Systematic Reviews of Topical Fluorides for Dental Caries: A Review of Reporting Practice

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Key Words

Dental caries · Meta-analysis · Systematic review · Topical fluoride

Abstract

This paper aims to assess systematic reviews on the caries-preventive effect of topical fluorides, identifying key content and reporting quality issues to be considered by researchers planning a review in this area. Published systematic reviews and meta-analyses of any topical fluoride intervention for caries control were included. Relevant databases were searched (December 2009), along with reference lists of included publications. Thirty-eight reports were identified and assessed. A majority of these focused on the child/adolescent population, fluoride toothpastes, no treatment/placebo comparisons, and had caries increment as the main outcome. Complete reporting of eligibility criteria (PICOS) was uncommon, except in Cochrane reviews. Less than half reported searching multiple sources and only one third reported a search strategy. Duplicate study selection and data extraction was reported in 27 (71%) and 16 (42%) reviews, respectively; quality assessment of included studies was not reported in one third of the reviews. Meta-analysis was reported in 20 (52%) reviews, with six not reporting the methods of synthesis used, 17 formally assessing heterogeneity, and 12 reporting analyses for its exploration. This study

shows that some content features have been covered more often than others in existing fluoride reviews, while some relevant features are yet to be addressed. Also, reporting of several methodological aspects are below an acceptable level, except for Cochrane reviews. Current reporting guidelines for systematic reviews of interventions (e.g. PRISMA) and