); non-placebo-controlled; 19% drop out after 2 years (study duration = 2 years).

Cobb 1980 *(Continued)*

	Reasons for attrition NR; differential group losses (but reported as NS difference).
Participants	193 children analysed at 2 years (available at final examination). Age range at start: 11-14 years. Surfaces affected at start: 5.7 DMFS (data from original sample only). Exposure to other fluoride: toothpaste assumed. Year study began: in/before 1977. Location: USA.
Interventions	FG+ptc versus NT+ptc (APF group = 12,300 ppm F). Operator-applied, with cotton-paint, twice a year, applied for 4 minutes.
Outcomes	2yDMFS increment - (CA). Reported at 0.5, 1, 1.5, and 2 years follow ups. Drop out.
Notes	Participants randomized (N = 237). Baseline characteristics (age, gender, ethnicity, regularity of dental care) described as 'balanced' (values NR); initial DMFS balanced. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Cons 1970

Methods	Random allocation; double-blind ('A'); placebo-controlled ('PL'); 26% drop out after 3 years (study duration = 3 years). Natural losses; exclusions based on presence in all follow-up examinations; differential group losses.
Participants	589 children analysed at 3 years (present for all examinations). Age range at start: 6-11 years (average = 8). Surfaces affected at start: 3 DMFS (first molar). Exposure to other fluoride: none assumed. Year study began: 1964. Location: USA.
Interventions	FG+ptc versus 'PL'+ptc (APF group = 12,300 ppm F). Operator-applied, with tray, once a year, applied for 4 minutes.
Outcomes	3yNet1stmDMFS increment - (E). Reported at 3 years follow up. NetDMFT(E).
Notes	Participants randomized (N = 795). Baseline characteristics (DMFS, DMFT) with some imbalance, but "adjustment made little difference in the magnitude of caries increment".

Cons 1970 *(Continued)*

	Clinical (VT) caries assessment by four examiners; diagnostic threshold NR; state of tooth eruption included = E; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Craig 1981

Methods	Stratified random allocation; single-blind (B); non-placebo-controlled; 11% drop out after 2 years (study duration = 2 years). Main reason for drop out: 12 children left the participating school; no differential losses between groups.
Participants	97 children analysed at 2 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 10.6 DFS. Exposure to other fluoride: toothpaste. Year study began: 1977. Location: New Zealand.
Interventions	FR+ptc versus NT+ptc** (NaF group = 900 ppm F). School use/supervised, fortnightly, 10 ml applied for 2 min.
Outcomes	2yDFS increment - (CA). Reported at 1 and 2 years follow ups. O-DFS. MD-DFS. BL-DFS. Drop out.
Notes	Participants randomized (N = 109). Baseline characteristics (DFS, dental age) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. State of tooth eruption included NR. Reproducibility checks for incremental clinical caries data in 15% sample at each examination (reversal rate less than 4% for both examiners). ** Prior professional prophylaxes with non-fluoride toothpaste in both groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

de Liefde 1989

Methods	Random allocation; double-blind (A); placebo-controlled; drop-out rate NR nor obtainable (study duration = 3 years).

de Liefde 1989 *(Continued)*

	Reasons for attrition NR; any differential group losses not assessable.
Participants	262 children analysed after 3 years (available at final examination). Age range at start: 7-10 years (average = 8). Surfaces affected at start: NR. Exposure to other fluoride: toothpaste assumed. Year study began: 1984. Location: New Zealand.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, fortnightly.
Outcomes	2yDMFS final scores* - (CA). Reported at 3 years follow up. DMFT.
Notes	Participants randomized (numbers NR). Baseline characteristics/values NR. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; diagnostic errors NR. * Only results of combined non-randomized and randomized groups reported (separate results for placebo group not available, data not suitable).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

DePaola 1977

Methods	Random allocation; double-blind (A); placebo-controlled; 23% drop out after 2 years (study duration = 2 years). Natural losses; any differential group losses not assessable.
Participants	475 children analysed at 2 years (available at final examination). Age range at start: 10-12 years (average = 11.7). Surfaces affected at start: 6.1 DFS. Exposure to other fluoride: none assumed***. Year study began: in/before 1974. Location: USA.
Interventions	FR (2 groups) versus PL (NH4F group = 1000 ppm F, NaF group = 1000 ppm F). School use/supervised, daily, 5 ml applied for 1 min.
Outcomes	2yNetDFS increment - (CA)cl+xr. Reported at 2 years follow up. DFS (U). Side effects (incomplete data).
Notes	Participants randomized (N = 614); numbers by group NR.

DePaola 1977 *(Continued)*

	Baseline characteristics (DFS) 'balanced'. Clinical (VT) caries assessment, diagnostic threshold = CA; state of tooth eruption included NR. Radiographic assessment (4 postBW); diagnostic threshold = ER; diagnostic errors NR. *** Although history of prior exposure to systemic F was reported by nearly half of panel.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

DePaola 1980

Methods	Random allocation; double-blind (A); placebo-controlled; drop-out rate NR nor obtainable (study duration = 2 years + 1 year post-study period). Exclusions based on compliance and presence in all follow-up examinations; any differential group losses not assessable.
Participants	270 children analysed at 1* year (after exclusions, present for entire trial period). Age range at start: 12-14 years (average = 13). Surfaces affected at start: NR. Exposure to other fluoride: toothpaste assumed. Year study began: in/before 1977. Location: USA.
Interventions	FG versus PL (APF group = 12,300 ppm F). Self applied under supervision, with tray, 10 consecutive applications (days) in 1st year, applied for 5 min.
Outcomes	1y*NetDFS increment - (CA)cl+xr. Reported at 1 and 2 years follow ups (and 1 year post-treatment).
Notes	Participants randomized (numbers NR). Baseline characteristics (age, dental age, DFS) described as 'balanced' (values NR). Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners (diagnostic threshold NR); diagnostic errors NR. *Intervention applied during 1st year of study only (final 2 years results not considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

DePaola 1980a

Methods	Random allocation; double-blind (A); placebo-controlled; drop-out rate NR nor obtainable (study duration = 2 years + 1 year post-study period). Exclusions based on compliance and presence in all follow-up examinations; any differential group losses not assessable.
Participants	271 children analysed at 2 years (after exclusions, present for entire trial period).

DePaola 1980a *(Continued)*

	Age range at start: 12-14 years (average = 13). Surfaces affected at start: NR. Exposure to other fluoride: toothpaste assumed. Year study began: in/before 1977. Location: USA.
Interventions	FR versus PL (NaF group = 230 ppm F). School use/supervised, daily, 10 ml applied for 1 min.
Outcomes	2yNetDFS increment - (CA)cl+xr. Reported at 1 and 2 years follow ups (and 1 year post-treatment).
Notes	Participants randomized (numbers NR). Baseline characteristics (age, dental age, DFS) described as 'balanced' (values NR). Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold NR; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Di Maggio 1980

Methods	Random allocation; double-blind (A); placebo-controlled; 16% drop out (for both study groups combined) after 2 years (study duration = 2 years). Main reason for attrition described: left institution; any differential group losses not assessable.
Participants	42 children analysed at 2 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 11.7 DMFS. Background exposure to fluoride: data not obtained for fluoridation status of site. Year study began: in/before 1977. Location: Italy.
Interventions	FT versus PL (SMFP-NaF group = 2500 ppm F). Institution use/supervised, three times a day. Abrasive system: not clearly specified.
Outcomes	2yDMFS increment - cl. Reported at 1 and 2 years follow ups. DMFT.
Notes	Participants randomized (N = 50). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical caries assessment by two examiners; diagnostic threshold NR; state of tooth eruption included NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement

Di Maggio 1980 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Dolles 1980

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 22% natural drop out after 2 years (study duration = 2 years). Reasons for attrition described with numbers by group: unacceptable staining (3,4), unacceptable taste (2,0), change of residence (0,2), other reasons/lack of co-operation (1,1); exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	47 children analysed at 2 years (present for all examinations). Average age at start: 13 years. Surfaces affected at start: NR. Background exposure to fluoride: none. Year study began: 1974. Location: Norway.
Interventions	FT(Chlor) versus PL(Chlor) ** (NaF toothpaste = 500 ppm F). Home use/unsupervised, daily frequency assumed (instructed to brush for 2 min twice a day). Abrasive system: plastic particles.
Outcomes	2yDS increment - (CA)cl+(ER)xr. Reported at 2 years follow up. Proportion of children with new carious surface.
Notes	Participants randomized (N = 60). Baseline characteristics NR. Clinical (VT) caries assessment, diagnostic threshold = CA; state of tooth eruption included NR. Radiographic assessment (postBW), diagnostic threshold = ER. Diagnostic errors NR. **Chlorhexidine present in both, the fluoride and the non-fluoride toothpaste groups (other outcomes measured, such as tooth staining, not considered relevant for the comparison of interest).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Driscoll 1982

Methods	Random allocation; double-blind (A); placebo-controlled; 46% drop out after 2.5 years (study duration = 2.5 years). Main reasons for high drop-out rate: children moving out or withdrawn by parents; no differential group losses.
Participants	524 children analysed at 2.5 years (present for entire trial period). Average age at start: 12.8 years. Surfaces affected at start: 4.8 DMFS. Exposure to other fluoride: water (and toothpaste assumed). Year study began: 1977. Location: USA.

Driscoll 1982 *(Continued)*

Interventions	FR (2 groups) versus PL. NaF Group 1: 230 ppm F, daily. NaF Group 2: 900 ppm F, weekly. School use/supervised, 10 ml applied for 1 min.
Outcomes	2.5yNetDMFS increment. Reported at 1.5 and 2.5 years follow ups. O-DMFS. MD-DMFS. BL-DMFS.
Notes	Participants randomized (N = 966). Baseline characteristics (DMFS) 'balanced'. Clinical caries assessment (VT) by two examiners; diagnostic threshold NR. State of tooth eruption included NR; differences between examiners assessment NS (but reproducibility assessment NR). Results presented separately by examiner (combined results considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Duany 1981

Methods	Random allocation; double-blind (A); placebo-controlled; drop-out rate not obtainable (study duration = 3 years). Reasons for attrition not obtainable; any differential group losses not assessable.
Participants	936 children analysed at 3 years. Age range at start and exposure to other fluoride not obtainable. Surfaces affected at start: 7 DMFS. Year study began: in/before 1977. Location: Puerto Rico.
Interventions	FR (3 groups) versus PL (NaF groups = 100 ppm F, 225 ppm F, 450 ppm F).
Outcomes	3yDMFS increment.
Notes	Baseline characteristics (DMFS) 'balanced'. Other data NR not obtainable.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Englander 1967

Methods	Stratified random allocation; single-blind (B); non-placebo-controlled; 13% drop out after 1.8 years (study duration = 1.8 years + 1.9 years post-intervention period).

Englander 1967 *(Continued)*

	Natural losses and losses due to other reasons (NR); exclusions based on presence in all follow-up examinations; differential group losses.
Participants	500 children analysed at 1.8 years (present for all examinations). Age range at start: 11-14 years (average = 12). Surfaces affected at start: 10.1 DMFS. Exposure to other fluoride: no. Year study began: 1964. Location: USA.
Interventions	FG (2 groups) versus NT (APF group = 5000 ppm F, NaF group = 5000 ppm F). Self applied under supervision, with tray, 140 times a year (average), 1-2 mg F (5-10 drops) applied for 6 minutes ***.
Outcomes	1.8yDMFS increment - (CA). Reported at 1.8 years follow up (and 1.9 years post-treatment). DMFT(CA). Drop out. Etching of enamel (incomplete data).
Notes	Participants randomized (N = 574). Baseline characteristics (age, gender, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; diagnostic errors NR. ***Gel application started 7 weeks after baseline examination.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Englander 1971

Methods	Stratified random allocation; single-blind (B); non-placebo-controlled; 38% drop out after 2.5 years (study duration = 2.5 years). Reason(s) for high drop-out rate NR; any differential group losses not assessable.
Participants	557 children analysed at 2.5 years (available at final examination). Age range at start: 11-15 years (average = 12.2). Surfaces affected at start: 3.7 DMFS. Exposure to other fluoride: water. Year study began: 1967. Location: USA.
Interventions	FG versus NT (APF group = 5000 ppm F). Self applied under supervision, with tray, 85 times a year (average), 1-2 mg applied for 3 min.
Outcomes	2.5yNetDMFS increment - (CA)(E). Reported at 2.5 years follow up.

Englander 1971 *(Continued)*

	Drop out (no data by group).
Notes	Participants randomized (N = 896); numbers by group NR. Baseline characteristics (age, gender, ethnicity, DMFS, SAR) 'balanced' . Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included = E; diagnostic errors NR. Results presented combined and separately by examiner; integrated results chosen.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Englander 1978

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 37% drop out after 1.5 years (study duration = 2.3 years). Main reason for high drop-out rate described (large number of families transferred from study location); no differential group losses.
Participants	145 children analysed at 1.5* years (available at 2nd examination). Age range at start: 2-6 years (average = 4.8). Surfaces affected at start: 3.7 defs (data from original sample only) - 43% caries-free. Exposure to other fluoride: water. Year study began: in/before 1974. Location: USA.
Interventions	FG versus PL (APF group = 5000 ppm F). Self applied under supervision, with tray, 76 times a year (average), 1 mg (5 drops) applied for 3 min.
Outcomes	1.5y*defs increment - (CA)(E). Reported at 0.5, 1.5 and 2.3 years follow ups. deft (CA)(E). Proportion of children remaining caries-free.
Notes	Participants randomized (N = 231). Baseline characteristics (age, deft, defs, TAR, SAR, % caries-free) 'balanced' . Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E; diagnostic errors NR. *Dramatic drop-out rate after 1.5 years of treatment (final 2.3 years results not considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Fanning 1968

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 22% natural drop out after 2 years (study duration = 2 years); no differential group losses (46% drop out based on analysis performed for randomized block design).
Participants	844 children analysed at 2 years (422 complete replicates of each group available). Age range at start: 12-14 years (average = 13). Surfaces affected at start: 17.7 DMFS (from sample randomized). Background exposure to fluoride: none. Year study began: 1964. Location: Australia.
Interventions	FT** versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP.
Outcomes	2yDMFS increment - (CA)cl+(ER)xr. Reported at 2 years follow up. Stain score.
Notes	Participants randomized (N = 1576). Baseline characteristics (DMFS, DMFT, SAR) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA. Radiographic assessment (5 BW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Intra- and inter-examiner reproducibility of clinical caries diagnosis (DFS) assessed annually by duplicate examination of 10% random sample ("error relatively small, NS difference between or within examiners"). **Na N-lauroyl sarcosinate/SMFP toothpaste group not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Finn 1975

Methods	Stratified random allocation; indication of blind caries assessment (C); placebo-controlled; 45% drop out after 2 years (study duration = 2 years). Main reason for high drop-out rate: 276 children transferred to non-participating schools; exclusions based on presence in both follow-up examinations; any differential group losses not assessable.
Participants	453 children analysed at 2 years (present in all examinations). Age range at start: 8-13 years (average = 11.7). Surfaces affected at start: 6 DMFS. Exposure to other fluoride: no. Year study began: in/before 1972. Location: USA.
Interventions	FR (2 groups) versus PL (APF group = 200 ppm F, NaF group = 100 ppm F).

Finn 1975 *(Continued)*

	School use/supervised, twice a day, 20 ml applied in 2 successive rinses of 30 seconds each (non-fluoride toothpaste and appropriate mouthrinse provided to all for home use).
Outcomes	2yNetDFS increment - cl+xr. Reported at 2 years follow up. DMFS. DMFT. Proportion of children with new DFS.
Notes	Participants randomized (N = 820); numbers by group NR. Baseline characteristics (DMFS, DMFT, age, gender) 'balanced' (DFS baseline data NR). Clinical (VT) caries assessment by one examiner, diagnostic threshold NR. Radiographic assessment (2-4 postBW+ 4 anterior) by one examiner; diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR. Reversals ranged beween 6% and 16% of observed DMFS increment in study groups for combined clin+xr findings, rates being higher in the test groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Fogels 1979

Methods	Random allocation; double-blind (A); placebo-controlled; 40% drop out after 3 years (study duration = 3 years). Reasons for attrition described: graduations, change of residence/school, parental requests, and ortho treatment; no differential group losses.
Participants	1339 children analysed at 3 years (available at final examination). Age range at start: 6-11 years (average = 9). Surfaces affected at start: 4.9 DFS. Background exposure to fluoride: none reported. Year study began: 1972. Location: USA.
Interventions	FT (2 groups) versus PL (both SnF2 groups = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: silica gel in one SnF2 and placebo toothpaste, Ca pyrophosphate in the other.
Outcomes	3yNetDFS increment - (CA)cl+(ER)xr. Reported at 3 years follow up. MD-DFS. DFS (U). DMFT. Oral soft tissues lesions (data NR). Proportion of children with tooth staining (data NR).
Notes	Participants randomized (N = 2218). Baseline characteristics (DFS) 'balanced'.

Fogels 1979 *(Continued)*

	Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. Radiographic assessment (postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included E/U. Results shown for each examiner and for the pooled data from both (F-ratios less than unit for examiner by treatment interactions); combined results considered.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Forsman 1974

Methods	Random allocation; double-blind (A); placebo-controlled; 18% drop out after 2 years (study duration = 2 years). Reasons for attrition described with respective total numbers: change of residence/school, ortho treatment, did not wish to continue; no differential group losses reported (but not assessable).
Participants	559 children analysed at 2 years (available at final examination). Age range at start: 10-11 years. Surfaces affected at start: 5.1 DMFS. Background exposure to fluoride: mouthrinse. Year study began: in/before 1970. Location: Sweden.
Interventions	FT (3 groups) versus PL (NaF group and one SMFP group = 250 ppm F, another SMFP group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: silica in all toothpastes.
Outcomes	2yDMFS increment - (NCA)cl. Reported at 2 years follow up. BLMD-DFS (clin). MD-DFS (x-ray). Proportion of children with new smooth surface caries.
Notes	Participants randomized (N = 681); numbers by group NR. Baseline characteristics (dental age, DMFS) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NCA. Radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Forsman 1974a

Methods	Random allocation; double-blind (A); placebo-controlled; 16% drop out after 2 years (study duration = 2 years). Reasons for attrition described with respective total numbers: change of residence/school, ortho treatment, did not wish to continue; no differential group losses reported (but not assessable).
Participants	394 children analysed at 2 years (available at final examination). Age range at start: 10-12 years. Surfaces affected at start: 12.9 DMFS. Background exposure to fluoride: mouthrinse. Year study began: in/before 1970. Location: Sweden.
Interventions	FT (2 groups) versus PL (one SMFP group = 250 ppm F, another SMFP group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca carbonate in all toothpastes.
Outcomes	2yDMFS increment - (NCA)cl. Reported at 2 years follow up. BLMD-DFS (clin). MD-DFS (x-ray). Proportion of children with new smooth surface caries.
Notes	Participants randomized (N = 469); numbers by group NR. Baseline characteristics (dental age, DMFS) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NCA. Radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Frostell 1991

Methods	Quasi-random allocation; single-blind (B); non-placebo-controlled; drop-out rate NR nor obtainable (study duration = 2 years). Exclusions based on compliance, any differential group losses not assessable.
Participants	206 children analysed at 2 years (after exclusions, available at final examination). Average age at start: 4 years. Surfaces affected at start: 4.79 dmfs. Exposure to other fluoride: toothpaste + others. Year study began: 1977. Location: Sweden.
Interventions	FV+ptc** versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied twice a year, with small brush, left to dry for 2 min.
Outcomes	2ydmfs increment - (E) (CA)cl+(DR)xr. Reported at 2 years follow up.

Frostell 1991 *(Continued)*

	dmft.
Notes	Participants randomized (numbers NR). Baseline characteristics (dmft/s) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included = E. Radiographic assessment (4postBW) by one examiner; diagnostic threshold = DR and ER. Diagnostic errors NR. **Prior prophylaxis with non-fluoride paste carried out in FV group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Gallagher 1974

Methods	Stratified quasi-random allocation; double-blind (A); placebo-controlled; 27% drop out after 2 years (study duration = 2 years). Natural losses; exclusions based on persistent swallowing of rinse; no differential group losses.
Participants	594 children analysed at 2 years (available at final examination). Age range at start: 11-13 years. Surfaces affected at start: 7.3 DMFS (from sample randomized). Exposure to other fluoride: none assumed. Year study began: 1970. Location: Canada. Dental treatment level (F/DMF): 42%.
Interventions	FR versus PL (NaF group = 1800 ppm F). School use/supervised, weekly, applied for 1 min.
Outcomes	2yDMFS increment - (E+U). Reported at 2 years follow up. DMFT. DT. DF.
Notes	Participants randomized (N = 809). Baseline characteristics (DMFS, DMFT, dental age) 'balanced' . Clinical (VT) caries assessment by one examiner, diagnostic threshold NR. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Gish 1966

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 34% drop out after 3 years (study duration = 5 years). Reasons for attrition NR; any differential group losses not assessable.
Participants	328 children analysed at 3 years (available at final examination). Age range at start: 6-14 years (average = 9). Surfaces affected at start: 3.9 DMFS. Background exposure to fluoride: water. Year study began: in/before 1963. Location: USA.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	3yDMFS increment - cl+xr. Reported at 1, 2, 3, 4 and 5 years follow ups. DMFT.
Notes	Participants randomized (N = 500); numbers by group NR. Baseline characteristics (age, DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = NR. Radiographic assessment (5-7 BW); diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Gisselsson 1999

Methods	Stratified quasi-random allocation; double-blind (A), placebo-controlled; 12% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers (29 moved away, 8 refused participation); differential group losses.
Participants	280 children analysed at 3 years (available at final examination). Average age at start: 13 years. Surfaces affected at start: 0.24 DFS*** - 39% caries-free. Exposure to other fluoride: toothpaste. Year study began: 1993. Location: Sweden. Dental treatment level (F/DF): 45%
Interventions	FG (2 groups) versus PL (NaF group = 4500 ppm F, SnF2 group = 2425 ppm F). Operator-applied, with floss+syringe, 4 times a year, 1 ml applied for 10 min.
Outcomes	3yMD-DFS increment - (CA)cl+ (DR)xr. Reported at 3 years follow up. DS.

Gisselsson 1999 *(Continued)*

	FS. Proportion of children remaining caries-free, proportion with one or more new DFS (at NCA/ER level).
Notes	Participants randomized (N = 317). Baseline characteristics (MD-DFS, DS, FS, % caries-free) with some imbalance (reported as NS difference). Clinical caries assessment by 11 examiners; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (postBW) by one examiner; diagnostic threshold = DR and ER. Diagnostic errors NR. *** Gel application started 12 weeks before (2nd) baseline examination.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Glass 1978

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 35% drop out after 3 years (study duration = 3 years). Natural losses, increased during 3rd year because an entire grade graduated; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	346 children analysed at 3 years (present for all examinations). Age range at start: 6-11 years (average = 9). Surfaces affected at start: 4.1 DFS. Background exposure to fluoride: none reported. Year study began: in/before 1974. Location: USA.
Interventions	FT versus PL (SMFP group = 1000 ppm F). School use/supervised, 1g applied daily (appropriate toothpastes and toothbrushes also provided for home use). Abrasive system: Ca carbonate.
Outcomes	3yNetDFS increment - (CA)cl+(ER)xr. Reported at 1, 2 and 3 years follow ups. MD-DFS. O-BL-DFS. DFT. CIR. O-BL-CIR. MD-CIR.
Notes	Participants randomized (N = 533); numbers by group NR. Baseline characteristics (age, DFS, DFT, SAR, TAR) 'balanced'. Clinical (VT) caries assessment (FOTI used) by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Reversals were small in both groups (about 6% of DFS increments) and equally common (NS different).

Glass 1978 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Glass 1983

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 16% drop out after 2.5 years (study duration = 2.5 years). Natural losses; no losses due to any adverse effects; any differential group losses not assessable.
Participants	853 children analysed at 2.5 years (available at final examination). Age range at start: 7-11 years (average = 9). Surfaces affected at start: 2.1 DFS. Background exposure to fluoride: water. Year study began: 1976. Location: USA.
Interventions	FT (2 groups) versus PL (both SMFP groups = 1000 ppm F). School use/supervised, daily (appropriate toothpastes and toothbrushes also provided for home use). Abrasive system: IMP (main abrasive) in one SMFP and placebo toothpaste, Ca carbonate in the other SMFP toothpaste.
Outcomes	2.5yNetDFS increment - (CA)cl+(ER)xr. Reported at 2.5 years follow up. DFT. CIR.
Notes	Participants randomized (N = 1017); numbers by group NR. Baseline characteristics (age, DFS, DFT, SAR, TAR) 'balanced' (for DFT/DFS). Clinical (VT) caries assessment by two examiners (independently); diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by two examiners (independently); diagnostic threshold = ER. Results of one examiner chosen (findings consistent throughout).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hagan 1985

Methods	Random allocation; double-blind (A); placebo-controlled; 26% drop out after 2 years (study duration = 2 years). Natural losses; any differential group losses described as "NS differences, ranging from 24% to 26%".
Participants	316 children analysed at 2 years (available at final examination). Age range at start: 11-15 years (average = 12.5). Surfaces affected at start: 4.6 DMFS.

Hagan 1985 *(Continued)*

	Exposure to other fluoride: toothpaste. Year study began: 1981. Location: USA.
Interventions	FG (2 groups)+ptc versus PL+ptc (APF group 1 = 12,300 ppm F, APF group 2 = 6000 ppm F). Operator-applied, with tray, twice a year, 2.5 ml applied.
Outcomes	2yDMFS increment - (E). Reported at 2 years follow up. PF-DMFS. MD-BL-DMFS. Nausea/vomiting within 15 min of gel application.
Notes	Participants randomized (N = 428); numbers by group NR. Baseline characteristics (age, gender, ethnicity, DMFS, regularity of dental care, previous exposure to other fluoride sources, etc.) described as 'balanced' ("NS higher DMFS value for one group"). Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included = E; reversal rate less than 0.002% of observed caries increment in all groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hanachowicz 1984

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 28% drop out after 3 years (study duration = 3 years). Natural losses and exclusions based on compliance; no differential group losses.
Participants	945 children analysed at 3 years (available at final examination and co-operative). Age range at start: 10-12 years. Surfaces affected at start: 5.4 DMFS. Background exposure to fluoride: none reported. Year study began: 1979. Location: France.
Interventions	FT versus PL (SMFP group = 1500 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yNetDMFS increment - (E)(CA)cl+xr. Reported at 3 years follow up. DMFT. DMFS (U). O-DMFS. MD-DMFS. BL-DMFS. premolarDMFT. premolarDMFS.

Hanachowicz 1984 *(Continued)*

	Proportion of children with new caries.
Notes	Participants randomized (N = 1318). Baseline characteristics (DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) by one examiner; diagnostic threshold NR. State of tooth eruption included = E/U. Consistency of clinical and x-ray diagnosis assessed by duplicate examinations of 6% sample (inter-examiner reproducibility ratios 0.24 for clinical and 0.13 for x-ray; intra-examiner reproducibility 0.27 for clinical and 0.14 for x-ray).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hargreaves 1973

Methods	Quasi-random allocation; double-blind (A); placebo-controlled; 4% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	303 children analysed at 3 years (present for all examinations). Age at start: 6 years. Surfaces affected at start: 13.9 dfs (data for deciduous dentition only). Background exposure to fluoride: none reported. Year study began: 1968. Location: UK.
Interventions	FT versus PL (SMFP group = 2400 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	1-3yNetDFS increment - (E+U)(CA)cl+(ER)xr. Reported at 3 years follow up. DFT. DMFS. DMFT. ECSI.
Notes	Participants randomized (N = 316); numbers by group NR. Baseline characteristics (age, tar, dfs, dmfs, dft, dmft, ecsi) 'balanced' (no DFS data at start). Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Hargreaves 1973a

Methods	Quasi-random allocation; double-blind (A); placebo-controlled; 5% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	284 children analysed at 3 years (present for all examinations). Age at start: 9 years. Surfaces affected at start: 6.3 DFS. Background exposure to fluoride: none reported. Year study began: 1968. Location: UK.
Interventions	FT versus PL (SMFP group = 2400 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yNetDFS increment - (E+U)(CA)cl+(ER)xr. Reported at 3 years follow up. DFT. DMFS. DMFT. ECSI.
Notes	Participants randomized (N = 298); numbers by group NR. Baseline characteristics (age, TAR, DFS, DMFS, DFT, DMFT, ECSI) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Hargreaves 1973b

Methods	Quasi-random allocation; double-blind (A); placebo-controlled; 6% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	297 children analysed at 3 years (present for all examinations). Age at start: 12 years. Surfaces affected at start: 9.2 DFS. Background exposure to fluoride: none reported. Year study began: 1968. Location: UK.
Interventions	FT versus PL (SMFP group = 2400 ppm F).

Hargreaves 1973b *(Continued)*

	Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yNetDFS increment - (E+U)(CA)cl+(ER)xr. Reported at 3 years follow up. DFT. DMFS. DMFT. ECSI.
Notes	Participants randomized (N = 317); numbers by group NR. Baseline characteristics (age, TAR, DFS, DMFS, DFT, DMFT, ECSI) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Heidmann 1992

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 17% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; any differential group losses not assessable.
Participants	1083 children analysed at 3 years. Age range at start: 6-12 years (average = 9). Surfaces affected at start: 1.5 DMFS. Exposure to other fluoride: toothpaste. Year study began: 1983. Location: Denmark. Dental treatment level (F/DMF): 98%.
Interventions	FR versus PL** (NaF group = 900 ppm F). School use/supervised, fortnightly.
Outcomes	3yCrude postDMFS increment - (CA)(E+U)cl. DMFS (U). O-DMFS. MD-DMFS. BL-DMFS. CIR - xr. Proportion of children with new post-MDDMFS.
Notes	Participants randomized (N = 1306); numbers by group NR. Baseline characteristics (DMFS, SAR) 'balanced'. Clinical (VT) caries assessment by dentists at public dental service, diagnostic threshold = CA. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included (E/U). Reproducibility of diagnosis assessed by duplicate radiographic examination of 10% random sample (kappa value 0.72).

Heidmann 1992 *(Continued)*

** Both groups had been using FR before study started.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Heifetz 1970

Methods	Stratified quasi-random allocation; double-blind ('A'); placebo-controlled ('PL'); 41% drop out after 2 years (study duration = 2 years). Reason(s) for high drop-out rate NR; exclusions based on compliance and presence in all follow-up examinations; no differential group losses.
Participants	309 children analysed at 2 years (after exclusions, present for all examinations). Age range at start: 12-13 years. Surfaces affected at start: 8.2 DMFS. Exposure to other fluoride: none assumed. Year study began: 1966. Location: USA.
Interventions	FG+ptc versus 'PL'+ptc (APF group = 12,300 ppm F). Self applied under supervision, with toothbrush, 5 times a year, 4 ml applied for 5 min.
Outcomes	2yNetDMFS increment - (E+U). Reported at 1 and 2 years follow ups. NetDMFT(E+U).
Notes	Participants randomized (N = 525). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold NR; state of tooth eruption included = E+U; reversal rate approximately 4% of observed DMFS increment for all groups combined.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Heifetz 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 56% drop out after 2 years (study duration = 2 years). Reasons for high drop-out rate described: high transiency of the population, dissatisfaction with taste, exclusions based on compliance and presence in both follow-up examinations; any differential group losses not assessable.
Participants	413 children analysed at 2 years (after exclusions, present in all examinations). Age range at start: 10-12 years. Surfaces affected at start: 10.8 DMFS. Exposure to other fluoride: none assumed.

Heifetz 1973 *(Continued)*

	Year study began: 1969. Location: USA.
Interventions	FR (2 groups) versus PL (2 groups) (APF group = 3000 ppm F, NaF group = 3000 ppm F). School use/supervised, weekly, 8 ml applied twice (16 ml) for 1 min.
Outcomes	2yNetDMFS increment - (E+U) cl+(ER)xr. Reported at 1 and 2 years follow ups.
Notes	Participants randomized (N = 947); numbers by group NR. Baseline characteristics (DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. Radiographic assessment (5 postBW) by two examiners; diagnostic threshold = ER. State of tooth eruption included (E/U). Diagnostic errors NR (but examiners calibrated regularly). Reversals ranged beween 5% and 10% of observed DMFS increment in study groups for combined clin+xr findings, rates being higher in the test groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Heifetz 1982

Methods	Random allocation; double-blind (A); placebo-controlled; 34% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; any differential group losses not assessable.
Participants	598 children analysed at 3 years (present for entire trial period). Age range at start: 10-12 years. Surfaces affected at start: 6.2 DMFS. Exposure to other fluoride: toothpaste. Year study began: 1976. Location: USA.
Interventions	FR (2 groups) versus PL NaF Group 1: 230 ppm F, daily. NaF Group 2: 900 ppm F, weekly. School use/supervised, 10 ml applied for 1 min.
Outcomes	3yNetDMFS increment - (CA)(E)clin. Reported at 1, 2 and 3 years follow ups. O-DMFS. MD-DMFS. BL-DMFS.
Notes	Participants randomized (N = 912); numbers by group NR. Baseline characteristics (DMFS) 'balanced' . Clinical caries assessment (VT) by two examiners; diagnostic threshold = CA (FOTI assessment - loss of translucency on transillumination - for approximal surfaces.) State of tooth eruption included = E; differences between examiners assessment NS (but reproducibility assessment NR). Results presented separately by examiner (combined results considered).

Heifetz 1982 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Held 1968

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 65% drop out after 3 years (study duration = 3 years). Reasons for high drop out due to age range at which many leave the institutions; no differential group losses.
Participants	63 children analysed at 3 years (available at final examination). Age range at start: 15-16 years. Surfaces affected at start: 14.3 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1962. Location: France.
Interventions	FT versus PL (NaF-SnF2 group = 1000 ppm F). Institution use/supervised, twice a day. Abrasive system: not clearly specified (silica used).
Outcomes	3yDMFS increment - (E) cl. Reported at 3 years follow up. DMFT. Annual CAR.
Notes	Participants randomized (N = 178). Baseline characteristics (DMFS, DMFT) not balanced. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included = E. Intra-examiner reproducibility checks done.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Held 1968a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 64% drop out after 3 years (study duration = 3 years). Reasons for high drop out due to age range at which many leave the institutions; no differential group losses.
Participants	36 children analysed at 3 years (available at final examination). Age range at start: 15-16 years. Surfaces affected at start: 9.6 DMFS. Background exposure to fluoride: data not available for fluoridation status of site.

Held 1968a *(Continued)*

	Year study began: 1961. Location: France.
Interventions	FT versus PL (NaF-SnF2 group = 1000 ppm F). Institution use/supervised, twice a day. Abrasive system: not clearly specified (silica used).
Outcomes	3yDMFS increment - (E) cl. Reported at 3 years follow up. DMFT. Annual CAR.
Notes	Participants randomized (N = 101). Baseline characteristics (DMFS, DMFT) not balanced. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included = E. Intra-examiner reproducibility checks done.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Held 1968b

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 62% drop out after 2 years (study duration = 3 years). Reasons for high drop out due to age range at which many leave the institutions; no differential group losses.
Participants	32 children analysed at 2* years (available at final examination). Average age at start: 15 years. Surfaces affected at start: 10.2 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1961. Location: France.
Interventions	FT versus PL (NaF group = 500 ppm F). Institution use/supervised, twice a day. Abrasive system: not clearly specified (silica used).
Outcomes	2y*DMFS increment - (E) cl. Reported at 2 and 3 years follow ups. DMFT. Annual CAR.
Notes	Participants randomized (N = 85). Baseline characteristics (DMFS, DMFT) not balanced. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included = E. Intra-examiner reproducibility checks done. *Results for 3 years follow up not considered due to very high drop-out rate.

Held 1968b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Hodge 1980

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 18% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers: 158 left school, 14 withdrawn by own choice, 8 lack of co-operation; any differential group losses not assessable.
Participants	799 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 7.3 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1976. Location: UK.
Interventions	FT (3 groups) versus PL (SMFP group = 1000 ppm F, both SMFP-NaF groups = 1450 ppm F). School use/supervised, daily, for 1 min (appropriate toothpastes also provided for home use). Abrasive system: alumina (in placebo toothpaste, SMFP and in one SMFP-NaF toothpaste), dicalcium phosphate (in another SMFP-NaF toothpaste).
Outcomes	3yNetDFS increment - (E) (CA)cl+(DR)xr. Reported at 3 years follow up. DMFT.
Notes	Participants randomized (N = 979); numbers by group NR. Baseline characteristics (DMFS, DMFT, SAR) 'balanced' (DFS baseline data NR). Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U; radiographic assessment (2 postBW) by one examiner; diagnostic threshold = DR. Reproducibility checks done in 10% sample clinically and radiographically (icc of incremental data between 0.92 and 0.97).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Holm 1979

Methods	Quasi-random allocation; single-blind (B); non-placebo-controlled; 10% drop out after 2 years (study duration = 2 years). Natural losses; no differential group losses.
Participants	225 children analysed at 2 years (available at final examination). Average age at start: 3 years. Surfaces affected at start: 0.88 defs (but no teeth filled or extracted) - 70% caries-free.

Holm 1979 *(Continued)*

	Exposure to other fluoride: toothpaste + others. Year study began: in/before 1976. Location: Sweden.
Interventions	FV versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied twice a year, with small brush, and left to dry.
Outcomes	2ydefs increment - (E) (CA)cl+(DR)xr Reported at 1 and 2 years follow ups. O-defs. MD-defs. BL-defs. ds. Proportion of children with one or more new defs (at CA level). Drop out.
Notes	Participants randomized (N = 250). Baseline characteristics (defs) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA and NCA; state of tooth eruption included = E. Radiographic assessment (if required) by one examiner; diagnostic threshold = DR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Holm 1984

Methods	Random allocation; indication of blind caries assessment (C); non-placebo-controlled; 16% drop out after 2 years (study duration = 2 years - of observation period for the individual 1st molars). Some of the reasons for attrition with sample sizes in each arm described (2 moved away, 2 refused participation) but reasons for 14 withdrawals NR; any differential group losses not assessable.
Participants	95 children analysed at 2 years (available at final examination). Average age at start: 6 years. Surfaces affected at start: 9.66 dmfs, 8% caries-free (zero DFS for erupting 1st molars). Exposure to other fluoride: water, rinse. Year study began: 1977. Location: Sweden.
Interventions	FV+ptc** versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied twice a year, with a pencil (probe used to press the varnish into fissure).
Outcomes	2y1stmDFS (fissures only) increment - (CA)(U). Reported at 2 years follow up. 1stmDFT increment.

Holm 1984 *(Continued)*

	Proportion of children with one or more new 1stmDFS (at CA level), proportion of carious 1st molars.
Notes	Participants randomized (N = 113); numbers by group NR. Baseline characteristics (dmfs) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = U; intra-examiner reproducibility checks for 1st molars (icc 0.98). **Prior prophylaxis with non-fluoride paste carried out in FV group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Homan 1969

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 19% drop out after 1.7 years (study duration = 1.7 years). Reasons for attrition not described; any differential group losses not assessable.
Participants	1874 children analysed at 1.7 years. Age range at start: 7-13 years. Surfaces affected at start: data not available nor obtainable. Background exposure to fluoride: none. Year study began: 1965. Location: Australia.
Interventions	FT (3 groups) versus PL (SnF2 and APF toothpaste concentrations NR nor obtainable). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in one SnF2 toothpaste, calcium-free abrasive in the other SnF2 toothpaste and in the APF toothpaste; abrasive in placebo toothpaste NR.
Outcomes	Caries increment data NR (not obtainable). Percentage DFS reductions by gender and age groups reported at 1.7 years follow up.
Notes	Participants randomized (N = 2317); numbers by group NR. Baseline characteristics NR. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included = E; radiographic assessment; diagnostic threshold = DR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Horowitz 1966

Methods	Quasi-random allocation; double-blind (A); placebo-controlled; 40% drop-out rate after 3 years (study duration = 3 years). Natural losses; no differential group losses.

Horowitz 1966 *(Continued)*

Participants	638 children analysed at 3 years (available at final examination). Age range at start: 6-10 years. Surfaces affected at start: 2.08 DMFS. Background exposure to fluoride: none reported. Year study began: 1961. Location: USA.
Interventions	FT versus PL ** (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	3yNetDMFS increment - (E+U) (CA)cl. Reported at 1, 2, and 3 years follow ups. DMFT.
Notes	Participants randomized (N = 1059). Baseline characteristics (DMFS, DMFT, TAR) 'balanced'. Clinical (VT) caries assessment by three examiners; diagnostic threshold = CA; state of tooth eruption included = E/U. Reversals were small in both groups (about 3% of DMFS increments) and equally common (NS different). ** Only relevant comparison (others were not randomized/quasi-randomized).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Horowitz 1971

Methods	Stratified quasi-random allocation; single-blind (B); non-placebo-controlled; 36% drop out after 3 years (study duration = 3 years+2 years post-intervention period). Natural losses; exclusions based on use of orthodontic bands; no differential group losses.
Participants	352 children analysed at 3 years (available at final examination). Age range at start: 10-12 years. Surfaces affected at start: 8.9 DMFS. Exposure to other fluoride: none assumed. Year study began: 1965. Location: Hawaii.
Interventions	FG+ptc versus NT+ptc (APF group = 12,300 ppm F). Operator-applied, with tray, once a year, applied for 4 min.
Outcomes	3yNetDMFS increment - (E). Reported at 1, 2 and 3 years follow ups (and 2 years post-treatment). O-DMFS. BL-DMFS. MD-DMFS. NetDMFT(E).

Horowitz 1971 *(Continued)*

	Drop out.
Notes	Participants randomized (N = 552). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included = E; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Horowitz 1971a

Methods	Stratified random allocation; double-blind (A); placebo-controlled (PL); 48% drop out after 1.6 years (study duration = 1.6 years). Main reason for high drop-out rate described (transiency of schools' neighbourhoods); exclusions based on presence in follow-up examinations; no differential group losses.
Participants	256 children analysed at 1.6 years (present for entire trial period). Age range at start: 6-7 years. Surfaces affected at start: 0.9 DMFS (sample available at end). Exposure to other fluoride: none assumed. Year study began: 1967. Location: USA.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, weekly, 10 ml applied for 1 min.
Outcomes	1.6yNetDMFS increment - (E+U). Reported at 1 and 1.6 years follow ups. DMFT (E/U). DMFS (U).
Notes	Participants randomized (N = 493). Baseline characteristics (DMFS, DMFT) 'balanced' . Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Horowitz 1971b

Methods	Stratified random allocation; double-blind (A); placebo-controlled (PL); 45% drop out after 1.6 years (study duration = 1.6 years).

Horowitz 1971b *(Continued)*

	Main reason for high drop-out rate described (transiency of schools' neighbourhoods); exclusions based on presence in follow-up examinations; no differential group losses.
Participants	208 children analysed at 1.6 years (present for entire trial period). Age range at start: 10-11 years. Surfaces affected at start: 6.7 DMFS (sample available at end). Exposure to other fluoride: none assumed. Year study began: 1967. Location: USA.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, weekly, 10 ml applied for 1 min.
Outcomes	1.6yNetDMFS increment - (E+U). Reported at 1 and 1.6 years follow ups. DMFT (E/U). DMFS (U).
Notes	Participants randomized (N = 381). Baseline characteristics (DMFS, DMFT) 'balanced' . Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Horowitz 1974

Methods	Stratified quasi-random allocation; double-blind ('A'); placebo-controlled ('PL'); 55% drop out after 3 years (study duration = 3 years). Main reason for high drop-out rate described (children leaving public school at an early age); exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	233 children analysed at 3 years (present for all examinations). Age range at start: 11-14 years (average = 11.5). Surfaces affected at start: 11.4 DMFS. Exposure to other fluoride: no. Year study began: 1967. Location: Brazil.
Interventions	FG+ptc versus 'PL'+ptc (APF group = 12,300 ppm F). Self applied under supervision, with toothbrush, 5 times a year, 4 ml applied for 2 min.
Outcomes	3yNetDMFS increment - (CA). Reported at 1, 2 and 3 years follow ups.
Notes	Participants randomized (N = 512). Baseline characteristics (age, dental age, DMFS) described as 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included NR; diagnostc errors NR.

Horowitz 1974 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Howat 1978

Methods	Random allocation; double-blind (A); placebo-controlled; 12% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers (56 left school, 7 withdrawn by own choice, 2 lack of co-operation); any differential group losses not assessable.
Participants	495 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 7.4 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1974. Location: UK.
Interventions	FT versus PL (SMFP group = 1000 ppm F). School use/supervised, daily, for 1 min (appropriate toothpastes also provided for home use). Abrasive system: silica zerogel.
Outcomes	3yNetDMFS increment - (E) (CA)cl+(DR)xr. Reported at 3 years follow up. antDMFS. postDMFS. PF-DMFS. MD-DMFS. MD-BL-DMFS. DMFT.
Notes	Participants randomized (N = 560); numbers by group NR. Baseline characteristics (DMFS, DMFT, SAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U; radiographic assessment (2 postBW) by one examiner; diagnostic threshold = DR. Reproducibility checks done in 10% sample clinically and radiographically (icc of incremental data between 0.96 and 0.99).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ingraham 1970

Methods	Random allocation; single-blind (B); non-placebo-controlled; 23% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses.

Ingraham 1970 *(Continued)*

Participants	119 children analysed at 2 years (available at final examination). Age range at start: 6-11 years (average = 9). Surfaces affected at start: 2.4 DMFS. Exposure to other fluoride: none assumed. Year study began: 1965. Location: USA.
Interventions	FG (2 groups)+ptc versus NT+ptc (APF groups 1 and 2, concentration(s) NR). Operator-applied, with tray (beeswax vs foam rubber), once a year (data extracted from Bryan 1968), applied for 4 min.
Outcomes	2yNetDMFS increment - (CA). Reported at 1 and 2 years follow ups. NetDMFT(CA). Nausea/vomiting on application seen as a reaction according to type of tray used (no data). Drop out.
Notes	Participants randomized (N = 155). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Jackson 1967

Methods	Quasi-random allocation; double-blind (A); placebo-controlled; 12% drop-out rate after 3 years (study duration = 3 years). Natural losses; no differential group losses.
Participants	871 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 8.7 DMFS. Background exposure to fluoride: none reported. Year study began: 1962. Location: UK.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: dicalcium pyrophosphate.
Outcomes	3yDMFS increment - (E+U)(CA)cl. Reported at 3 years follow up. DMFT. Proportion of caries-free teeth/surfaces (by tooth type/ surface type) which developed caries.

Jackson 1967 *(Continued)*

	Proportion of children who complained of tooth staining.
Notes	Participants randomized (N = 986). Baseline characteristics (age, DMFS, DMFT, TAR, level of treatment, staining) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Consistency of clinical diagnosis maintained by re-examination of 10% sample and calibration checks made against reserve examiner.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

James 1967

Methods	Random allocation; double-blind (A); placebo-controlled; 23% drop-out rate after 3 years (study duration = 3 years). Reasons for drop out described with respective total numbers: moved away, unco-operative, not present on examination day, disliked toothpaste, staining of teeth, others; no differential group losses.
Participants	803 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 11 DFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1962. Location: UK.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: dicalcium pyrophosphate.
Outcomes	3yDFS increment - (E) (CA)cl+(ER)xr. Reported at 3 years follow up. DMFS. DFT. DMFT. postMD-DFS. Proportion of children with tooth staining.
Notes	Participants randomized (N = 1043). Baseline characteristics (age, DFS, DFT, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

James 1977

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 19% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	782 children analysed at 3 years (present for all examinations). Age range at start: 11-12 years. Surfaces affected at start: 11.2 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1970. Location: UK.
Interventions	FT versus PL (SMFP group = 2400 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yDMFS increment - (CA)cl+(ER)xr. Reported at 3 years follow up. postMD-DMFS. O-DMFS. BL-DMFS. O-BL-MDDMFS. antDMFS.
Notes	Participants randomized (N = 964); numbers by group NR. Baseline characteristics (age, gender, DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW); state of tooth eruption included NR. Inter- and intra-examiner reliability for clinical and radiographic diagnosis revealed by re-examination of 10% sample.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kinkel 1972

Methods	Random allocation; double-blind (A); placebo-controlled; 25% drop-out rate after 3 years (study duration = 7 years). Reasons for drop out not described; any differential group losses not assessable.
Participants	699 children analysed at 3 years. Average age at start: 10 years. Surfaces affected at start: 2.2 DMFS. Background exposure to fluoride: data not available. Year study began: in/before 1969. Location: Switzerland.
Interventions	FT versus PL (SMFP group F concentration NR).

Kinkel 1972 *(Continued)*

	Home use/unsupervised, daily frequency assumed. Abrasive system: NR.
Outcomes	3yDMFS increment - (CA)cl+(DR)xr. Reported at 1, 2, 3, 4, 5 and 7 years follow ups.
Notes	Participants randomized (N = 927); numbers by group NR. Baseline characteristics (DMFS) 'balanced'. Clinical (V) caries assessment; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW); diagnostic threshold = DR and ER.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kleber 1996

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 10% drop out after 1 year (study duration = 1 year). Main reasons for attrition: changes in residence, few exclusions for initiation of ortho treatment; no differential group losses.
Participants	156 children analysed at 1 year (available at final examination). Age range at start: 10-11 years (average = 10.7). Surfaces affected at start: 4.2 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1994. Location: USA.
Interventions	FT(+Alrins) versus PL(+Alrins) ** (NaF toothpaste = 1100 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: silica.
Outcomes	1yDMFS increment - (CA)cl+(ER)xr. Reported at 0.6 and 1 year follow ups. DMFT. Proportion of children remaining caries-free. Proportion of children with new DMFS. Oral soft tissues lesions.
Notes	Participants randomized (N = 174). Baseline characteristics (age, gender DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (postBW) by two examiners (independently); diagnostic threshold = ER. Reversals were small in both groups and equally common. Results of one examiner chosen (findings consistent throughout). **Rinsing with 500 ppm Al solutions performed daily at school in both relevant groups compared.

Kleber 1996 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Koch 1967

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 23% drop out after 3 years (study duration = 3 years + 2 years post-intervention period). Natural losses; no differential group losses.
Participants	167 children analysed at 3 years (present for entire trial period). Age range at start: 9-11 years (average = 10). Surfaces affected at start: 14.5 DFS. Exposure to other fluoride: no. Year study began: 1962. Location: Sweden.
Interventions	FR versus PL (NaF group = 2250 ppm F). School use/supervised, fortnightly, 10 ml applied for 2 min.
Outcomes	3yDFS increment - (CA)(E)cl. Reported at 1 and 3 years follow ups (and 2 years post-treatment). DFT. O-DFS. MD-DFS. BL-DFS. CAR (annual). Secondary caries. Oral tissue inflammation (incomplete data).
Notes	Participants randomized (N = 217). Baseline characteristics (DFS, DFT, SAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Intra-examiner reproducibility checks for DFS in 10% sample (icc over 0.98); reversals very small in both groups and equally common. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967a

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 27% drop out after 3 years (study duration = 3 years).

Koch 1967a *(Continued)*

	Natural losses; no differential group losses.
Participants	251 children analysed at 3 years (present for entire trial period). Age range at start: 6-8 years (average = 7). Surfaces affected at start: 5.6 DFS. Exposure to other fluoride: none assumed. Year study began: 1962. Location: Sweden.
Interventions	FR versus PL (NaF group = 2250 ppm F). School clinic/supervised, 3 times a year, 10 ml applied for 2 min.
Outcomes	3yDFS increment - (CA)(E)cl. Reported at 1 and 3 years follow ups. DFT. CAR (annual). Secondary caries.
Notes	Participants randomized (N = 344). Baseline characteristics (DFS, DFT, SAR, TAR) 'balanced'. Clinical (VT) caries assessment by four examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Diagnostic errors NR. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967b

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 36% drop out after 3 years (study duration = 3 years). Natural losses; no differential group losses.
Participants	251 children analysed at 3 years (present for entire trial period). Age range at start: 7-11 years. Surfaces affected at start: 7 DFS. Exposure to other fluoride: none assumed. Year study began: 1962. Location: Sweden.
Interventions	FR versus PL (NaF group = 230 ppm F). School clinic/supervised, 3 times a year, 10 ml applied for 2 min.
Outcomes	3yDFS increment - (CA)(E)cl. Reported at 2 years follow up. DFT. CAR (annual). Secondary caries.

Koch 1967b *(Continued)*

Notes	Participants randomized (N = 392). Baseline characteristics (DFS, DFT, SAR, TAR) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Diagnostic errors NR. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967c

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 19% drop out after 3 years (study duration = 3 years + 2 years post-intervention period). Natural losses; no differential group losses.
Participants	124 children analysed at 3 years (present for entire trial period). Age range at start: 8-10 years (average = 9). Surfaces affected at start: 11.3 DFS. Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT versus PL (NaF group = 1000 ppm F). School use/supervised, daily, 1 g applied for 2 min (non-fluoride toothpaste provided to all for home use). Abrasive system: methacrylate polymer (acrylic).
Outcomes	3yDFS increment - cl(CA)(E). Reported at 1 and 3 years follow ups (and 2 years post-treatment). DFT. O-DFS. MD-DFS. BL-DFS. Annual CAR. Secondary caries.
Notes	Participants randomized (N = 153). Baseline characteristics (DFS, DFT, SAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Intra-examiner reproducibility checks for DFS in 10% sample (icc over 0.98); reversals very small in both groups and equally common. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967d

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 18% drop out after 3 years (study duration = 3 years + 2 years post-intervention period). Natural losses; no differential group losses.
Participants	120 children analysed at 3 years (present for entire trial period). Age range at start: 11-12 years (average = 11). Surfaces affected at start: 19.7 DFS. Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT versus PL (NaF group = 1000 ppm F). School use/supervised, daily, 1 g applied for 2 min (non-fluoride toothpaste provided to all for home use). Abrasive system: methacrylate polymer (acrylic).
Outcomes	3yDFS increment - cl(CA)(E). Reported at 1 and 3 years follow ups (and 2 years post-treatment). DFT. O-DFS. MD-DFS. BL-DFS. Annual CAR. Secondary caries.
Notes	Participants randomized (N = 146). Baseline characteristics (DFS, DFT, SAR, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Intra-examiner reproducibility checks for DFS in 10% sample (icc over 0.98); reversals very small in both groups and equally common. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967e

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 19% drop out after 2 years (study duration = 2 years). Natural losses; any differential group losses not assessable.
Participants	70 children analysed at 2 years (present for entire trial period). Age range at start: 13-14 years. Surfaces affected at start: 30.1 DFS. Background exposure to fluoride: none reported. Year study began: 1963. Location: Sweden.

Koch 1967e *(Continued)*

Interventions	FT versus PL (NaF group = 1000 ppm F). Home use/unsupervised, twice a day instructed frequency but daily frequency assumed, for 2 min. Abrasive system: methacrylate polymer (acrylic).
Outcomes	2yDFS increment - cl(CA)(E). Reported at 2 years follow up. DFT. O-DFS. MD-DFS. BL-DFS. Annual CAR. Secondary caries.
Notes	Participants randomized (N = 86); numbers by group NR. Baseline characteristics (FS, FT, SAR, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Diagnostic errors NR. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1967f

Methods	Stratified random allocation***; double-blind (A); placebo-controlled; 19% drop out after 3 years (study duration = 3 years). Natural losses; no differential group losses.
Participants	255 children analysed at 3 years (present for entire trial period). Age range at start: 7-10 years. Surfaces affected at start: 7.9 DFS. Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT versus PL (NaF group = 1000 ppm F). School clinic/supervised, 3 times a year, 1 g applied for 2 min (no provision of any toothpaste reported for home use). Abrasive system: methacrylate polymer (acrylic).
Outcomes	3yDFS increment - cl(CA)(E). Reported at 1 and 3 years follow ups. DFT. Annual CAR. Secondary caries.
Notes	Participants randomized (N = 316). Baseline characteristics (FS, FT, SAR, TAR) 'balanced'.

Koch 1967f *(Continued)*

	Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; radiographic assessment (2 postBW) used as an aid but not reported; state of tooth eruption included = E. Diagnostic errors NR. *** Allocation concealment considered adequate by consensus.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Koch 1975

Methods	Random allocation; single-blind (B); non-placebo-controlled; 10% drop out after 1 year (study duration = 1 year). Reasons for attrition NR; any differential group losses not assessable.
Participants	121 children analysed at 1 year (available at final examination). Average age at start: 15 years. Surfaces affected at start: 29.2 DMFS. Exposure to other fluoride: rinse. Year study began: 1973. Location: Sweden.
Interventions	FV+ptc** versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied twice a year, with a cotton swab, about 0.7 ml applied per child (full mouth treatment), left to dry for 2 min.
Outcomes	1yDMFS increment - (E) (CA)cl+(DR)xr. Reported at 1 year follow up. O-DMFS. MD-DMFS. BL-DMFS.
Notes	Participants randomized (135); numbers by group NR. Baseline characteristics (DMFS) balanced. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA and NCA; state of tooth eruption included = E. Radiographic assessment (full mouth BW) by one examiner; diagnostic threshold = DR and ER. Intra-examiner reproducibility checked for DMFS cl+xr examinations in 20% sample (mean difference of 0.2 DS). **Prior prophylaxis with non-fluoride paste carried out in FV group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Laswell 1975

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 44% drop out after 2.4 years (study duration = 2.4 years).

Laswell 1975 *(Continued)*

	Main reason for high drop-out rate NR. Exclusions based on presence in follow-up examinations and on compliance; no differential group losses.
Participants	323 children analysed at 2.4 years (after exclusions, present for entire trial period). Average age at start: 8.6 years. Surfaces affected at start: 3 DMFS. Exposure to other fluoride: water. Year study began: in/before 1971. Location: USA.
Interventions	FR (2 groups) versus PL. APF Group 1: 200 ppm F, daily. APF Group 2: 1000 ppm F, weekly. School use/supervised (non-fluoride toothpaste provided to all for home use, but no rinse provided).
Outcomes	2.4yNetDFS increment - (E+U). Reported at 2.4 years follow up. DMFS (U).
Notes	Participants randomized (N = 575). Baseline characteristics (DMFS, age) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. State of tooth eruption included = E/U. Diagnostic errors NR (results from only one examiner reported).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Lind 1974

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 17% drop-out rate after 3 years (study duration = 3 years). Main reasons for drop out: moved away, sickness; exclusions based on presence in one interim examination; no differential group losses.
Participants	1167 children analysed at 3 years (available at intermediate and final examination). Age range at start: 7-12 years (average = 10). Surfaces affected at start: 5.1 DMFS. Background exposure to fluoride: water. Year study began: 1970. Location: Denmark.
Interventions	FT versus PL (SMFP group = 2400 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate.
Outcomes	3yNetDMFS increment - (E+U)(CA)cl+(DR)xr. Reported at 1, 2, and 3 years follow ups. DMFT. ECSI.

Lind 1974 *(Continued)*

Notes	Participants randomized (N = 1407). Baseline characteristics (age, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA/NCA; radiographic assessment (2 postBW) by two examiners; diagnostic threshold = ER/DR; state of tooth eruption included = E/U. Inter-examiner diagnostic error reported to have no effect on results; reversal rates small and similar in both groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Mainwaring 1978

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 18% drop out (for all study groups combined) after 3 years (study duration = 3 years). Natural losses; any differential group losses not assessable.
Participants	631 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 7.9 DFS. Exposure to other fluoride: no. Year study began: in/before 1974. Location: UK.
Interventions	FG+ptc versus PL+ptc (APF group = 12,300 ppm F). Operator-applied, with tray, twice a year, applied for 4 min.
Outcomes	3yNet/Crude DFS increment - (CA)(E)cl+(ER)xr. Reported at 3 years follow up. PF-DFS cl. postMD-DFS xr. DFS (U) cl+xr. CIR.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, SAR, DFS) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Intra-examiner reproducibility checks for DFS in 10% sample (icc for VT/XR over 0.95); error variance less than 5% of total variance; reversal rate less than 4% of observed DFS increment in all groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Mainwaring 1978a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 18% drop out (for all study groups combined) after 3 years (study duration = 3 years). Natural losses; any differential group losses not assessable.
Participants	1107 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 7.9 DFS. Background exposure to fluoride: none reported. Year study began: in/before 1974. Location: UK.
Interventions	FT (2 groups) versus PL (both SMFP groups = 1000 ppm F). Home use/unsupervised, for 1 min, daily frequency assumed. Abrasive system: Ca carbonate in all toothpastes.
Outcomes	3yNetDFS increment - (E)(CA)cl+(ER)xr. Reported at 3 years follow up. PF-DFS . postMD-DFS. CIR.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, SAR, DFS) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Intra-examiner reproducibility checks for DFS in 10% sample (icc for VT/XR over 0.95); error variance less than 5% of total variance; reversal rate less than 5% of observed DFS increment in all groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Mainwaring 1983

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 19% drop out (for all study groups combined) after 4 years (study duration = 4 years). Natural losses, no losses due to any adverse effects; any differential group losses not assessable.
Participants	682 children analysed at 4 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 6.9 DFS. Background exposure to fluoride: none reported. Year study began: in/before 1978. Location: UK.
Interventions	FT (2 groups)** versus PL (SMFP group = 1000 ppm F, SMFP-NaF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca carbonate in all toothpastes.
Outcomes	4yNetDFS increment - (CA)cl+(ER)xr.

Mainwaring 1983 *(Continued)*

	Reported at 4 years follow up. O-DFS. MD-DFS. postMD-DFS. MD-BL-DFS.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, SAR, DFS, FS) 'balanced'. Clinical (VT) caries assessment (FOTI used) by one examiner; diagnostic threshold = CA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Intra-examiner reproducibility checks for DFS in 10% sample (icc for VT/XR over 0.95). **Ca glycerophosphate/SMFP toothpaste group not considered (additional non-F active agent in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marthaler 1965

Methods	Random allocation; double-blind (A); placebo-controlled; 43% drop out (for all study groups combined) after 3 years (study duration = 7 years). Exclusions based on variation in toothpaste provision and presence in follow-up examinations; any differential group losses not assessable.
Participants	269 children analysed at 3 years (present for all examinations). Age range at start: 6-9 years (average = 8). Surfaces affected at start: 3.3 DMFS. Background exposure to fluoride: salt (suboptimal). Year study began: 1958. Location: Switzerland.
Interventions	FT versus PL (AmF group = 1250 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP.
Outcomes	3yNetDFS increment - (CA)cl+(DR)xr. Reported at 1.5, 3, 5 and 7 years follow ups. postMD-DFS. antMD-DFS. BL-DFS. O-DFS. DMFT. FT. FS. MT.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DMFS, DMFT) 'balanced' (DFS baseline data NR).

Marthaler 1965 *(Continued)*

	Clinical (V) caries assessment by one examiner; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = DR and ER; partial recording. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Marthaler 1965a

Methods	Random allocation; double-blind (A); placebo-controlled; 66% drop out (for all study groups combined) after 3 years (study duration = 3 years). Main reason for high drop out: children leaving public school on completion of last compulsory year; exclusions based on variation in toothpaste provision and presence in follow-up examinations; any differential group losses not assessable.
Participants	74 children analysed at 3 years (present for all examinations). Age range at start: 11-14 years (average = 13). Surfaces affected at start: 18.9 DMFS. Background exposure to fluoride: salt (suboptimal). Year study began: 1958. Location: Switzerland.
Interventions	FT versus PL (AmF group = 1250 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP.
Outcomes	3yNetDFS increment - (CA)cl+(DR)xr. Reported at 3 years follow up. postMD-DFS. antMD-DFS. BL-DFS. O-DFS. DMFT. FT. FS. MT.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DMFS, DMFT) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by one examiner; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = DR and ER; partial recording. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Marthaler 1970

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 18% drop out (for all study groups combined) after 3 years (study duration = 3 years). Exclusions based on use of orthodontic bands and presence in all follow-up examinations; any differential group losses not assessable.
Participants	120 children analysed at 3 years (present for all examinations). Age range at start: 6-7 years. Surfaces affected at start: 0.81 DMFS. Exposure to other fluoride: salt. Year study began: 1966. Location: Switzerland.
Interventions	FG versus PL (AmF/NaF group = 12,500 ppm F). Self applied under supervision, with toothbrush, 20 times a year, 1 g applied for 6 min.
Outcomes	3yNetDFS increment - (CA)cl+(DR)xr. Reported at 1 and 3 years follow ups. 1stmPF-DFS (CA)cl. 1stmMD-DFS (CA)xr.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DFMS, 1stmDMFS) 'balanced'. Clinical (V) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR and ER; partial recording. "Sufficient agreement of the two examiners known from earlier work".

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marthaler 1970a

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 30% drop out (for all study groups combined) after 4 years (study duration = 4 years). Exclusions based on use of orthodontic bands, and presence in all follow-up examinations; any differential group losses not assessable.
Participants	41 children analysed at 2&4* years (present for all examinations). Age range at start: 7-9 years. Surfaces affected at start: 2.5 DMFS. Exposure to other fluoride: salt. Year study began: 1966. Location: Switzerland.
Interventions	FG versus PL (AmF/NaF group = 12,500 ppm F). Self applied under supervision, with toothbrush, 22 times a year, 1 g applied for 6 min.
Outcomes	2y*NetDFS increment - (CA)cl+(DR)xr. Reported at 2 and 4 years follow ups.

Marthaler 1970a *(Continued)*

	1stmPF-DFS (CA) cl. 1stmMD-DFS (DR) xr.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DMFS, 1stmDMFS) 'balanced'. Clinical (V) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR and ER; partial recording. "Sufficient agreement of examiners known from earlier work". *FG replaced by F solution after 2 years (final 4 years results not considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marthaler 1970b

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 18% drop out (for all study groups combined) after 3 years (study duration = 3 years). Exclusions based on use of orthodontic bands and presence in all follow-up examinations; any differential group losses not assessable.
Participants	100 children analysed at 3 years (present for all examinations). Age range at start: 6-7 years (average = 7). Surfaces affected at start: 1 DMFS. Background exposure to fluoride: salt (suboptimal). Year study began: 1966. Location: Switzerland.
Interventions	FT versus PL (AmF group = 1250 ppm F). Home use/unsupervised, twice/three times a day/680 times a year estimated. Abrasive system: IMP.
Outcomes	3yNetDFS increment - (CA)cl+(DR)xr. Reported at 1 and 3 years follow ups. 1stmPF-DFS. 1stmMD-DFS.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DMFS, 1stmDMFS) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR and ER; partial recording. "Sufficient agreement of the two examiners known from earlier work".

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marthaler 1970c

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 30% drop out (for all study groups combined) after 4 years (study duration = 4 years). Exclusions based on: use of orthodontic bands, and presence in all follow-up examinations; any differential group losses not assessable.
Participants	43 children analysed at 4* years (present for all examinations). Age range at start: 7-9 years (average = 8). Surfaces affected at start: 2.3 DMFS. Background exposure to fluoride: salt (suboptimal). Year study began: 1966. Location: Switzerland.
Interventions	FT versus PL (AmF group = 1250 ppm F). Home use/unsupervised, twice/three times a day/800 times a year estimated. Abrasive system: IMP.
Outcomes	2y*NetDFS increment - (CA)cl+(DR)xr. Reported at 2 and 4 years follow ups. 1stmPF-DFS. 1stmMD-DFS.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, DMFS, 1stmDMFS) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR and ER; partial recording. "Sufficient agreement of examiners known from earlier work". *F solution used by all children after 2 years (final 4 years results not considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Marthaler 1974

Methods	Random allocation; double-blind (A); placebo-controlled; 32% drop out after 6 years (study duration = 6 years). Exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	109 children analysed at 6* years (present for all examinations). Age range at start: 6-9 years (average = 7.5). Surfaces affected at start: 2.6 DMFS. Background exposure to fluoride: in solution/salt (suboptimal). Year study began: 1966. Location: Switzerland.
Interventions	FT versus PL (AmF group = 1250 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP.
Outcomes	6y*NetDFS increment - (E) (CA)cl+(DR)xr. Reported at 2 and 6 years follow ups.

Marthaler 1974 *(Continued)*

	PF-DFS. postMD-DFS. antMD-B-DFS. DFT. Proportion of children with new DFS.
Notes	Participants randomized (N = 161). Baseline characteristics (DMFS, DMFT, FS, FT, TAR) 'balanced' (DFS baseline data NR). Clinical (V) caries assessment by two examiners; diagnostic threshold = CA and NCA; state of tooth eruption included = E. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR and ER; partial recording. "Sufficient agreement of examiners known from earlier work". *Results at 6 years follow up chosen (reported for all outcomes).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

McConchie 1977

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 38% drop out after 2 years (study duration = 2 years + 1 year post-intervention period). Main reason for high drop-out rate: children moved out of participating schools (plus absenteeism). Exclusions based on compliance; any differential group losses not assessable.
Participants	743 children analysed at 2 years (available at final examination). Average age at start: 10 years. Surfaces affected at start: 6.2 DFS. Exposure to other fluoride: no. Year study began: 1970. Location: Canada.
Interventions	FR (2 groups) versus PL (SnF2 groups = 200 ppm F, and 100 ppm F). School use/supervised, daily, 20 ml applied in 2 successive rinses 30 seconds each (non-fluoride toothpaste provided to all for home use, but no rinse provided).
Outcomes	2yNetDFS increment - (E+U)cl+xr. Reported at 2 years follow up (and 1 year post-treatment). DMFS. DMFT. Increments standardised to 28 teeth and 122 surfaces (E/U). Children with tooth staining/pigmentation, unacceptance to the taste, side effects (incomplete data).
Notes	Participants randomized (N = 1202); numbers by group NR. Baseline characteristics (DFS, DMFS, DMFT, SAR, TAR, age) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. Radiographic assessment (postBW) by two examiners; diagnostic threshold NR. State of tooth eruption included = E/U. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement

McConchie 1977 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Mergele 1968

Methods	Stratified random allocation; double-blind ('A'); placebo-controlled; 22% drop out (for all study groups combined) after 3 years (study duration = 3 years). Reasons for attrition: natural losses to follow up; any differential group losses not assessable.
Participants	387 children analysed at 3 years (available at final examination). Age range at start: 10-13 years (average = 11). Surfaces affected at start: 6.5 DMFS. Background exposure to fluoride: water. Year study began: in/before 1964. Location: USA.
Interventions	FT** versus 'PL' (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in fluoride toothpaste, IMP in control toothpaste.
Outcomes	3yNetDMFS increment - cl. Reported at 3 years follow up. DMFT.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, SAR, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR. **Na N-lauroyl sarcosinate/SMFP toothpaste groups not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Mestrinho 1983

Methods	Stratified quasi-random allocation; blind caries assessment stated but unclear (C); non-placebo-controlled; 20% drop out after 1 year (study duration = 1 year). Exclusions based on 'statistical reasons' (made 'at random' to keep groups of equal sizes, after 8% natural loss).
Participants	174 children analysed at 1 year (after exclusions, available at final examination). Age range at start: 7-10 years. Surfaces affected at start: NR. Exposure to other fluoride: none assumed. Year study began: 1981. Location: Brazil.

Mestrinho 1983 *(Continued)*

Interventions	FG+ptc** versus NT (APF group = 12300 ppm F). Operator-applied, with tray, twice a year, 2.5 ml applied.
Outcomes	1yDMFS increment. Reported at 1 year follow up. O-DMFS. BL-DMFS. MD-DMFS. DMFT. Nausea on application, discomfort in using trays. Drop out (no data by group).
Notes	Participants randomized (N = 218); numbers by group NR. Baseline characteristics (dental age, DMFS) described as 'balanced' (values NR). Clinical (VT) caries assessment by three examiners; diagnostic threshold NR; state of tooth eruption included NR; diagnostic errors NR. **Prior toothbrushing with non-fluoride toothpaste and abrasive paste performed in FG group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Modeer 1984

Methods	Random allocation; single-blind (B); non-placebo-controlled; 18% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective numbers in each group (8 moved away, 14 ortho treated, 20 - all in varnish group, refused participation); differential group losses.
Participants	194 children analysed at 3 years (available at final examination). Average age at start: 14 years. Surfaces affected at start: 1.43 DFS. Exposure to other fluoride: toothpaste + rinse. Year study began: 1979. Location: Sweden. Dental treatment level (F/DF): 86%.
Interventions	FV+ptc** versus NT (NaF Group (Duraphat®) = 22,600 ppm F). Applied four times a year, with small brush, 0.3-0.5 ml applied per child.
Outcomes	3yMD-DFS increment - (E) (DR)xr. Reported at 3 years follow up. Caries progression rate. Drop out.
Notes	Participants randomized (N = 236).

Modeer 1984 *(Continued)*

	Baseline characteristics (toothbrushing frequency, toothpaste use, participation in rinsing program, SES) described as 'balanced' (values NR); initial DFS unbalanced. No clinical assessment of caries. Radiographic assessment (4postBW) by one examiner; diagnostic threshold = ER/DR; intra-examiner reproducibility checks (icc = 0.89). **Prior prophylaxis with non-fluoride paste carried out in FV group only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Molina 1987

Methods	Random allocation; double-blind (A); placebo-controlled; 62% drop out after 2.5 years (study duration = 2.5 years). Main reason for high drop-out rate: children moved out of participating schools (during 1985 earthquake). No differential group losses.
Participants	295 children analysed at 2.5 years (available at final examination). Age range at start: 5-13 years. Surfaces affected at start: 4.3 DMFS. Exposure to other fluoride: data not obtained for dentifrice or water. Year study began: 1983. Location: Chile.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, applied weekly.
Outcomes	2.5yDMFS increment. Reported at 2.5 years follow up. DMFT.
Notes	Participants randomized (N = 767). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment, diagnostic threshold NR. State of tooth eruption included NR. Consistency of diagnosis assessed by duplicate examinations annually. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Moreira 1972

Methods	Stratified quasi-random allocation; double-blind (A); non-placebo-controlled; 39% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses (but exclusions may have been based on 'statistical reasons', made 'at random' to keep groups of equal sizes, after natural losses).

Moreira 1972 *(Continued)*

Participants	200 children analysed at 2 years (after exclusions, available at final examination). Age range at start: 6.5-7.5 years. Surfaces affected at start: 4.6 DMFS (from sample randomized). Exposure to other fluoride: none assumed. Year study began: 1968. Location: Brazil.
Interventions	FR (3 groups) versus PL** (NaF group = 450 ppm F). NaF Group 1: 3 times a week. NaF Group 2: weekly. NaF Group 3: fortnightly. School use/supervised, 25 ml applied in 2 successive rinses of 30 seconds each.
Outcomes	2yDMFS increment. Reported at 1 and 2 years follow ups.
Notes	Participants randomized (N = 330). Baseline characteristics (DMFS, dental age, age) 'balanced'. Clinical (VT) caries assessment, diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR. ** Rinsing with tap water was carried out first, in all 4 groups (followed by another rinse with tap water in the PL group).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Moreira 1981

Methods	Stratified quasi-random allocation; single-blind (B); non-placebo-controlled; 29% drop out after 2.5 years (study duration = 2.5 years). Reasons for attrition NR; differential group losses.
Participants	164 children analysed at 2.5 years (available at final examination). Age range at start: 7-8 years. Surfaces affected at start: 1.4 DMFS. Exposure to other fluoride: water. Year study began: 1974. Location: Brazil.
Interventions	FR versus NT (NaF group = 900 ppm F). School use/supervised, weekly, 20 ml applied in 2 successive rinses of 30 seconds each.
Outcomes	2.5yDMFS increment. Reported at 2.5 years follow up. CAR. Drop out.

Moreira 1981 *(Continued)*

Notes	Participants randomized (N = 230). Baseline characteristics (DMFS, dental age, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Muhler 1955

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 22% drop out after 1 year (study duration = 1 year). Reasons for attrition NR; differential group losses.
Participants	444 children analysed at 1 year (available at final examination). Age range at start: 6-16 years. Surfaces affected at start: 9.3 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: in/before 1954. Location: USA.
Interventions	FT** versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: heat-treated Ca orthophosphate.
Outcomes	1yDMFS increment - cl+xr. Reported at 6 m and 1 year follow ups. DMFT.
Notes	Participants randomized (N = 568). Baseline characteristics (DMFS) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Criteria for caries diagnosis reported to have been carefully standardised, diagnostic errors NR. **NaF-heat treated Ca orthophosphate toothpaste group not considered (abrasive system known to be incompatible with NaF).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Muhler 1970

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 15% drop out after 1 year (study duration = 1 year). Reasons for attrition NR; differential group losses.

Muhler 1970 *(Continued)*

Participants	436 children analysed at 1 year (available at final examination). Age range at start: 5-16 years (average = 10). Surfaces affected at start: 10.3 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: in/before 1967. Location: USA.
Interventions	FT** versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	1yDMFS increment - cl+xr. Reported at 6 m and 1 year follow ups. DMFT.
Notes	Participants randomized (N = 510). Baseline characteristics (age, gender, DMFS) with some imbalance. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-7 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR. **Na N-lauroyl sarcosinate/SMFP toothpaste group not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Murray 1980

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 23% drop out after 3 years (study duration = 3 years). Natural losses; exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	1106 children analysed at 3 years (present for all examinations). Age range at start: 11-13 years (average = 11.9). Surfaces affected at start: 9.9 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: 1974. Location: UK.
Interventions	FT (2 groups) versus PL (both SMFP groups = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Al oxide trihydrate (low and normal abrasivity).
Outcomes	3yNetDMFS increment - cl+ xr. Reported at 3 years follow up. DMFS (U).

Murray 1980 *(Continued)*

Notes	Participants randomized (N = 1431). Baseline characteristics (age, DMFS, TAR) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold = NR; radiographic assessment (2 postBW) by two examiners; diagnostic threshold = NR; state of tooth eruption included = E/U. Reproducibility ratios were less than 0.23 for intra-examiner reproducibility for clinical caries diagnosis and less than 0.16 for radiographic caries diagnosis; inter-examiner reproducibility ratios was 0.26 and 0.1 respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Naylor 1967

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 17% drop out (for all study groups combined) after 3 years (study duration = 3 years). Natural losses; any differential group losses not assessable.
Participants	973 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 9.5 DMFS. Background exposure to fluoride: none reported. Year study began: 1961. Location: UK.
Interventions	FT** versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP (main abrasive) in fluoride toothpaste, dicalcium phosphate (dihydrate) in placebo toothpaste.
Outcomes	3ycrudeDFS increment - (E+U) (CA)cl+(ER)xr. Reported at 3 years follow up. DMFT. DMFS. postMD-DFS. 1stmoMD-DFS. Proportion of children with tooth staining.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, gender, SAR, DMFS, DMFT, postMD-DFS) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Reversal rate less than 4% of observed DFS increment in all groups. High accuracy of diagnosis revealed by 10% sample checks (clinically and radiographically). **Na N-lauroyl sarcosinate/SMFP toothpaste group not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement

Naylor 1967 *(Continued)*

Allocation concealment?	Low risk	A - Adequate

Naylor 1979

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 20% drop out (for all study groups combined) after 3 years (study duration = 3 years). Natural losses; any differential group losses not assessable.
Participants	625 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 7.9 DFS. Background exposure to fluoride: none reported. Year study began: 1973. Location: UK.
Interventions	FT** versus PL (SMFP group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca carbonate.
Outcomes	3yDFS increment - (E) (CA)cl+(ER)xr. Reported at 3 years follow up. DFT. DFT (U). O-BL-DFS. MD-DFS. CIR.
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (age, SAR, TAR, DFS, DFT) 'balanced'. Clinical (VT) caries assessment (FOTI used) by two examiners (independently); diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by two examiners (independently); diagnostic threshold = ER. Results of one examiner chosen (findings consistent throughout). **Ca glycerophosphate/SMFP toothpaste group not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Olivier 1992

Methods	Random allocation; double-blind (A); placebo-controlled; 12% drop out after 2 years (study duration = 2 years). Natural losses; "exclusions not based on compliance"; no differential group losses.
Participants	431 children analysed at 2 years (available at final examination). Age range at start: 6-7 years. Surfaces affected at start: 0.68 DMFS. Exposure to other fluoride: toothpaste.

Olivier 1992 *(Continued)*

	Year study began: 1985. Location: Canada.
Interventions	FG versus PL (APF group = 12,300 ppm F). Operator-applied, with tray, twice a year, applied for 4 min.
Outcomes	2yDMFS increment - (CA). Reported at 2 years follow up.
Notes	Participants randomized (N = 488). Baseline characteristics (age, DFMS, defs, daily sugar consumption, daily toothbrushing, exposure to other fluoride, etc.) 'balanced'. Clinical (VT) caries assessment by five examiners; diagnostic threshold = CA; state of tooth eruption included NR; inter- and intra-examiner reproducibility checks for DMFS in 10% sample (icc over 0.96).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Packer 1975

Methods	Random allocation; indication of blind caries assessment (C); placebo-controlled; 39% drop out after 2.4 years (study duration = 2.4 years). Main reason for high drop-out rate NR. Exclusions based on presence in follow-up examinations and on compliance; no differential group losses.
Participants	285 children analysed at 2.4 years (after exclusions, present for entire trial period). Average age at start: 8.7 years. Surfaces affected at start: 6.6 DMFS. Exposure to other fluoride: no. Year study began: in/before 1971. Location: USA.
Interventions	FR (2 groups) versus PL. APF Group 1: 200 ppm F, daily. APF Group 2: 1000 ppm F, weekly. School use/supervised (non-fluoride toothpaste provided to all for home use, but no rinse provided).
Outcomes	2.4yNetDFS increment - (E+U). Reported at 2.4 years follow up. DMFS (U).
Notes	Participants randomized (N = 464). Baseline characteristics (DMFS, age) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. State of tooth eruption included = E/U. Diagnostic errors NR (results from only one examiner reported).

Risk of bias

Bias	Authors' judgement	Support for judgement

Packer 1975 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Peterson 1967

Methods	Stratified random allocation; double-blind ('A'); placebo-controlled; 16% drop out after 2 years (study duration = 3 years). Reasons for attrition not described; any differential group losses not assessable.
Participants	954 children analysed at 2 years (available at this examination). Age range at start: 9-15 years. Surfaces affected at start: 14.3 DMFS. Background exposure to fluoride: data not available for fluoridation status of site. Year study began: in/before 1964. Location: USA.
Interventions	FT (2 groups) versus 'PL' (SnF2 group = 1000 ppm F, APF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in SnF2 toothpaste, IMP in APF toothpaste, control toothpaste abrasive NR.
Outcomes	2y*DMFS increment - cl+xr. Reported at 1, 2 and 3 years follow ups. DMFT. O-DMFS. BL-DMFS. MD-DMFS.
Notes	Participants randomized (N = 1136); numbers by group NR. Baseline characteristics (DMFS, DMFT, dental age) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included NR; radiographic assessment (3 BW) by one examiner; diagnostic threshold NR. Diagnostic errors NR. *Results for 3 years follow up not considered (not fully reported).

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Peterson 1979

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 25% drop out after 2.5 years (study duration = 2.5 years). Natural losses; exclusions based on presence in all follow-up examinations; any differential group losses not assessable.
Participants	712 children analysed at 2.5 years (present for all examinations). Age range at start: 8-12 years (average = 10). Surfaces affected at start: 2.9 DFS. Background exposure to fluoride: water. Year study began: 1971.

Peterson 1979 *(Continued)*

	Location: USA.
Interventions	FT (2 groups) versus PL (both SMFP groups = 1000 ppm F). School use/supervised, daily, (appropriate toothpastes also provided for home use). Abrasive system: Ca carbonate in one toothpaste and in placebo toothpaste, IMP in the other SMFP toothpaste.
Outcomes	2.5yDFS increment - cl+xr. Reported at 2.5 years follow up. DMFT. MD-DFS.
Notes	Participants randomized (N = 950); numbers by group NR. Baseline characteristics (DFS, MD-DFS, DFT) 'balanced'. Clinical (VT) caries assessment (FOTI used) by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Petersson 1998a

Methods	Random allocation; double-blind (A); placebo-controlled; drop-out rate NR nor obtainable (study duration = 3 years). Reasons for attrition NR. Any differential group losses not assessable.
Participants	139 children analysed at 3 years. Average age at start: 13 years. Surfaces affected at start: 1.3 DFS. Exposure to other fluoride: toothpaste. Year study began: in/before 1994. Location: Sweden.
Interventions	FR versus PL (NaF group = 200 ppm F). School use/supervised, for 3 days every 6 months (6 times a year), 10 ml applied.
Outcomes	3ypostMD-DFS increment. Reported at 3 years follow up.
Notes	Participants randomized (numbers NR). Baseline characteristics (DFS) 'balanced'. Radiographic assessment (4 postBW) by one examiner; diagnostic threshold = DR and ER. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement

Petersson 1998a *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Poulsen 1984

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 8% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; no differential group losses.
Participants	365 children analysed at 3 years (available at final examination). Age range at start: 7-10 years (average = 9). Surfaces affected at start: 3.6 DMFS. Exposure to other fluoride: toothpaste. Year study began: 1979. Location: Denmark.
Interventions	FR versus PL (NaF group = 900 ppm F). School use/supervised, fortnightly, 10 ml applied.
Outcomes	3yNetDMFS increment - (CA)(E)cl. Reported at 3 years follow up. DMFS (U). O-DMFS. MD-DMFS. BL-DMFS. postMDDMFS.
Notes	Participants randomized (N = 398). Baseline characteristics (DMFS, erupted surfaces, age) 'balanced'. Clinical (VT) caries assessment by dentists at public dental service, diagnostic threshold = CA. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = DR. State of tooth eruption included (E/U). Reproducibility of diagnosis assessed by duplicate radiographic examination of 10% random sample (kappa value 0.72).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Powell 1981

Methods	Stratified random allocation; double-blind (A); placebo-controlled; drop-out rate NR nor obtainable (study duration = 4 years). Reasons for attrition NR; any differential group losses not assessable.
Participants	125 children analysed at 4 years (subjects who developed caries). Age range at start: 12-14 years. Surfaces affected at start: 21.4 DMFS (from sample above). Background exposure to fluoride: none reported. Year study began: 1963. Location: Australia.

Powell 1981 *(Continued)*

Interventions	FT (pp/Plsol) versus PL(pp/Plsol)** (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	Caries increment data NR (not obtainable). Progression rate of initial carious lesions in MD surfaces of permanent posterior teeth at annual intervals (for 4 years).
Notes	Participants randomized (numbers NR). Baseline characteristics (age, gender, DMFS) 'balanced'. Radiographic (post BW) enamel caries progression assessment by one examiner; state of tooth eruption included = E. High reproducibility of radiographic diagnosis (icc = 0.91). **Prior prophylaxis with lava pumice followed by professional application of placebo solution performed every 6 months for 2 years in both relevant groups compared.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Radike 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 18% drop out after 1.6 years (study duration = 1.6 years). Reasons for attrition NR; no differential group losses.
Participants	726 children analysed at 1.6 years (available at final examination). Age range at start: 8-13 years (average = 10.4). Surfaces affected at start: 4.9 DMFS. Exposure to other fluoride: water. Year study began: in/before 1970. Location: USA. Dental treatment level (F/DMF): 50%.
Interventions	FR versus PL (SnF2 group = 250 ppm F). School use/supervised, daily, 60 ml applied in 3 successive rinses of 10, 30, and 30 seconds each (non-fluoride toothpaste provided to all for home use, but no rinse provided).
Outcomes	1.6yDMFS increment - cl+xr. Reported at 8 months and 1.6 years follow ups. DMFT. Children with tooth staining/pigmentation (incomplete data).
Notes	Participants randomized (N = 890). Baseline characteristics (DMFS, DMFT, age, gender) 'balanced'.

Radike 1973 *(Continued)*

	Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. Radiographic assessment (4 postBW) by two examiners; diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR. Results of one examiner chosen (findings of both examiners consistent throughout).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ran 1991

Methods	Random allocation; double-blind (A); placebo-controlled; 20% drop out (for all study groups combined) after 1.5 years (study duration = 1.5 years + 0.5 year post-intervention period). Reasons for attrition/ handling of exclusions NR; any differential group losses not assessable.
Participants	83 children analysed at 1.5 years; all male. Average age at start: 13 years. Surfaces affected at start: 6.5 DMFS. Exposure to other fluoride: data not obtained for dentifrice. Year study began: in/before 1989. Location: Israel.
Interventions	FG (2 groups) versus PL (AmF group 1= 4000 ppm F, AmF group 2 = 12,500 ppm F). Self applied under supervision, with toothbrush, 25 times a year, 1 g applied for 4 min.
Outcomes	1.5yNetDMFS increment - (CA). Reported at 0.5 and 1.5 years follow ups (and 0.5 year post-treatment).
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (DFMS) with some imbalance (reported as NS difference). Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR; intra-examiner reproducibility checks for DMFS (icc reaching 0.97).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ran 1991a

Methods	Random allocation; double-blind (A); placebo-controlled; 20% drop out (for all study groups combined) after 1.5 years (study duration = 1.5 years + 0.5 year post-intervention period). Reasons for attrition/ handling of exclusions NR; any differential group losses not assessable.
Participants	55 children analysed at 1.5 years; all male. Average age at start: 13 years. Surfaces affected at start: 6.4 DMFS. Background exposure to other fluoride: data not obtained for home use of toothpaste. Year study began: in/before 1989. Location: Israel.

Ran 1991a *(Continued)*

Interventions	FT versus PL (AmF group = 1250 ppm F). School use/supervised, fortnightly/20 times a year, 1 g applied for 4 min, no post-brushing rinse done (no provision of any toothpaste reported for home use). Abrasive system: NR.
Outcomes	1.5yNetDMFS increment - (CA). Reported at 0.5 and 1.5 years follow ups (and 0.5 year post-treatment).
Notes	Participants randomized (numbers for relevant groups NR). Baseline characteristics (DMFS) with some imbalance (reported as NS difference). Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR. Intra-examiner reproducibility checks for DMFS (icc reaching 0.97).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Reed 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 28% drop out after 2 years (study duration = 2 years). Reasons for attrition not described; no differential group losses.
Participants	1525 children analysed at 2 years (available at final examination). Age range at start: 6-13 years (average = 9). Surfaces affected at start: 3.3 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1970. Location: USA.
Interventions	FT (3 groups) versus PL (NaF groups = 1000 ppm F, 500 ppm F, 250 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	2yDMFS increment - cl+xr. Reported at 1 and 2 years follow ups. DMFT.
Notes	Participants randomized (N = 2104). Baseline characteristics (age, gender, DMFS, DMFT) 'balanced' . Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included NR. Radiographic assessment (up to 7 BW) by one examiner; diagnostic threshold NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement

Reed 1973 *(Continued)*

Allocation concealment?	Unclear risk	B - Unclear

Reed 1975

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 39% drop out after 2 years (study duration = 2 years). Reasons for high drop out not described; no differential group losses.
Participants	344 children analysed at 2 years (available at final examination). Age range at start: 8-13 years (average = 10). Surfaces affected at start: 5 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1968. Location: USA.
Interventions	FT versus PL (NaF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	2yDMFS increment - cl+xr. Reported at 1 and 2 years follow ups. DMFT.
Notes	Participants randomized (N = 567). Baseline characteristics (age, gender, DMFS, DMFT) with some imbalance. Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included NR. Radiographic assessment (up to 7 BW) by one examiner; diagnostic threshold NR. Diagnostic errors NR.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Ringelberg 1979

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 40% drop out after 2.5 years (study duration = 2.5 years). Reason(s) for attrition NR; no differential group losses.
Participants	527 children analysed at 2.5 years (available at final examination). Average age at start: 11 years. Surfaces affected at start: 4.3 DMFS. Exposure to other fluoride: no. Year study began: 1973. Location: USA.
Interventions	FR (2 groups) versus PL(2 groups). (AmF group = 250 ppm F, NaF group = 250 ppm F).

Ringelberg 1979 *(Continued)*

	School use/supervised, daily, 10 ml applied for 1 min.
Outcomes	2.5yNetDMFS increment - (CA)cl + (DR)xr. Reported at 2.5 years follow up. DMFT. Stain score.
Notes	Participants randomized (N = 878). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. Radiographic assessment (5 BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Reversal rate between 4 and 9% of observed caries increment in the groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ringelberg 1979a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 37% drop out after 2.5 years (study duration = 2.5 years). Reasons for attrition not described; no differential group losses.
Participants	556 children analysed at 2.5 years (available at final examination). Average age at start: 11 years. Surfaces affected at start: 4.2 DMFS. Background exposure to fluoride: none reported. Year study began: 1973. Location: USA.
Interventions	FT (2 groups) versus PL (2 groups) (AmF group = 1250 ppm F, SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in SnF2 toothpaste and its placebo, NR for AmF and its placebo.
Outcomes	2.5yNetDMFS increment - (CA)cl + (DR)xr. Reported at 2.5 years follow up. DMFT. Stain score.
Notes	Participants randomized (N = 888). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. Radiographic assessment (5 BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Reversal rate between 4 and 9% of observed caries increment in the groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ringelberg 1982

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 39% drop out after 2 years (study duration = 2 years). Reason(s) for high drop out related to "migratory" nature of community; no differential group losses.
Participants	1238 children analysed at 2 years (available at final examination). Average age at start: 12.5 years. Surfaces affected at start: 4.7 DMFS. Exposure to other fluoride: toothpaste assumed. Year study began: in/before 1979. Location: USA.
Interventions	FR (4 groups) versus PL. NaF Group 1: 230 ppm F, daily. NaF Group 2: 900 ppm F, daily. NaF Group 3: 230 ppm F, weekly. NaF Group 4: 900 ppm F, weekly. School use/supervised, 10 ml applied for 1 min.
Outcomes	2yNetDMFS increment. Reported at 1.5 and 2.5 years follow ups. posMD-DFS.
Notes	Participants randomized (N = 2014). Baseline characteristics (DMFS) with some imbalance but "adjustment made no difference in the results". Clinical (VT) caries assessment by two examiners, diagnostic threshold NR. Radiographic assessment by two examiners; diagnostic threshold NR. State of tooth eruption included NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Rugg-Gunn 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 12% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers: 1 found it difficult to rinse, 56 moved away or were absent from school at final examination; no differential group losses.
Participants	434 children analysed at 3 years (available at final examination). Age range at start: 10-11 years. Surfaces affected at start: 8.8 DMFS. Exposure to other fluoride: no. Year study began: in/before 1969. Location: UK.
Interventions	FR versus PL (NaF group = 230 ppm F). School use/supervised, daily, 7.5 ml applied for 2 min.

Rugg-Gunn 1973 *(Continued)*

Outcomes	3yNetDMFS increment - (E+U)(CA)cl+(DR)xr. Reported at 1, 2 and 3 years follow ups. DMFT (E/U). PF-DMFS. FS-DMFS. AntMD-DMFS. PostMD-DMFS. DMFS (U). Signs of sensitivity in oral mucosa.
Notes	Participants randomized (N = 491). Baseline characteristics (DMFS, DMFT, gender, exposure to fluoride toothpaste) 'balanced'. Clinical (V) caries assessment by one examiner, diagnostic threshold = CA/NCA. Radiographic assessment (2postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = E/U. Intra-examiner reproducibility checks for incremental caries data in 10% sample (icc score 0.9 for DMFS). Reversal rate 4% and 7% of observed DMFS increment in control and study groups respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Ruiken 1987

Methods	Cluster random allocation; indication of blind caries assessment (C); non-placebo-controlled; 59% drop out after 3 years (study duration = 3 years). Main reasons for attrition: natural losses and results reported only for chidren with readable x-rays; any differential group losses not assessable.
Participants	207 children analysed at 3 years (present at final examination, for which there were readable x-rays). Average age at start: 8 years. Surfaces affected at start: 2.7 DFS. Exposure to other fluoride: toothpaste, tablets. Year study began: 1981. Location: The Netherlands.
Interventions	FR versus NT (NaF group = 900 ppm F). School use/supervised, weekly, 10 ml applied for 1 min.
Outcomes	3yNetDFS increment - cl+xr. Reported at 3 years follow up.
Notes	Schools (N = 29) randomized (and 2nd grade children in these taken as units of analysis); number of children by group NR. Baseline characteristics (DFS, erupted surfaces, age) described as 'balanced'. Clinical (V) caries assessment by two examiners; diagnostic threshold = CA/NCA; state of tooth eruption included NR. Radiographic assessment (2 postBW) by two examiners; diagnostic threshold = DR/ER; partial recording. Diagnostic errors NR.

Risk of bias

Ruiken 1987 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Rule 1984

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 24% drop out after 2 years (study duration = 2 years). Reasons for attrition not described; exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	876 children analysed at 2 years (present for all examinations). Age range at start: 9-12 years (average = 11). Surfaces affected at start: 8.6 DMFS. Background exposure to fluoride: none reported. Year study began: 1977. Location: USA.
Interventions	FT versus PL (SMFP group = 1000 ppm F). School use/supervised, daily, for 1 min (appropriate toothpastes also provided for home use). Abrasive system: silica zerogel.
Outcomes	2yDFS increment - (E+U) (CA)cl+(ER)xr. Reported at 1 and 2 years follow ups. DFT. DMFS. DMFT. O-DFS. MD-DFS. Oral soft tissue lesions.
Notes	Participants randomized (N = 1154). Baseline characteristics (age, gender, TAR, DMFS, DMFT, DS, DT) 'balanced' (DFS baseline data NR). Clinical (VT) caries assessment (FOTI used) by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Reproducibility checks done in 10% sample clinically and radiographically.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Segal 1967

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 23% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; differential group losses.
Participants	648 children analysed at 2 years (available at final examination).

Segal 1967 *(Continued)*

	Age range at start: 7-12 years. Surfaces affected at start: NR. Background exposure to fluoride: none reported. Year study began: in/before 1964. Location: USA.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). School use/supervised, daily, (appropriate toothpastes also provided for home use). Abrasive system: IMP (mainly).
Outcomes	2yDFS increment - (CA)cl+xr. Reported at 1 and 2 years follow ups. DFS (U).
Notes	Participants randomized (N = 845). Baseline characteristics (SAR) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA. Radiographic assessment as a supplementary aid; diagnostic threshold = NR. State of tooth eruption included E/U. Inter- and intra-examiner reproducibility checks done.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Shern 1976

Methods	Random allocation; double-blind (A); placebo-controlled; 8% drop out after 1 year (study duration = 2 years). Natural losses only; "losses distributed evenly among groups".
Participants	562 children analysed at 1* year (available at 1st examination). Age range at start: 6-13 years. Surfaces affected at start: 2.7 DMFS (data from original sample only). Exposure to other fluoride: none assumed. Year study began: in/before 1973. Location: Venezuela.
Interventions	FG (3groups)+ptc versus PL(2 groups)+ptc (APF group 1 = 12,300 ppm F, AmF group 1 = 12,500 ppm F, AmF group 2 = 12,500 ppm F). Operator-applied, with tray 5 consecutive applications (every day/week) in 1st year, 3 mg (about 14 drops) applied for 5 min.
Outcomes	1y*NetDMFS increment. Reported at 1 and 2 years follow ups. O-DMFS. MD-BL-DMFS. Side effects (incomplete data).
Notes	Participants randomised (N = 614). Baseline characteristics (DFMS) 'balanced'.

Shern 1976 *(Continued)*

	Clinical (VT) caries assessment by one examiner; diagnostic threshold NR; state of tooth eruption included NR; diagnostic errors NR. *Intervention applied during 1st year of study only (final 2 years results not considered).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Slack 1964

Methods	Random allocation; double-blind (A); placebo-controlled; 32% drop-out rate after 2 years (study duration = 2 years). Natural losses and other reasons; exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	719 children analysed at 2 years (present for all examinations). Age range at start: 11-13 years. Surfaces affected at start: NR. Background exposure to fluoride: none reported. Year study began: 1962. Location: UK.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, 3 times/day instructed but daily frequency assumed. Abrasive system: IMP in fluoride toothpaste, dicalcium phosphate (dihydrate) in placebo toothpaste.
Outcomes	Caries increment data NR (not obtainable). Proportion of carious teeth/surfaces (by tooth type) reported at 1 and 2 years follow ups. Proportion of caries-free teeth/surfaces (by tooth type) which developed caries after each year. Proportion of children with tooth staining.
Notes	Participants randomized (N = 1059). Baseline characteristics 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Slack 1967

Methods	Random allocation; double-blind (A); placebo-controlled; 21% drop-out rate after 3 years (study duration = 3 years). Reasons for drop out described with numbers: left school, moved away, staining of teeth, on parents request; exclusions based on presence in all follow-up examinations; no differential group losses.

Slack 1967 *(Continued)*

Participants	696 children analysed at 3 years, all female (present for all examinations). Average age at start: 11 years. Surfaces affected at start: 8.9 DFS. Background exposure to fluoride: none reported. Year study began: 1963. Location: UK.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP (dicalcium phosphate (dihydrate) in placebo toothpaste also).
Outcomes	3yNetDFS increment - (E)(CA)cl. Reported at 3 years follow up. DFT. DMFS. DMFT. postMD-DFS. Proportion of children with tooth staining.
Notes	Participants randomized (N = 886). Baseline characteristics (age, dental age, DFS, DFT, DMFS, DMFT, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Consistency of clinical diagnosis maintained by re-examination of 10% sample and calibration checks made against reserve examiner.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Slack 1967a

Methods	Random allocation; double-blind (A); placebo-controlled; 21% drop-out rate after 3 years (study duration = 3 years). Reasons for drop out described with numbers: left school, moved away, staining of teeth, on parents request; exclusions based on presence in all follow-up examinations; no differential group losses.
Participants	757 children analysed at 3 years, all female (present for all examinations). Age range at start: 11-12 years. Surfaces affected at start: 7 DFS. Background exposure to fluoride: none reported. Year study began: 1962. Location: UK.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: dicalcium pyrophosphate.
Outcomes	3yDFS increment - (E) (CA)cl.

Slack 1967a *(Continued)*

	Reported at 3 years follow up. DFT. DMFS. DMFT. postMD-DFS. Proportion of children with tooth staining.
Notes	Participants randomized (N = 961). Baseline characteristics (age, dental age, DFS, DFT, DMFS, DMFT, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = E/U. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Consistency of clinical diagnosis maintained by re-examination of 10% sample and calibration checks made against reserve examiner.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Slack 1971

Methods	Random allocation; double-blind ('A'); placebo-controlled; 33% drop-out rate after 3 years (study duration = 3 years). Main reasons for drop out: moved away, left school, away on examination day, disliked toothpaste taste, brown staining of teeth; no differential group losses.
Participants	1110 children analysed at 3 years (available at final examination). Age range at start: 11-12 years. Surfaces affected at start: 11.6 DMFS. Background exposure to fluoride: none reported. Year study began: 1965. Location: UK.
Interventions	FT (3 groups) versus 'PL' (Both SnF2 groups = 1000 ppm F, APF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: IMP in one SnF2 toothpaste and in APF toothpaste, dicalcium pyrophosphate in another SnF2 toothpaste; control toothpaste abrasive NR.
Outcomes	3yCrudeDMFS increment - (CA)cl+(ER)xr. Reported at 3 years follow up.
Notes	Participants randomized (N = 1665). Baseline characteristics (age, gender, DMFS, previous F toothpaste use) 'balanced'. Clinical (VT) caries assessment by one examiner; diagnostic threshold = CA; state of tooth eruption included = NR. Radiographic assessment (2 postBW) by one examiner; diagnostic threshold = ER. Consistency of clinical diagnosis revealed by 10% sample checks at each examination.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Spets-Happonen 1991

Methods	Random allocation; double-blind (A); placebo-controlled; 17% drop out after 3 years (study duration = 3 years). Reasons for attrition NR; differential group losses not assessable but "greatest proportion of drop outs in the fluoride group".
Participants	95 children analysed at 3 years (available at final examination). Average age at start: 11 years. Surfaces affected at start: 5.8 DMFS (from 1 y sample). Exposure to other fluoride: varnish (toothpaste assumed). Year study began: 1985. Location: Finland.
Interventions	FR(Chlor)+ptc versus PL(Chlor)+ptc ** (NaF mouthrinse = 180 ppm F). School use/supervised, 5 days every 3 weeks, 5 ml applied for 1 min. Same schedule at home (but no instruction for use of toothpaste).
Outcomes	3yDMFS increment - (CA)cl+(DR)xr. Reported at 3 years follow up.
Notes	Participants randomized (numbers NR). Baseline characteristics (DMFS, gender) with some imbalance, but "adjustment made no difference in the results". Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA (FOTI assessment - loss of translucency on transillumination - for approximal surfaces of anterior teeth); state of tooth eruption included NR. Radiographic assessment; diagnostic threshold = DR ; kappa 0.7 and 0.79 for inter- and intra-examiner reliability. ** Chlorhexidine present in both, the fluoride and the non-fluoride mouthrinse (thus, other outcomes, such as tooth staining, not relevant for the comparison of interest). Prior toothbrushing without toothpaste done.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Szwejda 1972

Methods	Random allocation; double-blind ('A'); placebo-controlled ('PL'); drop-out rate NR nor obtainable (study duration = 3 years). Exclusions based on lifetime exposure to fluoridated water, compliance to treatment, and presence in all follow-up examinations; any differential group losses not assessable.
Participants	316 children analysed at 3 years (after exclusions, present for all examinations). Age range at start: 7-9 years. Surfaces affected at start: 0.86 DMFS. Exposure to other fluoride: water. Year study began: in/before 1968. Location: USA.
Interventions	FG+ptc versus 'PL'+ptc (APF, concentration NR).

Szwejda 1972 *(Continued)*

	Operator-applied, with tray once a year.
Outcomes	3yNetDMFS increment - (E). Reported at 3 years follow up. O-DMFS. MD-DMFS. BL-DMFS. NetDMFT(E/U).
Notes	Participants randomized (numbers NR). Baseline characteristics (age, DMFT, DMFS, TAR, SAR) 'balanced'. Clinical (VT) caries assessment by more than one examiner; diagnostic threshold NR; state of tooth eruption included = E and U; reversal rate 3.9% and 2.2% of observed DMFT increment, and 3.2% and 1.5% of observed DMFS increment in FG and PL groups respectively (3rd year results only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Tewari 1990

Methods	Stratified random allocation; double-blind ('A'); placebo-controlled ('PL'); 6% drop out after 2.5 years (study duration = 4.5 years). Natural losses; no differential group losses.
Participants	618 children analysed at 2.5* years (available at 2nd examination). Age range at start: 6-12 years (average = 8.5). Surfaces affected at start: 2.53 DMFS. Exposure to other fluoride: data not obtained for dentifrice. Year study began: in/before 1982. Location: India.
Interventions	FV+ptc versus 'PL'+ptc (NaF group (Duraphat®) = 22,600 ppm F). Applied twice a year, with single tufted brush, about 0.5 ml applied per child, left to dry for 4 min.
Outcomes	2.5y*NetDMFS increment - (CA)(E). Reported at 1.5 and 2.5 year follow ups. ODMFS. MDDMFS. BLDMFS. DMFT.
Notes	Participants randomized (N = 657). Baseline characteristics (age, DMFS, DMFT) balanced. Clinical (VT) caries assessment by two examiners; diagnostic threshold = NCA/CA; state of tooth eruption included = E/U; constant duplicate examination of 10% sample between same and both examiners (results NR). *Final 4.5 years results not available (results closest to 3 years chosen).

Risk of bias

Tewari 1990 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Thomas 1966

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 32% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses.
Participants	464 children analysed at 2 years (present for the entire study period). Average age at start: 7-16 years (average = 12). Surfaces affected at start: 10.7 DFS. Background exposure to fluoride: none reported. Year study began: 1961. Location: USA.
Interventions	FT (2 groups) versus PL (Both SnF2 groups = 1000 ppm F). Institution use/supervised, twice a day. Abrasive system: IMP in one SnF2 and placebo toothpaste, Ca pyrophosphate in another SnF2 toothpaste.
Outcomes	2yDFS increment - cl+xr. Reported at 6 m, 1, 1.5 and 2 years follow ups. DFT.
Notes	Participants randomized (N = 679). Baseline characteristics (DFS, DFT, TAR) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Check of diagnostic errors done.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Torell 1965

Methods	Random allocation; single-blind (B); non-placebo-controlled; 17% drop-out rate after 2 years (study duration = 2 years). Natural losses mainly; no differential group losses.
Participants	494 children analysed at 2 years (available at final examination). Average age at start: 10 years. Surfaces affected at start: 14.5 DMFS (from sample randomized). Exposure to other fluoride: none assumed. Year study began: 1962. Location: Sweden.

Torell 1965 *(Continued)*

Interventions	FR (2 groups) versus NT. NaF Group 1: 230 ppm F, 10 ml applied daily, unsupervised at home (instructed to be done after tooth-brushing). NaF Group 2: 900 ppm F, 10 ml applied fortnightly, supervised at school.
Outcomes	2yDMFS increment - (CA)cl. Reported at 1 and 2 years follow ups. MD-DMFS. FS. Proportion of children with new carious lesions - (U)xr.
Notes	Participants randomized (N = 597). Baseline characteristics (DMFS, MD-DMFS) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA; radiographic assessment (BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Inter- and intra-examiner reproducibility checks done for clinical caries in 4 and 2% sample respectively; duplicate examination of x-rays records done and any discrepancies discussed before final diagnosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Torell 1965a

Methods	Random allocation; double-blind (A); placebo-controlled; 13% drop-out rate after 2 years (study duration = 2 years). Natural losses mainly; no differential group losses.
Participants	668 children analysed at 2 years (available at final examination). Average age at start: 10 years. Surfaces affected at start: 14.5 DMFS (from sample randomized). Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT (2 groups) versus PL (2 groups) (SnF2 group = 1000 ppm F, NaF group = 1100 ppm F). Home use/unsupervised, twice a day instructed but daily frequency assumed, post-brushing water rinse instructed. Abrasive system: Ca pyrophosphate in SnF2 toothpaste and its placebo, Na bicarbonate in NaF toothpaste and its placebo.
Outcomes	2yDMFS increment - (CA)cl. Reported at 1 and 2 years follow ups. MD-DMFS. FS. Proportion of children with new carious lesions (U)xr.
Notes	Participants randomized (N = 766). Baseline characteristics (DMFS, MD-DMFS) 'balanced'.

Torell 1965a *(Continued)*

	Clinical (VT) caries assessment by two examiners, diagnostic threshold = CA; radiographic assessment (BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Inter- and intra-examiner reproducibility checks done for clinical caries in 4 and 2% sample respectively; duplicate examination of x-rays records done and any discrepancies discussed before final diagnosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Torell 1965b

Methods	Random allocation; double-blind (A); placebo-controlled; 20% drop-out rate after 2 years (study duration = 2 years). Natural losses mainly; differential group losses.
Participants	285 children analysed at 2 years (available at final examination). Average age at start: 10 years. Surfaces affected at start: 11.7 DMFS (from sample randomized). Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT versus PL (SMFP group = 1000 ppm F). Home use/unsupervised, twice a day instructed but daily frequency assumed, post-brushing water rinse instructed. Abrasive system: Ca carbonate.
Outcomes	2yDMFS increment - (CA)cl. Reported at 2 years follow up. MD-DMFS. FS.
Notes	Participants randomized (N = 357). Baseline characteristics (DMFS, MD-DMFS) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = CA; radiographic assessment (BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Intra-examiner reproducibility check done for clinical caries in a sample; duplicate examination of x-rays records done and any discrepancies discussed before final diagnosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Torell 1965c

Methods	Random allocation; double-blind (A); placebo-controlled; 15% drop-out rate after 2 years (study duration = 2 years).

Torell 1965c *(Continued)*

	Natural losses mainly; differential group losses.
Participants	368 children analysed at 2 years (available at final examination). Average age at start: 11 years. Surfaces affected at start: 15 DMFS (from sample randomized). Background exposure to fluoride: none reported. Year study began: 1962. Location: Sweden.
Interventions	FT versus PL (SMFP group = 1000 ppm F). Home use/unsupervised, twice a day instructed but daily frequency assumed, post-brushing water rinse instructed. Abrasive system: Ca carbonate.
Outcomes	2yDMFS increment - (CA)cl. Reported at 2 years follow up. MD-DMFS. FS.
Notes	Participants randomized (N = 432). Baseline characteristics (DMFS, MD-DMFS) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = CA; radiographic assessment (BW) by two examiners; diagnostic threshold = DR. State of tooth eruption included NR. Intra-examiner reproducibility check done for clinical caries in a sample; duplicate examination of x-rays records done and any discrepancies discussed before final diagnosis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Treide 1988

Methods	Random allocation; double-blind (A); placebo-controlled; 33% drop out after 3 years (study duration = 3 years). No differential group losses.
Participants	433 children analysed at 3 years. Average age at start: 3.5 years. Surfaces affected at start: NR (but dmft data reported from original sample only = 0.8). Exposure to other fluoride: no. Year study began: 1983. Location: GDR.
Interventions	FG (3 groups) +ptc versus PL+ptc (NaF+hexaf group = 12,500 ppm F, NaF group = 12,500 ppm F, AmF group = NR). Self applied under supervision, with toothbrush, approximately 130 times a year.
Outcomes	3ydmfs increment - (E). Reported at 1, 2 and 3 years follow ups. dmft (E).
Notes	Participants randomized (N = 643).

Treide 1988 *(Continued)*

	Baseline characteristic (dmft) 'balanced'. Clinical (VT) caries assessment by two examiners; diagnostic threshold NR; state of tooth eruption included = E.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Trubman 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 46% drop out after 3 years (study duration = 3 years). Main reason(s) for high drop-out rate NR; exclusions based on presence in all follow-up examinations; differential group losses.
Participants	311 children analysed at 3 years (present for all examinations). Average age at start: 8.1 years. Surfaces affected at start: 2.1 DMFS. Exposure to other fluoride: none assumed. Year study began: in/before 1969. Location: USA.
Interventions	FG+ptc versus PL+ptc (APF group = 12,300 ppm F). Self applied under supervision, with tray 4 times a year, applied for 4 min.
Outcomes	3yNetDMFS increment - (CA). Reported at 2 and 3 years follow ups. NetDMFT(CA).
Notes	Participants randomized (N = 575). Baseline characteristics (age, DMFT, DMFS) with some imbalance (DMFS) "but adjustment results in trivial changes in crude means". Clinical (VT) caries assessment by two examiners; diagnostic threshold = CA; state of tooth eruption included NR; reversal rate 18.4% and 9.2% of observed DMFT increment in FG and PL groups respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

van Wyk 1986

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 38% drop out after 3 years (study duration = 3 years). Reasons for attrition described with respective total numbers, main reasons: changing of school and scholastic failure; no differential group losses.
Participants	569 children analysed at 3 years (available at final examination). Age range at start: 12-13 years. Surfaces affected at start: 1.6 DFS.

van Wyk 1986 *(Continued)*

	Exposure to other fluoride: no. Year study began: 1981. Location: South Africa.
Interventions	FR (2 groups) versus PL (NaF groups = 900 ppm F and 230 ppm F). School use/supervised, weekly, 10 ml applied for 1 min.
Outcomes	2yNetDFS increment - (CA)cl. Reported at 1, 2 and 3 years follow ups.
Notes	Participants randomized (N = 925). Baseline characteristics (DFS, gender) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = CA. State of tooth eruption included NR. Intra-examiner reproducibility checks for incremental caries data in 40% sample (icc score 0.91).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Weisenstein 1972

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 42% drop out after 1.8 years (study duration = 1.8 years). Reasons for high drop out described: change of residence, absent on examination day; no differential group losses.
Participants	402 children analysed at 1.8 years (available at final examination). Age range at start: 5-15 years (average = 9.5). Surfaces affected at start: 6.8 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1969. Location: USA.
Interventions	FT versus PL (NaF group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	1.8yDMFS increment - cl+xr. Reported at 9 m, 1.4 and 1.8 years follow ups. DMFT.
Notes	Participants randomized (N = 694). Baseline characteristics (age, gender, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by two examiners, diagnostic threshold = NR. Radiographic assessment (7 BW) by two examiners; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR. Results of one examiner chosen.

Risk of bias

Weisenstein 1972 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Zacherl 1970

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 43% drop out after 2.5 years (study duration = 2.5 years). Reasons for high drop out NR; no differential group losses.
Participants	512 children analysed at 2.5 years (available at final examination). Age range at start: 6-9 years. Surfaces affected at start: 4.6 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1963. Location: USA.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	2.5yDMFS increment - cl+xr. Reported at 10 m, 1.5 and 2.5 years follow ups. DMFT.
Notes	Participants randomized (N = 902). Baseline characteristics (dental age, gender, DMFS, DMFT, oral hygiene) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Zacherl 1970a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 35% drop out after 2.5 years (study duration = 2.5 years). Reasons for attrition NR; no differential group losses.
Participants	528 children analysed at 2.5 years (available at final examination). Age range at start: 13-14 years. Surfaces affected at start: 23.5 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1963. Location: USA.
Interventions	FT versus PL

Zacherl 1970a *(Continued)*

	(SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate.
Outcomes	2.5yDMFS increment - cl+xr. Reported at 10 m, 1.5 and 2.5 years follow ups. DMFT.
Notes	Participants randomized (N = 811). Baseline characteristics (dental age, gender, DMFS, DMFT, oral hygiene) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

Zacherl 1972

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 34% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses.
Participants	447 children analysed at 2 years (available at final examination). Age range at start: 6-15 years (average = 10). Surfaces affected at start: 11.7 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1969. Location: Canada.
Interventions	FT versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in SnF2 toothpaste, placebo toothpaste abrasive NR.
Outcomes	2yDMFS increment - cl+xr. Reported at 1 and 2 years follow ups. DMFT.
Notes	Participants randomized (N = 677). Baseline characteristics (age, gender, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Zacherl 1972a

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 36% drop out after 1.7 years (study duration = 1.7 years). Reasons for high drop out NR; exclusions based on presence in both examinations; no differential group losses.
Participants	894 children analysed at 1.7 years (present for both examinations). Age range at start: 7-14 years (average = 9). Surfaces affected at start: 7.3 DMFS. Background exposure to fluoride: water. Year study began: in/before 1969. Location: Canada.
Interventions	FT (4 groups) versus PL (SnF2 group, NaF group, SMFP group, APF group = 1000 ppm F each). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in all toothpastes.
Outcomes	1.7yDMFS increment - cl+xr. Reported at 1 and 1.7 years follow ups. DMFT.
Notes	Participants randomized (N = 1405). Baseline characteristics (age, gender, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Zacherl 1973

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 34% drop out after 2 years (study duration = 2 years). Reasons for attrition NR; no differential group losses.
Participants	444 children analysed at 2 years (available at final examination). Age range at start: 5-12 years (average = 9). Surfaces affected at start: 8.5 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1970. Location: USA.
Interventions	FT** versus PL (SnF2 group = 1000 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in SnF2 toothpaste, placebo toothpaste abrasive NR.
Outcomes	2yDMFS increment - cl+xr.

Zacherl 1973 *(Continued)*

	Reported at 1 and 2 years follow ups. DMFT.
Notes	Participants randomized (N = 677). Baseline characteristics (age, DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment by one examiner, diagnostic threshold = NR. Radiographic assessment (5-10 BW) by one examiner; diagnostic threshold = NR. State of tooth eruption included = NR. Diagnostic errors NR. **Na N-lauroyl sarcosinate/SMFP toothpaste group not considered (additional non-F active agent used in this group only).

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Zacherl 1981

Methods	Stratified random allocation; double-blind (A); placebo-controlled; 43% drop out after 3 years (study duration = 3 years). Reasons for attrition described: change of residence, absent on examination day, poor quality of x-rays; no differential group losses.
Participants	1754 children analysed at 3 years (available at final examination). Age range at start: 6-13 years (average = 9). Surfaces affected at start: 5.8 DMFS. Background exposure to fluoride: none reported. Year study began: in/before 1977. Location: USA.
Interventions	FT (2 groups) versus PL (SnF2 group = 1000 ppm F, NaF group = 1100 ppm F). Home use/unsupervised, daily frequency assumed. Abrasive system: Ca pyrophosphate in SnF2 and placebo toothpastes, silica in NaF toothpaste.
Outcomes	3yDMFS increment - (CA)cl+(ER)xr. Reported at 1, 2 and 3 years follow ups. DMFT.
Notes	Participants randomized (N = 3093). Baseline characteristics (DMFS, DMFT) 'balanced'. Clinical (VT) caries assessment (FOTI used) by one examiner, diagnostic threshold = CA. Radiographic assessment (postBW) by one examiner; diagnostic threshold = ER. State of tooth eruption included = NR. Intra-examiner reproducibility checks for incremental clinical and radiographic caries data in 10% sample (icc score 0.9). Reversal rate very low and similar among groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Drop-out rate based only on groups relevant to review, on relevant follow ups, unless otherwise stated. Baseline caries experience averaged among relevant study arms, and based on the study sample analysed at the end of study period (final sample), unless otherwise stated. Age range (average age when reported) at the time the study started based on all study participants (or on groups relevant to the review when data were available).
1stm = first permanent molar; 'A' = classified as double-blind but participants may not be blind (as a 'PL' was used); Al = aluminium; Alumina = Al oxide trihydrate (Al2O3); AmF = amine fluoride; APF = acidulated phosphate fluoride; Ca = calcium; Ca carbonate = CaCO3; CA = lesions showing loss of enamel continuity that can be recorded clinically (undermined enamel, softened floor/walls) or showing frank cavitation; CAR = caries attack rate; CIR = caries incidence rate; CFS = caries-free surfaces; CFT = caries-free teeth; Chlor = chlorhexidine diguclonate; cl = clinical examination; d(e)ft/s = decayed, (extracted) and filled deciduous teeth or surface; dmft/s = decayed, missing (or extracted) and filled deciduous teeth or surface; D(M)FS/T = decayed, (missing) and filled permanent surfaces or teeth; DR = radiolucency into dentin; E = teeth erupted at baseline; ECSI = Extrapolated Caries Surface Index (assesses caries progression into enamel/dentin/pulp); ER = any radiolucency in enamel/enamel-dentin junction; F = fluoride; FG = fluoride gel; FR = fluoride mouthrinse; FT = fluoride toothpaste; FV = fluoride varnish; icc = intra-class correlation coefficient (for inter-rater reliability); IMP = insoluble Na metaphosphate; NH4F = Ammonium fluoride; M = missing permanent teeth; MD = mesio and distal surfaces; N = numbers; Na = sodium; NaF = sodium fluoride; Na bicarbonate = NaHCO3; NCA = non-cavitated enamel lesions visible as white spots or discoloured fissures; NR = not reported; NS = not significant; NT = no treatment control; O = occlusal surfaces; PF = pit and fissure surfaces; PL = placebo; 'PL' = fluoride-free but not a true placebo (e.g. different in taste or colour); post BW = posterior bite-wing x-ray assessment; ppm F = parts per million of fluoride; ptc = prior tooth-cleaning performed with or without a non-fluoride paste; Silica = silicon dioxide (SiO2); SMFP = sodium monofluorophosphate; SnF2 = stannous fluoride; U = teeth unerupted at baseline; VT = visual-tactile assessment; xr = radiographic examination.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aasenden 1972	Fluoride solution swallowed after rinsing (even though no systemic effect should be anticipated for this age group).
Antia 1974	Random or quasi-random allocation not stated.
Arcieri 1981	Random or quasi-random allocation not stated. Blind outcome assessment not stated.
Axelsson 1976	Additional fluoride-based intervention associated to fluoride mouthrinse/toothpaste. Blind outcome assessment not stated.
Badersten 1975	Additional non-fluoride based intervention associated to fluoride mouthrinse. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Bellini 1981	Additional fluoride based intervention associated to fluoride gel. Blind outcome assessment not stated and unlikely. Note - no relevant outcome reported.
Bibby 1945	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Billy-Pryga 1983	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Birkeland 1973	Length of follow up of less than 1 year/school year. Relevant outcomes not reported. Blind outcome assessment not stated.
Bixler 1962	Group of participants more than 16 years old selected. Random or quasi-random allocation not stated.
Bixler 1966	Group of young adults selected.
Bixler 1966a	Additional fluoride-based intervention associated to fluoride toothpaste. Group of participants more than 16 years old selected. Blind outcome assessment not stated.

Study	Reason for exclusion
Bohannan 1985a	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Boyd 1985	Additional fluoride based intervention associated to fluoride gel/rinse. Clearly not randomized or quasi-randomized. Blind outcome assessment not stated. Length of follow up of less than 1 year/ school year.
Bristow 1975	Additional interventions associated to fluoride mouthrinse. Only two clusters (schools), each assigned to one of the two study groups.
Brodeur 1989	Open outcome assessment.
Castellanos 1983	Open outcome assessment reported after contacting author.
Chikte 1996	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Clark 1985a	Clearly not randomized or quasi-randomized (concurrent control group taken from another study).
Corpus 1973	Clearly not randomized or quasi-randomized (systematic allocation according to participants' characteristics). Blind outcome assessment not stated or indicated.
de Canton 1983	Additional fluoride and non-fluoride based interventions associated to fluoride mouthrinse. Random or quasi-random allocation not stated.
DePaola 1967	Additional fluoride-based intervention associated to fluoride mouthrinse. Blind outcome assessment not stated.
Disney 1989	Additional non-fluoride based intervention associated to fluoride mouthrinse. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Downer 1976	Additional fluoride-based intervention associated to fluoride toothpaste.
Ennever 1980	Random or quasi-random allocation not stated or indicated.
Esteva Canto 1991	Clearly not randomized or quasi-randomized. Blind outcome assessment not stated or indicated.
Fernandez 1979	Open outcome assessment. Random or quasi-random allocation not stated or indicated.
Finn 1963	Medically compromised group of institutionalised children selected.
Frankl 1972	Fluoride solution swallowed after rinsing (even though no systemic effect should be anticipated for this age group).
Gish 1965	Additional fluoride-based intervention associated to fluoride toothpaste. Blind outcome assessment not stated.
Gray 1980	Additional fluoride-based intervention associated to fluoride mouthrinse.
Grodzka 1982	No random or quasi-random allocation used. Open outcome assessment reported after contacting author.
Gutherz 1968	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Halikis 1966	Random or quasi-random allocation not stated or indicated.

Study	Reason for exclusion
Heifetz 1979	Additional fluoride based intervention associated to fluoride gel/rinse. Note - inappropriate 'placebo' used.
Hetzer 1973	Additional non-fluoride based intervention associated to fluoride varnish. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Heuser 1968	No random or quasi-random allocation used (non-random concurrent control). Blind outcome assessment not stated and unlikely. Varnish applied once in 15 months.
Hill 1959	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Hochstein 1975	Medically compromised group of children selected. No random or quasi-random allocation used (non-random concurrent control). Open outcome assessment.
Irmisch 1974	Additional active agent associated to fluoride in mouthrinse. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Ivanova 1990	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Jiraskova 1965	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Jordan 1959	Only two clusters (schools), each randomized to one of the two interventions compared.
Kani 1973	Random or quasi-random allocation not stated. Blind outcome assessment not stated.
Kasakura 1966	Random or quasi-random allocation not stated. Blind outcome assessment not stated or indicated.
Kitsugi 1978	Additional intervention associated to fluoride mouthrinse.
Kolehmainen 1979	Split-mouth design - sites within a participant's mouth were allocated to treatment and placebo groups.
Kolehmainen 1981	Split-mouth design - sites within a participant's mouth were allocated to treatment and placebo groups.
Kukleva 1983	Random or quasi-random allocation not stated or indicated. Open outcome assessment reported after contacting author.
Kukleva 1998	Random or quasi-random allocation not stated or indicated. Open outcome assessment reported after contacting author.
Kunin 1991	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Kunzel 1977	Additional fluoride-based intervention associated to fluoride toothpaste.
Kunzel 1978	Only two clusters (schools), each assigned to one of the two study groups. Blind outcome assessment not stated or indicated.
Lagutina 1978	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Lehnhoff 1966	Participants more than 16 years old selected.

Study	Reason for exclusion
Lieser 1978	No random or quasi-random allocation used (non-random concurrent control - by matching procedure). Blind outcome assessment not stated and unlikely.
Lindquist 1989	Fluoride based intervention associated to control group.
Louw 1995	Random or quasi-random allocation to groups not stated or indicated. Blind outcome assessment not stated or indicated.
Lu 1985	Additional active agent associated to fluoride in toothpaste.
Luoma 1978	Additional fluoride-based intervention associated to fluoride mouthrinse/toothpaste.
Maiwald 1973	Random or quasi-random allocation not stated or indicated.
Maiwald 1978	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Mari 1988	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Mari 1988a	Random or quasi-random allocation not stated or indicated. Note - two clusters, each assigned to one of the two groups.
McCormick 1970	Random or quasi-random allocation not stated. Note - only post-treatment effects reported.
Mellberg 1978	Blind outcome assessment not stated and unlikely in any element /phase of assessment.
Mendonca 1995	Open outcome assessment reported after contacting author.
Mergele 1968a	Medically compromised group of institutionalised young adults and children selected.
Moller 1968	Additional active agent associated to fluoride in test toothpaste.
Morgan 1998	Additional non-fluoride based intervention associated to fluoride mouthrinse. Blind outcome assessment not stated.
Morozova 1983	Additional intervention associated to fluoride mouthrinse. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Muhler 1955a	Random or quasi-random allocation not stated.
Muhler 1957	Random or quasi-random allocation not stated.
Muhler 1958	Participants more than 16 years old selected. Random or quasi-random allocation not stated.
Muhler 1960	Participants more than 16 years old selected. Random or quasi-random allocation not stated. Blind outcome assessment not stated.
Muhler 1962	Participants more than 16 years old selected.
Murray 1977	Split-mouth design - sites within a participant's mouth were allocated to treatment and placebo groups.
Niwa 1975	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.

Study	Reason for exclusion
Onisi 1970	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated or indicated.
Onisi 1974	Additional active agent associated to fluoride in toothpaste. Only two clusters (villages), each assigned to one of the two interventions compared.
Pashaev 1977	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups. Random or quasi-random allocation not stated. Blind outcome assessment not stated and unlikely.
Patz 1970	Participants more than 16 years old selected. Blind outcome assessment not stated.
Peffley 1960	Participants more than 16 years old selected. Random or quasi-random allocation not stated. Blind outcome assessment not stated.
Petersson 1998	No random or quasi-random allocation used (non-random concurrent controls - by matching procedure). Blind outcome assessment not stated and unlikely .
Piccione 1979	Blind outcome assessment not stated or indicated.
Pinto 1993	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Ramos 1995	Open outcome assessment.
Riethe 1975	Blind outcome assessment not stated or indicated.
Riethe 1977	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Roberts 1948	Clearly not randomized or quasi-randomized (concurrent control group selected by matching procedure).
Rodriguez Miro 1983	Additional active agent associated to fluoride in mouthrinse. Only three clusters (school classes), each assigned to one of the three interventions compared.
Rodriguez Miro 1988	Additional non-fluoride based intervention associated to fluoride varnish.
Ruszynska 1978	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Salem 1979	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Schmidt 1970	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Seppa 1982	Split-mouth design - sites within a participant's mouth were allocated to treatment and control groups.
Shobha 1987	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely. Note - main outcome data not reported in control group (and not obtainable).
Spears 1978	No random or quasi-random allocation used (non-random concurrent control). Blind outcome assessment not stated and unlikely .

Study	Reason for exclusion
	Note - dramatic drop-out rate during the study period.
Stadtler 1982	Medically compromised group of institutionalised children selected.
Stookey 1975	Random or quasi-random allocation not stated.
Suntsov 1991	Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely. Note - only post-treatment effects reported.
Swerdloff 1969	Length of follow up of less than 1 year/school year.
Szoke 1989	Additional fluoride or non-fluoride based intervention associated to fluoride gel. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
Szwejda 1971	No random or quasi-random allocation used (concurrent control taken from another study).
Todorashko 1983	Additional fluoride based intervention associated to fluoride varnish. Random or quasi-random allocation not stated or indicated. Blind outcome assessment not stated and unlikely.
van Eck 1984	No random or quasi-random allocation used (non-random concurrent control - by matching procedure).
Wegner 1976	Medically compromised group of children selected. No random or quasi-random allocation used (non-random concurrent control). Blind outcome assessment not stated and unlikely .
Weisz 1960	Clearly not randomized or quasi-randomized (concurrent control group taken from a different population). Open outcome assessment.
Widenheim 1989	Clearly not randomized or quasi-randomized (concurrent control group taken from a different population). Open outcome assessment.
Wilson 1978	Random or quasi-random allocation not stated.
Winter 1975	No random or quasi-random allocation used (non-random concurrent control). Blind outcome assessment not stated and unlikely .
Wrinkler 1953	Random or quasi-random allocation clearly not used (non-random concurrent control: by matching procedure).
Wycoff 1991	Clearly not randomized or quasi-randomized. Blind outcome assessment not stated or indicated.
Zickert 1982	Additional fluoride-based intervention associated to fluoride mouthrinse/toothpaste.
Zimmer 1999	No random or quasi-random allocation used (non-random concurrent control). Blind outcome assessment not used.

Characteristics of ongoing studies *[ordered by study ID]*

Mancunian

Trial name or title	The Mancunian Fluoride Varnish Project.
Methods	

Mancunian *(Continued)*

Participants	Inclusion criteria: Years 2 and 3 children (aged 6 to 8 years at start). Setting: 24 schools in South Manchester, UK.
Interventions	FV - Duraphat vs NT (NaF group = 22600 ppm F twice a year).
Outcomes	Primary measure: 2-year caries incidence in primary and permanent dentitions.
Starting date	Starting date: 2000.
Contact information	Dr Gill Davies Mancunian Community Health NHS Trust, Mauldeth House, Mauldeth Road West, Chorlton Manchester M21 7RL England +44 161 958 4049 +44 161 958 4045 gill@daviesg28.fsnet.co.uk
Notes	Cluster randomized controlled trial with a single blindness. Expected or actual study completion date: 1 Jun 2003. Participating organisations: University of Manchester. Funding organisation: Inequalities in Health Research Initiative - DOH.

PECC

Trial name or title	Prevention of Early Childhood Caries.
Methods	
Participants	Inclusion criteria: Children aged 6 to 36 months at enrollment, no gender or ethnicity restriction (most are Chinese or Hispanic), with 4 erupted maxillary anterior teeth, without white spots, caries-free on all teeth. Setting: General Hospital and Family Dental Center in California, USA.
Interventions	FV - Duraphat (2 groups) vs PL (NaF group 1 = 22600 ppm F once a year, NaF group 2 = 22600 ppm F twice a year).
Outcomes	Primary measure: 2-year caries incidence in primary dentition.
Starting date	Recruitment phase: 2001.
Contact information	Prof Jane A. Weintraub Division of Oral Epidemiology and Dental Public Health, Department of Preventive and Restorative Dental Sciences, San Francisco School of Dentistry, University of California 3333 California Street, Suite 495 San Francisco CA 94143-1361 USA +1 415 476 3033 +1 415 502 8447

PECC *(Continued)*	
	janew@itsa.ucsf.edu
Notes	Double-blind, parallel design, randomized controlled trial. Expected or actual study completion date: Spring 2004. Participating organizations: University of California, San Francisco. Funding organization: NIH/NIDCR.

DATA AND ANALYSES

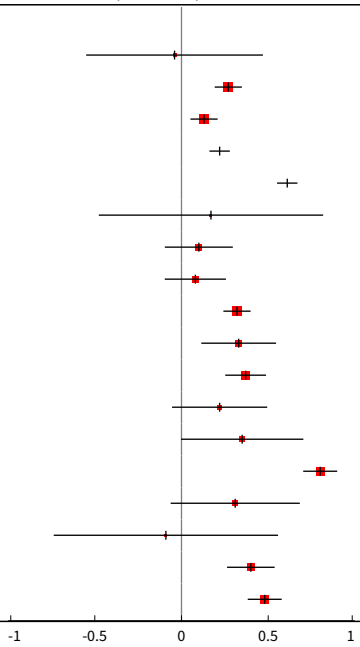
Comparison 1. Topical fluoride versus placebo/no-treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 D(M)FS increment (PF) - nearest to 3 years (133 trials)	133	65179	Prevented Fraction (Random, 95% CI)	0.26 [0.23, 0.29]
1.1 Fluoride toothpaste versus placebo	70	41796	Prevented Fraction (Random, 95% CI)	0.24 [0.21, 0.28]
1.2 Fluoride gel versus placebo	13	4142	Prevented Fraction (Random, 95% CI)	0.21 [0.14, 0.28]
1.3 Fluoride varnish versus placebo	3	1654	Prevented Fraction (Random, 95% CI)	0.40 [0.09, 0.72]
1.4 Fluoride mouthrinse versus placebo	30	13324	Prevented Fraction (Random, 95% CI)	0.26 [0.22, 0.29]
1.5 Fluoride gel versus no-treatment	9	2677	Prevented Fraction (Random, 95% CI)	0.38 [0.23, 0.53]
1.6 Fluoride varnish versus no-treatment	4	624	Prevented Fraction (Random, 95% CI)	0.52 [0.35, 0.69]
1.7 Fluoride mouthrinse versus no-treatment	4	962	Prevented Fraction (Random, 95% CI)	0.33 [0.27, 0.40]
2 D(M)FT increment (PF) - nearest to 3 years (79 trials)	79	41391	Prevented Fraction (Random, 95% CI)	0.26 [0.21, 0.30]
2.1 Fluoride toothpaste versus placebo	53	32186	Prevented Fraction (Random, 95% CI)	0.23 [0.19, 0.28]
2.2 Fluoride gel versus placebo	4	1525	Prevented Fraction (Random, 95% CI)	0.18 [0.09, 0.27]
2.3 Fluoride varnish versus placebo	2	978	Prevented Fraction (Random, 95% CI)	0.49 [0.02, 0.96]
2.4 Fluoride mouthrinse versus placebo	13	4920	Prevented Fraction (Random, 95% CI)	0.24 [0.18, 0.30]

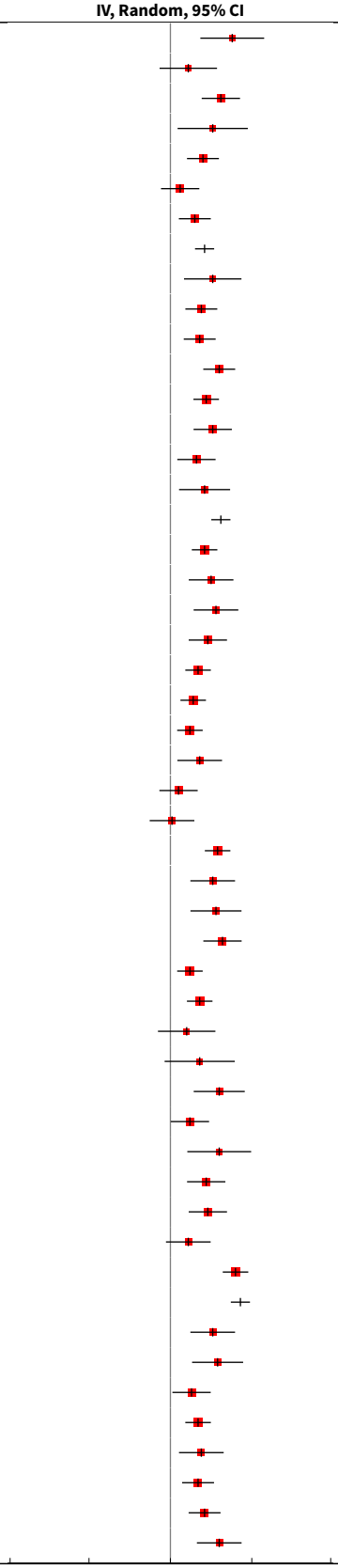
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.5 Fluoride gel versus no-treatment	6	1673	Prevented Fraction (Random, 95% CI)	0.43 [0.29, 0.57]
2.6 Fluoride varnish versus no-treatment	1	109	Prevented Fraction (Random, 95% CI)	0.6 [0.36, 0.84]
3 d(e)fs increment (PF) - nearest to 3 years (5 trials)	5	1685	Prevented Fraction (Random, 95% CI)	0.33 [0.22, 0.44]
3.1 Fluoride gel versus placebo	2	578	Prevented Fraction (Random, 95% CI)	0.26 [-0.11, 0.63]
3.2 Fluoride varnish versus placebo	1	676	Prevented Fraction (Random, 95% CI)	0.2 [0.02, 0.38]
3.3 Fluoride varnish versus no-treatment	2	431	Prevented Fraction (Random, 95% CI)	0.41 [0.26, 0.55]
4 Developing one or more new caries (12 trials)	13	5297	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.82, 0.95]
5 Unacceptability of treatment as measured by leaving study early (10 trials)	10	2897	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.85, 1.70]

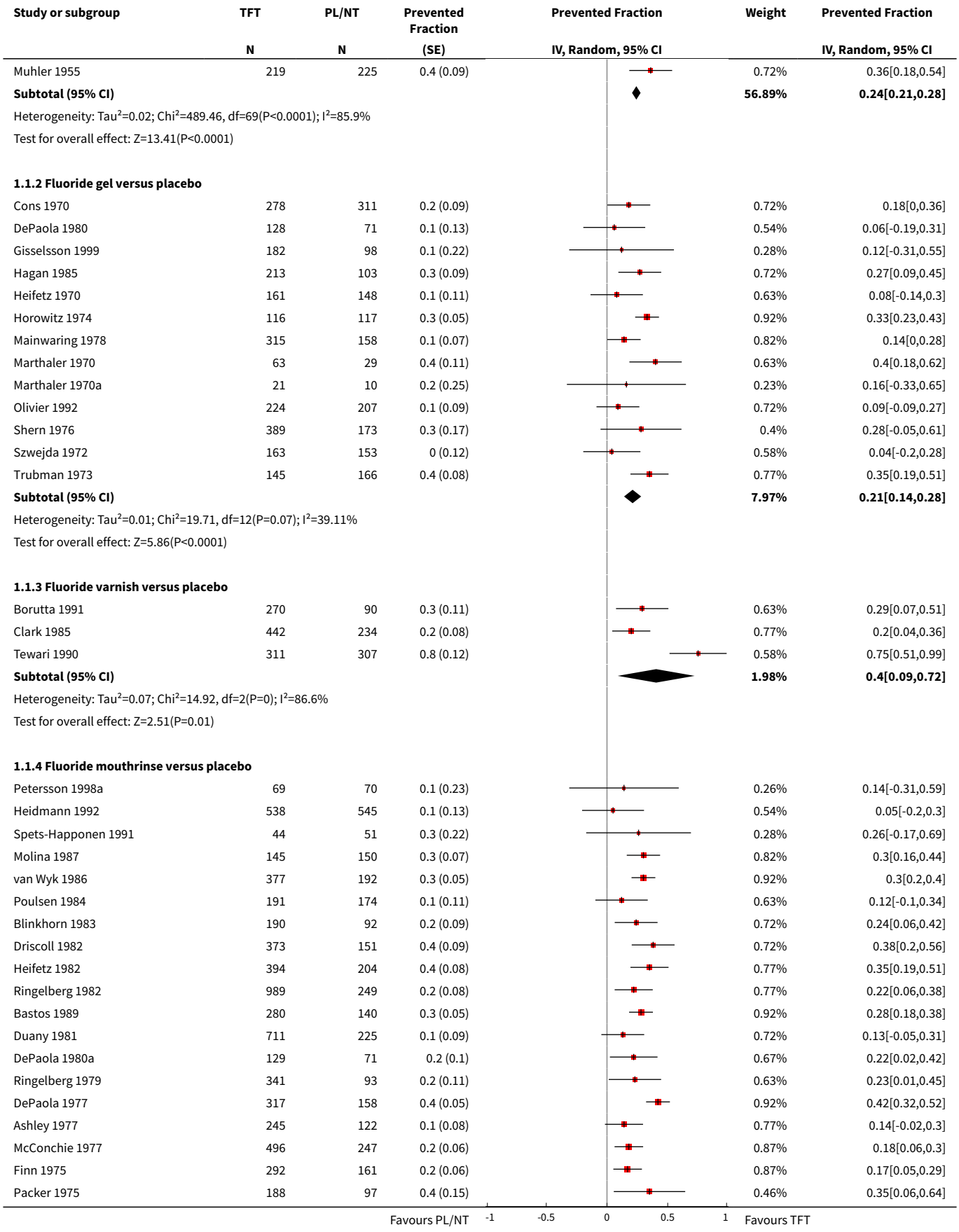
Analysis 1.1. Comparison 1 Topical fluoride versus placebo/no-treatment, Outcome 1 D(M)FS increment (PF) - nearest to 3 years (133 trials).

Study or subgroup	TFT N	PL/NT N	Prevented Fraction (SE)	Prevented Fraction IV, Random, 95% CI	Weight	Prevented Fraction IV, Random, 95% CI
1.1.1 Fluoride toothpaste versus placebo						
Kleber 1996	77	79	-0 (0.26)		0.22%	-0.04[-0.55,0.47]
Hanachowicz 1984	473	472	0.3 (0.04)		0.96%	0.27[0.19,0.35]
Cahen 1982	1300	708	0.1 (0.04)		0.96%	0.13[0.05,0.21]
Buhe 1984	859	427	0.2 (0.03)		1%	0.22[0.16,0.28]
Di Maggio 1980	22	20	0.6 (0.03)		1%	0.61[0.55,0.67]
Dolles 1980	24	23	0.2 (0.33)		0.15%	0.17[-0.48,0.82]
Forsman 1974	414	145	0.1 (0.1)		0.67%	0.1[-0.1,0.3]
Forsman 1974a	262	132	0.1 (0.09)		0.72%	0.08[-0.1,0.26]
Lind 1974	592	575	0.3 (0.04)		0.96%	0.32[0.24,0.4]
Marthaler 1974	50	59	0.3 (0.11)		0.63%	0.33[0.11,0.55]
Kinkel 1972	354	345	0.4 (0.06)		0.87%	0.37[0.25,0.49]
Marthaler 1970b	43	28	0.2 (0.14)		0.5%	0.22[-0.05,0.49]
Marthaler 1970c	23	10	0.4 (0.18)		0.37%	0.35[-0,0.7]
Held 1968	32	31	0.8 (0.05)		0.92%	0.8[0.7,0.9]
Held 1968a	19	17	0.3 (0.19)		0.35%	0.31[-0.06,0.68]
Held 1968b	14	18	-0.1 (0.33)		0.15%	-0.09[-0.74,0.56]
Koch 1967c	64	60	0.4 (0.07)		0.82%	0.4[0.26,0.54]
Koch 1967d	60	60	0.5 (0.05)		0.92%	0.48[0.38,0.58]

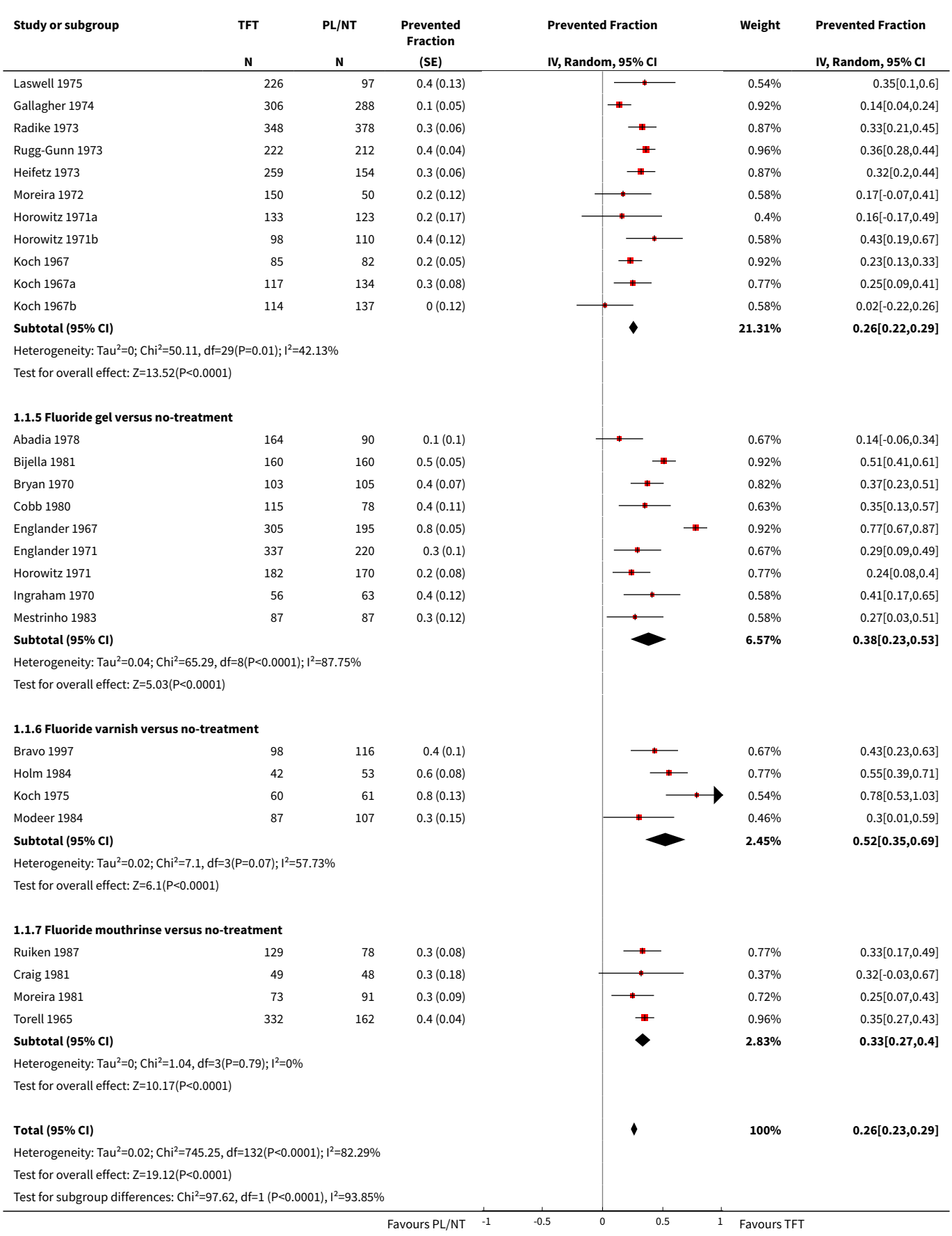


Study or subgroup	TFT N	PL/NT N	Prevented Fraction (SE)	Prevented Fraction IV, Random, 95% CI	Weight	Prevented Fraction IV, Random, 95% CI
Koch 1967e	32	38	0.4 (0.1)		0.67%	0.38[0.18,0.58]
Koch 1967f	127	128	0.1 (0.09)		0.72%	0.11[-0.07,0.29]
Marthaler 1965	145	124	0.3 (0.06)		0.87%	0.31[0.19,0.43]
Marthaler 1965a	42	32	0.3 (0.11)		0.63%	0.26[0.04,0.48]
Torell 1965a	335	333	0.2 (0.05)		0.92%	0.2[0.1,0.3]
Torell 1965b	148	137	0.1 (0.06)		0.87%	0.06[-0.06,0.18]
Torell 1965c	188	180	0.2 (0.05)		0.92%	0.15[0.05,0.25]
Fanning 1968	422	422	0.2 (0.03)		1%	0.21[0.15,0.27]
Blinkhorn 1983a	184	92	0.3 (0.09)		0.72%	0.26[0.08,0.44]
Mainwaring 1983	458	224	0.2 (0.05)		0.92%	0.19[0.09,0.29]
Hodge 1980	597	202	0.2 (0.05)		0.92%	0.18[0.08,0.28]
Murray 1980	750	356	0.3 (0.05)		0.92%	0.3[0.2,0.4]
Naylor 1979	319	306	0.2 (0.04)		0.96%	0.22[0.14,0.3]
Howat 1978	253	242	0.3 (0.06)		0.87%	0.26[0.14,0.38]
Mainwaring 1978a	791	158	0.2 (0.06)		0.87%	0.16[0.04,0.28]
Ashley 1977a	246	121	0.2 (0.08)		0.77%	0.21[0.05,0.37]
James 1977	403	379	0.3 (0.03)		1%	0.31[0.25,0.37]
Andlaw 1975	364	376	0.2 (0.04)		0.96%	0.21[0.13,0.29]
Hargreaves 1973	163	140	0.3 (0.07)		0.82%	0.25[0.11,0.39]
Hargreaves 1973a	146	138	0.3 (0.07)		0.82%	0.28[0.14,0.42]
Hargreaves 1973b	146	151	0.2 (0.06)		0.87%	0.23[0.11,0.35]
Slack 1971	821	289	0.2 (0.04)		0.96%	0.17[0.09,0.25]
Naylor 1967	494	479	0.1 (0.04)		0.96%	0.14[0.06,0.22]
Jackson 1967	438	433	0.1 (0.04)		0.96%	0.12[0.04,0.2]
James 1967	406	397	0.2 (0.07)		0.82%	0.18[0.04,0.32]
Slack 1967a	376	381	0.1 (0.06)		0.87%	0.05[-0.07,0.17]
Slack 1967	356	340	0 (0.07)		0.82%	0.01[-0.13,0.15]
Rule 1984	460	416	0.3 (0.04)		0.96%	0.29[0.21,0.37]
Glass 1983	567	286	0.3 (0.07)		0.82%	0.26[0.12,0.4]
Glass 1978	178	168	0.3 (0.08)		0.77%	0.28[0.12,0.44]
Zacherl 1981	1500	254	0.3 (0.06)		0.87%	0.32[0.2,0.44]
Abrams 1980	761	380	0.1 (0.04)		0.96%	0.12[0.04,0.2]
Fogels 1979	890	449	0.2 (0.04)		0.96%	0.18[0.1,0.26]
Peterson 1979	467	245	0.1 (0.09)		0.72%	0.1[-0.08,0.28]
Ringelberg 1979a	370	93	0.2 (0.11)		0.63%	0.18[-0.04,0.4]
Reed 1975	168	176	0.3 (0.08)		0.77%	0.3[0.14,0.46]
Reed 1973	1128	397	0.1 (0.06)		0.87%	0.12[0,0.24]
Zacherl 1973	220	224	0.3 (0.1)		0.67%	0.3[0.1,0.5]
Zacherl 1972	231	216	0.2 (0.06)		0.87%	0.22[0.1,0.34]
Zacherl 1972a	684	210	0.2 (0.06)		0.87%	0.23[0.11,0.35]
Weisenstein 1972	206	196	0.1 (0.07)		0.82%	0.11[-0.03,0.25]
Zacherl 1970	251	261	0.4 (0.04)		0.96%	0.4[0.32,0.48]
Zacherl 1970a	260	268	0.4 (0.03)		1%	0.43[0.37,0.49]
Gish 1966	165	163	0.3 (0.07)		0.82%	0.26[0.12,0.4]
Muhler 1970	201	235	0.3 (0.08)		0.77%	0.29[0.13,0.45]
Mergele 1968	197	190	0.1 (0.06)		0.87%	0.13[0.01,0.25]
Peterson 1967	634	320	0.2 (0.04)		0.96%	0.17[0.09,0.25]
Segal 1967	338	310	0.2 (0.07)		0.82%	0.19[0.05,0.33]
Horowitz 1966	329	309	0.2 (0.05)		0.92%	0.17[0.07,0.27]
Brudevold 1966	955	323	0.2 (0.05)		0.92%	0.21[0.11,0.31]
Thomas 1966	309	155	0.3 (0.07)		0.82%	0.3[0.16,0.44]



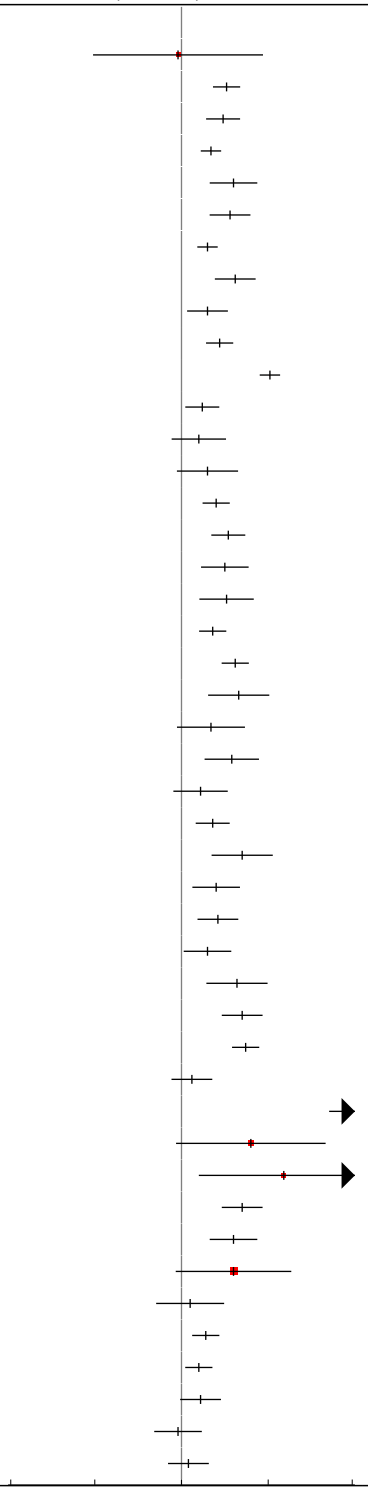


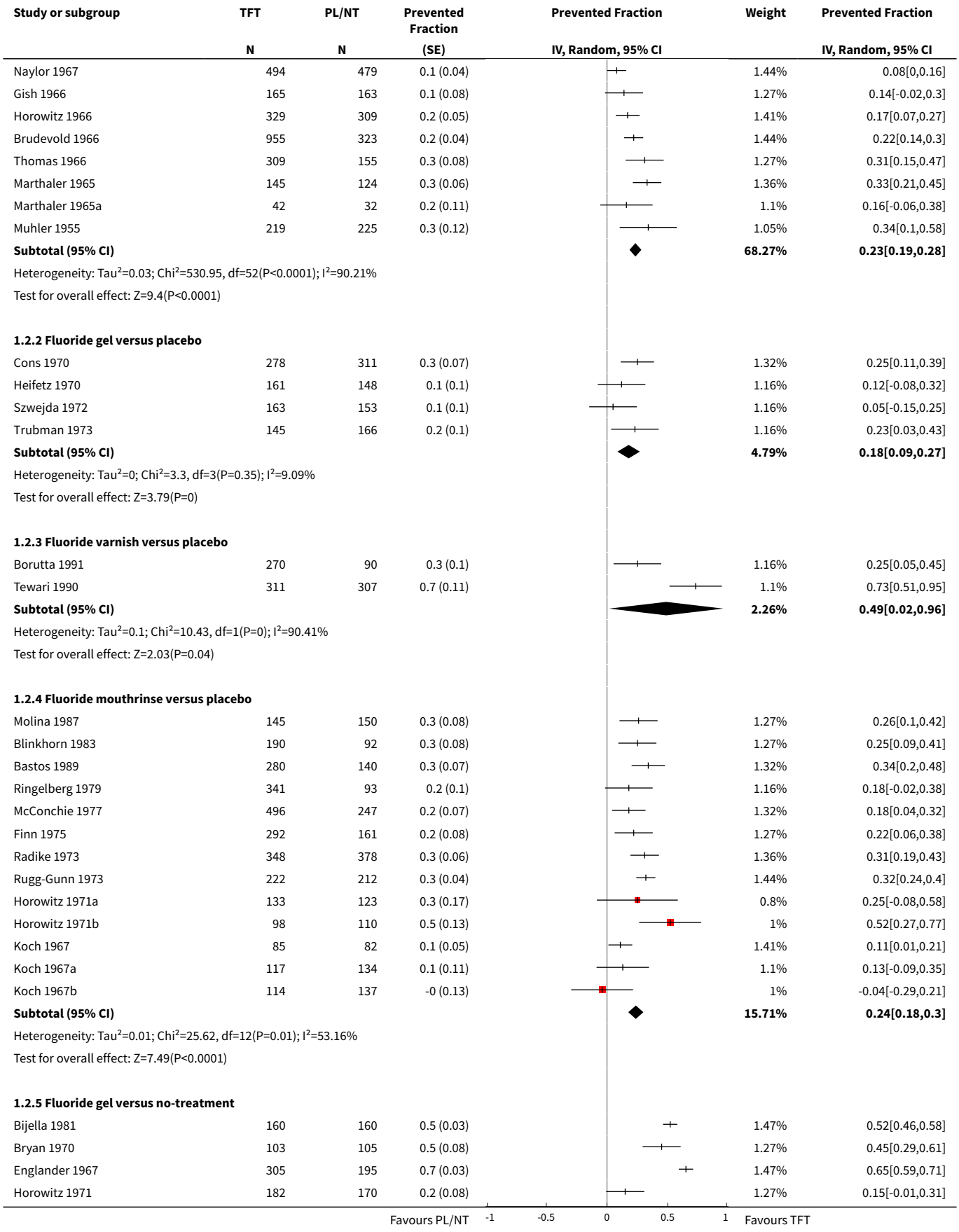
Study or subgroup	TFT N	PL/NT N	Prevented Fraction (SE)	Prevented Fraction IV, Random, 95% CI	Weight	Prevented Fraction IV, Random, 95% CI
Muhler 1955	219	225	0.4 (0.09)		0.72%	0.36[0.18,0.54]
Subtotal (95% CI)					**56.89%**	**0.24[0.21,0.28]**
Heterogeneity: Tau²=0.02; Chi²=489.46, df=69(P<0.0001); I²=85.9%						
Test for overall effect: Z=13.41(P<0.0001)						
1.1.2 Fluoride gel versus placebo						
Cons 1970	278	311	0.2 (0.09)		0.72%	0.18[0,0.36]
DePaola 1980	128	71	0.1 (0.13)		0.54%	0.06[-0.19,0.31]
Gisselsson 1999	182	98	0.1 (0.22)		0.28%	0.12[-0.31,0.55]
Hagan 1985	213	103	0.3 (0.09)		0.72%	0.27[0.09,0.45]
Heifetz 1970	161	148	0.1 (0.11)		0.63%	0.08[-0.14,0.3]
Horowitz 1974	116	117	0.3 (0.05)		0.92%	0.33[0.23,0.43]
Mainwaring 1978	315	158	0.1 (0.07)		0.82%	0.14[0,0.28]
Marthaler 1970	63	29	0.4 (0.11)		0.63%	0.4[0.18,0.62]
Marthaler 1970a	21	10	0.2 (0.25)		0.23%	0.16[-0.33,0.65]
Olivier 1992	224	207	0.1 (0.09)		0.72%	0.09[-0.09,0.27]
Shern 1976	389	173	0.3 (0.17)		0.4%	0.28[-0.05,0.61]
Szwejda 1972	163	153	0 (0.12)		0.58%	0.04[-0.2,0.28]
Trubman 1973	145	166	0.4 (0.08)		0.77%	0.35[0.19,0.51]
Subtotal (95% CI)					**7.97%**	**0.21[0.14,0.28]**
Heterogeneity: Tau²=0.01; Chi²=19.71, df=12(P=0.07); I²=39.11%						
Test for overall effect: Z=5.86(P<0.0001)						
1.1.3 Fluoride varnish versus placebo						
Borutta 1991	270	90	0.3 (0.11)		0.63%	0.29[0.07,0.51]
Clark 1985	442	234	0.2 (0.08)		0.77%	0.2[0.04,0.36]
Tewari 1990	311	307	0.8 (0.12)		0.58%	0.75[0.51,0.99]
Subtotal (95% CI)					**1.98%**	**0.4[0.09,0.72]**
Heterogeneity: Tau²=0.07; Chi²=14.92, df=2(P=0); I²=86.6%						
Test for overall effect: Z=2.51(P=0.01)						
1.1.4 Fluoride mouthrinse versus placebo						
Petersson 1998a	69	70	0.1 (0.23)		0.26%	0.14[-0.31,0.59]
Heidmann 1992	538	545	0.1 (0.13)		0.54%	0.05[-0.2,0.3]
Spets-Happonen 1991	44	51	0.3 (0.22)		0.28%	0.26[-0.17,0.69]
Molina 1987	145	150	0.3 (0.07)		0.82%	0.3[0.16,0.44]
van Wyk 1986	377	192	0.3 (0.05)		0.92%	0.3[0.2,0.4]
Poulsen 1984	191	174	0.1 (0.11)		0.63%	0.12[-0.1,0.34]
Blinkhorn 1983	190	92	0.2 (0.09)		0.72%	0.24[0.06,0.42]
Driscoll 1982	373	151	0.4 (0.09)		0.72%	0.38[0.2,0.56]
Heifetz 1982	394	204	0.4 (0.08)		0.77%	0.35[0.19,0.51]
Ringelberg 1982	989	249	0.2 (0.08)		0.77%	0.22[0.06,0.38]
Bastos 1989	280	140	0.3 (0.05)		0.92%	0.28[0.18,0.38]
Duany 1981	711	225	0.1 (0.09)		0.72%	0.13[-0.05,0.31]
DePaola 1980a	129	71	0.2 (0.1)		0.67%	0.22[0.02,0.42]
Ringelberg 1979	341	93	0.2 (0.11)		0.63%	0.23[0.01,0.45]
DePaola 1977	317	158	0.4 (0.05)		0.92%	0.42[0.32,0.52]
Ashley 1977	245	122	0.1 (0.08)		0.77%	0.14[-0.02,0.3]
McConchie 1977	496	247	0.2 (0.06)		0.87%	0.18[0.06,0.3]
Finn 1975	292	161	0.2 (0.06)		0.87%	0.17[0.05,0.29]
Packer 1975	188	97	0.4 (0.15)		0.46%	0.35[0.06,0.64]



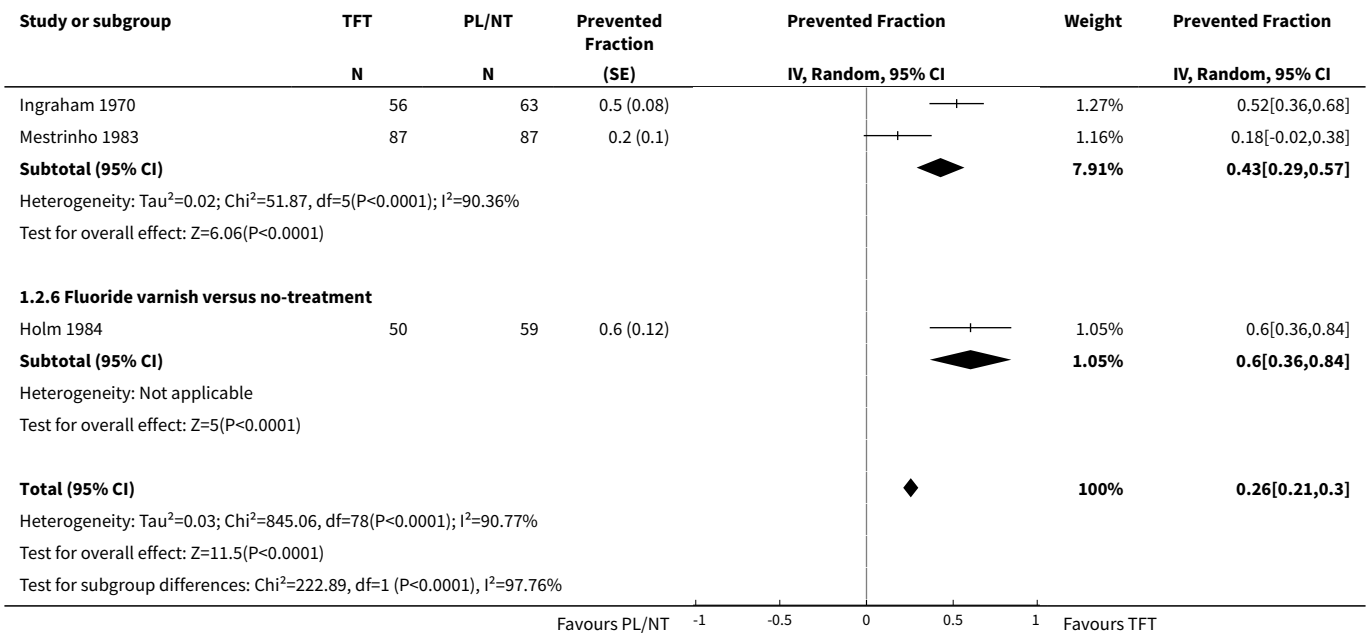
Analysis 1.2. Comparison 1 Topical fluoride versus placebo/no-treatment, Outcome 2 D(M)FT increment (PF) - nearest to 3 years (79 trials).

Study or subgroup	TFT N	PL/NT N	Prevented Fraction (SE)	Prevented Fraction IV, Random, 95% CI	Weight	Prevented Fraction IV, Random, 95% CI
1.2.1 Fluoride toothpaste versus placebo						
Kleber 1996	77	79	-0 (0.25)		0.52%	-0.02[-0.51,0.47]
Hanachowicz 1984	473	472	0.3 (0.04)		1.44%	0.26[0.18,0.34]
Rule 1984	460	416	0.2 (0.05)		1.41%	0.24[0.14,0.34]
Buhe 1984	859	427	0.2 (0.03)		1.47%	0.17[0.11,0.23]
Blinkhorn 1983a	184	92	0.3 (0.07)		1.32%	0.3[0.16,0.44]
Glass 1983	567	286	0.3 (0.06)		1.36%	0.28[0.16,0.4]
Cahen 1982	1300	708	0.2 (0.03)		1.47%	0.15[0.09,0.21]
Zacherl 1981	1500	254	0.3 (0.06)		1.36%	0.31[0.19,0.43]
Abrams 1980	761	380	0.2 (0.06)		1.36%	0.15[0.03,0.27]
Hodge 1980	597	202	0.2 (0.04)		1.44%	0.22[0.14,0.3]
Di Maggio 1980	22	20	0.5 (0.03)		1.47%	0.51[0.45,0.57]
Fogels 1979	890	449	0.1 (0.05)		1.41%	0.12[0.02,0.22]
Peterson 1979	467	245	0.1 (0.08)		1.27%	0.1[-0.06,0.26]
Ringelberg 1979a	370	93	0.2 (0.09)		1.21%	0.15[-0.03,0.33]
Naylor 1979	319	306	0.2 (0.04)		1.44%	0.2[0.12,0.28]
Howat 1978	253	242	0.3 (0.05)		1.41%	0.27[0.17,0.37]
Glass 1978	178	168	0.3 (0.07)		1.32%	0.25[0.11,0.39]
Reed 1975	168	176	0.3 (0.08)		1.27%	0.26[0.1,0.42]
Andlaw 1975	364	376	0.2 (0.04)		1.44%	0.18[0.1,0.26]
Lind 1974	592	575	0.3 (0.04)		1.44%	0.31[0.23,0.39]
Marthaler 1974	50	59	0.3 (0.09)		1.21%	0.33[0.15,0.51]
Hargreaves 1973	163	140	0.2 (0.1)		1.16%	0.17[-0.03,0.37]
Hargreaves 1973a	146	138	0.3 (0.08)		1.27%	0.29[0.13,0.45]
Hargreaves 1973b	146	151	0.1 (0.08)		1.27%	0.11[-0.05,0.27]
Reed 1973	1128	397	0.2 (0.05)		1.41%	0.18[0.08,0.28]
Zacherl 1973	220	224	0.4 (0.09)		1.21%	0.35[0.17,0.53]
Zacherl 1972	231	216	0.2 (0.07)		1.32%	0.2[0.06,0.34]
Zacherl 1972a	684	210	0.2 (0.06)		1.36%	0.21[0.09,0.33]
Weisenstein 1972	206	196	0.2 (0.07)		1.32%	0.15[0.01,0.29]
Muhler 1970	201	235	0.3 (0.09)		1.21%	0.32[0.14,0.5]
Zacherl 1970	251	261	0.4 (0.06)		1.36%	0.35[0.23,0.47]
Zacherl 1970a	260	268	0.4 (0.04)		1.44%	0.37[0.29,0.45]
Mergele 1968	197	190	0.1 (0.06)		1.36%	0.06[-0.06,0.18]
Held 1968	32	31	0.9 (0.04)		1.44%	0.93[0.85,1.01]
Held 1968a	19	17	0.4 (0.22)		0.61%	0.4[-0.03,0.83]
Held 1968b	14	18	0.6 (0.25)		0.52%	0.59[0.1,1.08]
Koch 1967c	64	60	0.4 (0.06)		1.36%	0.35[0.23,0.47]
Koch 1967d	60	60	0.3 (0.07)		1.32%	0.3[0.16,0.44]
Koch 1967e	32	38	0.3 (0.17)		0.8%	0.3[-0.03,0.63]
Koch 1967f	127	128	0.1 (0.1)		1.16%	0.05[-0.15,0.25]
Peterson 1967	636	320	0.1 (0.04)		1.44%	0.14[0.06,0.22]
Jackson 1967	438	433	0.1 (0.04)		1.44%	0.1[0.02,0.18]
James 1967	406	397	0.1 (0.06)		1.36%	0.11[-0.01,0.23]
Slack 1967	356	340	-0 (0.07)		1.32%	-0.02[-0.16,0.12]
Slack 1967a	376	381	0 (0.06)		1.36%	0.04[-0.08,0.16]

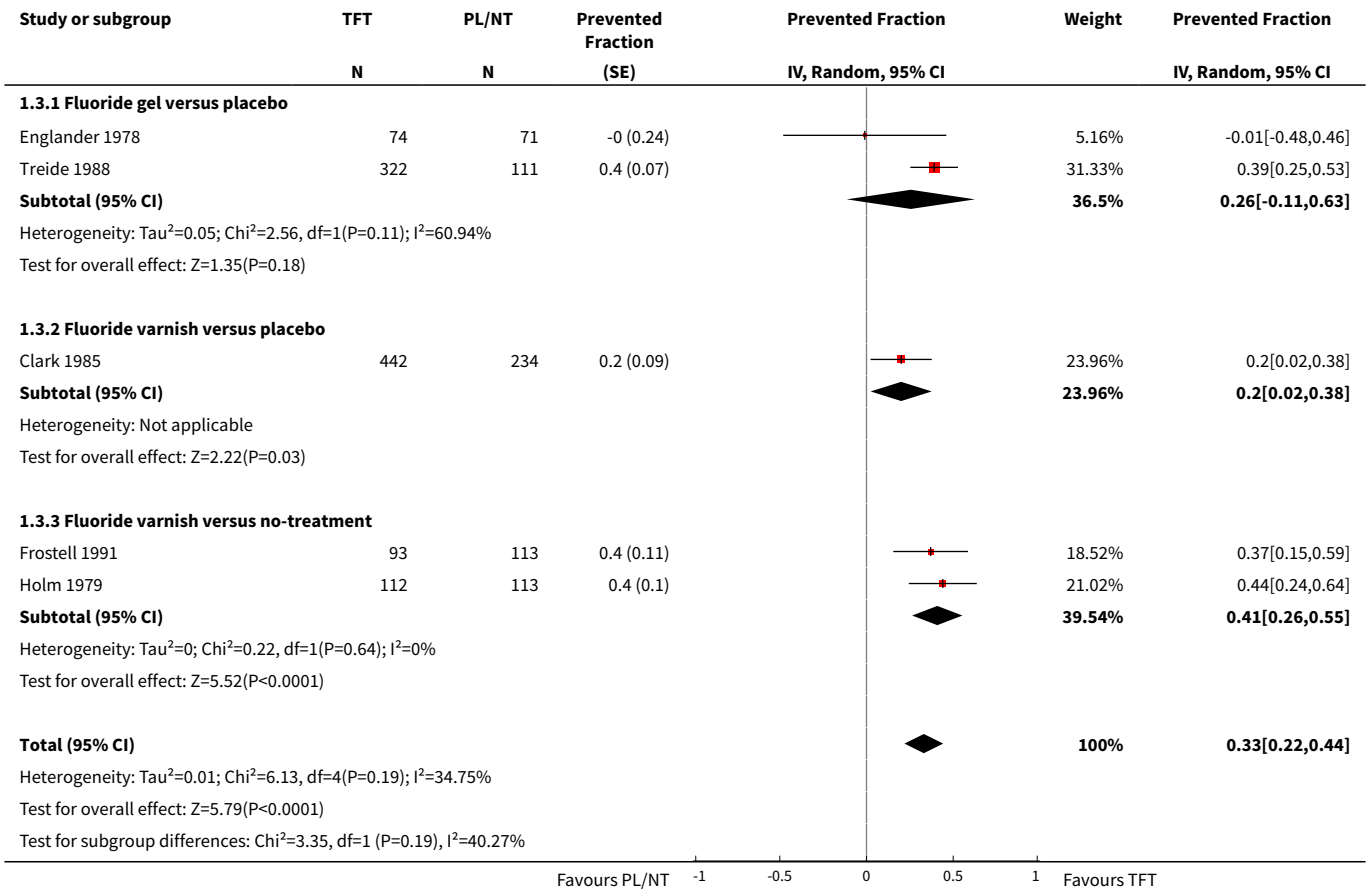




Study or subgroup	TFT N	PL/NT N	Prevented Fraction (SE)	Prevented Fraction IV, Random, 95% CI	Weight	Prevented Fraction IV, Random, 95% CI
Naylor 1967	494	479	0.1 (0.04)		1.44%	0.08[0,0.16]
Gish 1966	165	163	0.1 (0.08)		1.27%	0.14[-0.02,0.3]
Horowitz 1966	329	309	0.2 (0.05)		1.41%	0.17[0.07,0.27]
Brudevold 1966	955	323	0.2 (0.04)		1.44%	0.22[0.14,0.3]
Thomas 1966	309	155	0.3 (0.08)		1.27%	0.31[0.15,0.47]
Marthaler 1965	145	124	0.3 (0.06)		1.36%	0.33[0.21,0.45]
Marthaler 1965a	42	32	0.2 (0.11)		1.1%	0.16[-0.06,0.38]
Muhler 1955	219	225	0.3 (0.12)		1.05%	0.34[0.1,0.58]
Subtotal (95% CI)					**68.27%**	**0.23[0.19,0.28]**
Heterogeneity: Tau²=0.03; Chi²=530.95, df=52(P<0.0001); I²=90.21%						
Test for overall effect: Z=9.4(P<0.0001)						
1.2.2 Fluoride gel versus placebo						
Cons 1970	278	311	0.3 (0.07)		1.32%	0.25[0.11,0.39]
Heifetz 1970	161	148	0.1 (0.1)		1.16%	0.12[-0.08,0.32]
Szwejda 1972	163	153	0.1 (0.1)		1.16%	0.05[-0.15,0.25]
Trubman 1973	145	166	0.2 (0.1)		1.16%	0.23[0.03,0.43]
Subtotal (95% CI)					**4.79%**	**0.18[0.09,0.27]**
Heterogeneity: Tau²=0; Chi²=3.3, df=3(P=0.35); I²=9.09%						
Test for overall effect: Z=3.79(P=0)						
1.2.3 Fluoride varnish versus placebo						
Borutta 1991	270	90	0.3 (0.1)		1.16%	0.25[0.05,0.45]
Tewari 1990	311	307	0.7 (0.11)		1.1%	0.73[0.51,0.95]
Subtotal (95% CI)					**2.26%**	**0.49[0.02,0.96]**
Heterogeneity: Tau²=0.1; Chi²=10.43, df=1(P=0); I²=90.41%						
Test for overall effect: Z=2.03(P=0.04)						
1.2.4 Fluoride mouthrinse versus placebo						
Molina 1987	145	150	0.3 (0.08)		1.27%	0.26[0.1,0.42]
Blinkhorn 1983	190	92	0.3 (0.08)		1.27%	0.25[0.09,0.41]
Bastos 1989	280	140	0.3 (0.07)		1.32%	0.34[0.2,0.48]
Ringelberg 1979	341	93	0.2 (0.1)		1.16%	0.18[-0.02,0.38]
McConchie 1977	496	247	0.2 (0.07)		1.32%	0.18[0.04,0.32]
Finn 1975	292	161	0.2 (0.08)		1.27%	0.22[0.06,0.38]
Radike 1973	348	378	0.3 (0.06)		1.36%	0.31[0.19,0.43]
Rugg-Gunn 1973	222	212	0.3 (0.04)		1.44%	0.32[0.24,0.4]
Horowitz 1971a	133	123	0.3 (0.17)		0.8%	0.25[-0.08,0.58]
Horowitz 1971b	98	110	0.5 (0.13)		1%	0.52[0.27,0.77]
Koch 1967	85	82	0.1 (0.05)		1.41%	0.11[0.01,0.21]
Koch 1967a	117	134	0.1 (0.11)		1.1%	0.13[-0.09,0.35]
Koch 1967b	114	137	-0 (0.13)		1%	-0.04[-0.29,0.21]
Subtotal (95% CI)					**15.71%**	**0.24[0.18,0.3]**
Heterogeneity: Tau²=0.01; Chi²=25.62, df=12(P=0.01); I²=53.16%						
Test for overall effect: Z=7.49(P<0.0001)						
1.2.5 Fluoride gel versus no-treatment						
Bijella 1981	160	160	0.5 (0.03)		1.47%	0.52[0.46,0.58]
Bryan 1970	103	105	0.5 (0.08)		1.27%	0.45[0.29,0.61]
Englander 1967	305	195	0.7 (0.03)		1.47%	0.65[0.59,0.71]
Horowitz 1971	182	170	0.2 (0.08)		1.27%	0.15[-0.01,0.31]

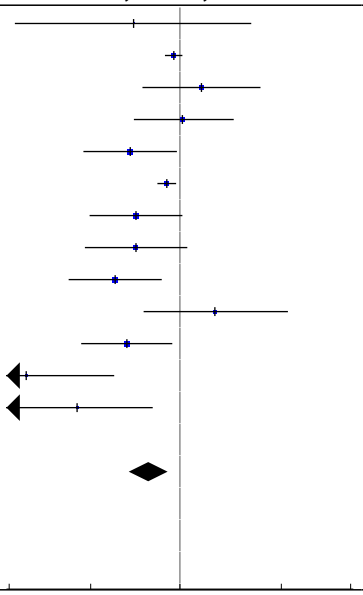


Analysis 1.3. Comparison 1 Topical fluoride versus placebo/no-treatment, Outcome 3 d(e)fs increment (PF) - nearest to 3 years (5 trials).



Analysis 1.4. Comparison 1 Topical fluoride versus placebo/no-treatment, Outcome 4 Developing one or more new caries (12 trials).

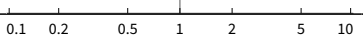
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Dolles 1980	13/24	15/23		2.29%	0.83[0.52,1.33]
Finn 1975	278/292	157/161		14.95%	0.98[0.94,1.01]
Forsman 1974	174/414	56/145		6.42%	1.09[0.86,1.38]
Forsman 1974a	139/262	69/132		7.68%	1.01[0.83,1.24]
Gisselsson 1999	102/182	67/98		8.18%	0.82[0.68,0.99]
Hanachowicz 1984	425/473	447/472		14.91%	0.95[0.91,0.98]
Heidmann 1992	134/426	162/432		8.21%	0.84[0.7,1.01]
Holm 1979	64/112	77/113		7.48%	0.84[0.68,1.03]
Holm 1984	36/50	55/59		8.19%	0.77[0.64,0.93]
Kleber 1996	45/77	40/79		4.95%	1.15[0.87,1.54]
Marthaler 1974	37/50	54/59		8.37%	0.81[0.67,0.97]
Torell 1965	51/332	46/162		3.71%	0.54[0.38,0.77]
Torell 1965a	56/335	84/333		4.63%	0.66[0.49,0.9]
Total (95% CI)	**3029**	**2268**		**100%**	**0.88[0.82,0.95]**
Total events: 1554 (Treatment), 1329 (Control)					
Heterogeneity: Tau^2=0.01; Chi^2=53.88, df=12(P<0.0001); I^2=77.73%					
Test for overall effect: Z=3.19(P=0)					



Favours TFT — Favours control

Analysis 1.5. Comparison 1 Topical fluoride versus placebo/no-treatment, Outcome 5 Unacceptability of treatment as measured by leaving study early (10 trials).

Study or subgroup	TFT n/N	NT n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Abadia 1978	29/193	8/98		8.58%	1.84[0.87,3.87]
Bryan 1970	36/139	43/148		12.14%	0.89[0.61,1.3]
Cobb 1980	15/130	29/107		10.27%	0.43[0.24,0.75]
Craig 1981	5/54	7/55		5.95%	0.73[0.25,2.15]
Englander 1967	64/369	10/205		9.53%	3.56[1.87,6.77]
Holm 1979	13/125	12/125		8.58%	1.08[0.51,2.28]
Horowitz 1971	94/276	106/276		13.4%	0.89[0.71,1.11]
Ingraham 1970	17/73	19/82		10.22%	1.01[0.57,1.78]
Modeer 1984	31/118	11/118		9.58%	2.82[1.49,5.34]
Moreira 1981	42/115	24/91		11.75%	1.38[0.91,2.11]
Total (95% CI)	**1592**	**1305**		**100%**	**1.2[0.85,1.7]**
Total events: 346 (TFT), 269 (NT)					
Heterogeneity: Tau^2=0.22; Chi^2=40.85, df=9(P<0.0001); I^2=77.97%					
Test for overall effect: Z=1.02(P=0.31)					



Favours TFT — Favours NT

ADDITIONAL TABLES

Table 1. Random-effects metaregression analyses of prevented fractions: D(M)FS

Characteristic	Number of studies	Slope estimate	95% CI	Slope interpretation	P-value
F Gel vs F Varnish (indirect comparison)	29	-15%	(-28% to -1.6%)	PF lower among Fluoride Gel trials	0.03
F Mouthrinse vs F Varnish (indirect comparison)	41	-14%	(-27% to -0.5%)	PF lower among Fluoride Mouthrinse trials	0.04
F Toothpaste vs F Varnish (indirect comparison)	77	-14%	(-27% to -0.6%)	PF lower among Fluoride Toothpaste trials	0.04
Control group	133	14%	(5% to 23%)	Higher PF for no-treatment compared with placebo	0.002
Mean baseline caries	126	0.7%	(0.2% to 1.2%)	Increase in PF per unit increase in mean baseline caries	0.004
Fluoridated water	116	2.9%	(-3.3% to 9.1%)	Higher PF in presence of water fluoridation	0.4
Background fluorides	115	-1.5%	(-6.7% to 3.7%)	Lower PF in presence of any background fluoride	0.6
Operator vs unsupervised (indirect comparison)	76	-3.4%	(-18% to 11%)	PF lower among operator applied TFT	0.7
Self applied supervised vs unsupervised (indirect comparison)	111	11%	(3.7% to 17%)	PF higher among self applied supervised TFT	0.002
Mode of use	133	13%	(0.12% to 27%)	PF higher among self applied (supervised plus unsupervised) TFT	0.5
Intensity (frequency x concentration)	128 (excludes Di Maggio 1980)	2.5%	(1% to 3.9%)	Increase in PF equivalent to doubling from 100 to 200 applications and increasing by 1000 ppmF	0.001
Frequency of application	131 (excludes Di Maggio 1980)	3%	(0.4% to 5.7%)	Increase in PF per 100 extra applications/year	0.03
Fluoride concentration	129	-0.3%	(-1.4% to 0.9%)	Decrease in PF per 1000 ppm F	0.6
Method of application	133	-3.8%	(-21% to 14%)	Lower PF for tray or paint compared with brush or rinse	0.7
Allocation concealment	133	2.6%	(-5% to 10%)	Higher PF with poorly concealed allocation	0.6
Blind outcome assessment	133	1.4%	(-8.7% to 12%)	Higher PF with blind outcome assessment not clearly stated	0.8
Double-blinding	133	4.9%	(-8.7% to 18%)	Higher PF with lack of double-blinding	0.5

Table 1. Random-effects metaregression analyses of prevented fractions: D(M)FS *(Continued)*

Drop out	128	1.7%	(-0.2% to 3.5%)	Increase in PF per 10 drop outs	0.08
Language of publication	132 (excludes Di Maggio 1980)	5.9%	(-3.1% to 15%)	Higher PF with publications only in languages other than English	0.2
Length of follow up	133	-0.04%	(-3.9% to 3.8%)	Decrease in PF per extra year of follow up	0.98
APF vs AmF (indirect comparison)	26	-3.9%	(-22% to 14%)	PF lower among APF trials	0.67
NaF vs AmF (indirect comparison)	48	-7.6%	(-20% to 5%)	PF lower among NaF trials	0.25
SMFP vs AmF (indirect comparison)	29	-8%	(-20% to 4%)	PF lower among SMFP trials	0.19
SnF2 vs AmF (indirect comparison)	28	-9.8%	(-22% to 2%)	PF lower among SnF2 trials	0.11

APPENDICES

Appendix 1. MEDLINE search strategy

(a) [("DENTAL-CARIES" explode all subheadings or "DENTAL-CARIES-ACTIVITY-TESTS" all subheadings or "DENTAL-CARIES-SUSCEPTIBILITY" all subheadings or CARIE* or DMF*) and (("FLUORIDES" explode all subheadings or "FLUORIDES,-TOPICAL" explode all subheadings or FLUOR* or AMF or AMINE F OR SNF2 OR STANNOUS F OR NAF OR SODIUM F OR APF OR SMFP OR MFP OR MONOFLUOR*) or ("CARIOSTATIC-AGENTS" explode all subheadings or "DENTAL-PROPHYLAXIS" explode all subheadings or "DENTIFRICES" explode all subheadings or "MOUTHWASHES" explode all subheadings or CARIOSTA* or PROPHYLA* or ANTICARI* or ANTI CARI* or VARNISH* or LACQUER* or DURAPHAT or GEL* or TOOTHPASTE* or TOOTH PASTE* or PASTE* or DENTIFRIC* or MOUTHRINS* or MOUTH RINS* or RINS* or MOUTHWASH* or MOUTH WASH*))].
(b) [((explode FLUORIDES/ all subheadings) or (explode FLUORIDES-TOPICAL/ ALL SUBHEADINGS) or (FLUOR*) or (AMF or AMINE F OR SNF2 OR STANNOUS F OR NAF OR SODIUM F OR APF OR MFP OR SMFP OR MONOFLUOR* OR DURAPHAT)) and ((CARI*) or (DMF*) or (TOOTH*) or (TEETH*) or (DENT* in TI, in AB, in MESH)) or ((explode CARIOSTATIC-AGENTS/ all subheadings) or (ANTICARI* or ANTI CARI*) or (explode MOUTHWASHES/ all subheadings) or (MOUTHWASH* or MOUTH WASH*) or (MOUTHRINS* or MOUTH RINS*) or (VARNISH* or LACQUER*))].

Appendix 2. LILACS/BBO search strategy

[(fluor$ or ppmf or ppm f or amf or snf or naf or apf or mfp or smfp or monofluor$ or duraphat$) and (carie$ or dmf$ or cpo$ or tooth$ or teeth$ or dent$ or dient$ or anticarie$ or cario$ or mouthrins$ or mouth rins$ or rinse$ or bochech$ or enjuag$ or verniz$ or varnish$ or barniz$ or laca$ or gel or gels)] and [random$ or aleatori$ or acaso$ or azar$ or blind$ or mask$ or cego$ or cega$ or ciego$ or ciega$ or placebo$ or(clinic$ and (trial$ or ensaio$ or estud$)) or (control$ and (trial$ or ensaio$ or estud$))].

Appendix 3. Supplementary MEDLINE search strategy

[(CARIE* or (DENT* near CAVIT*) or TOOTH* DECAY* or DMF* or (explode "DENTAL-CARIES"/ ALL SUBHEADINGS))
and (FLUOR* or APF* or NAF* or AMINE F OR SNF* or ACIDULATED* PHOSPHATE* FLUORID* or ACIDULATED* FLUORID* or PHOSPHATE* FLUORID* or SODIUM* FLUORID* or AMINE* FLUORID* or STANNOUS* FLUORID* or (explode "FLUORIDES"/ ALL SUBHEADINGS))
and
(1) (TOOTHPASTE* or TOOTH* PASTE* or DENTIFRICE* or PASTE*) or (explode "DENTIFRICES"/ all subheadings)].
(2) ((RINS* or MOUTH* RINS* or WASH* or MOUTH* WASH*) or (MOUTHRINS* or MOUTHWASH*)) or (explode "MOUTHWASHES"/ all subheadings)].
(3) (FLUOR* or ...or ELMEX* or (explode "FLUORIDES"/ ALL SUBHEADINGS))
and (GEL* or TRAY*)].
(4) (FLUOR* or (DURAPHAT* or FLUOR PROTECTOR*) or (explode "FLUORIDES"/ ALL SUBHEADINGS)) and (VARNISH*) or (LACQUER* or LAQUER*) or (VERNIZ*) or (LACKER*) or (LAKK*) or (SILANE* or POLYURETHANE*)].

WHAT'S NEW

Date	Event	Description
29 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

All authors contributed to the development of the protocol and execution of the review. Valeria Marinho (VM) wrote the protocol, designed and implemented the search strategies, contacted authors, selected studies, assessed validity, and extracted data. Julian Higgins (JH) duplicated study selection, quality assessment, and data extraction in a sample of studies and Stuart Logan (SL) or Aubrey Sheiham (AS) were consulted where necessary. VM entered and analysed the data in consultation with JH. VM prepared the full review. All authors contributed to its revision, interpretation of results and approval.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Department of Epidemiology and Public Health (UCL), UK.
- Systematic Reviews Training Unit, Institute of Child Health (UCL), UK.
- Medical Research Council, UK.

External sources

- CAPES - Ministry of Education, Brazil.

INDEX TERMS

Medical Subject Headings (MeSH)

Cariostatic Agents [*therapeutic use]; Dental Caries [*prevention & control]; Fluorides, Topical [*therapeutic use]; Gels; Mouthwashes [*therapeutic use]; Toothpastes [*therapeutic use]

MeSH check words

Adolescent; Child; Humans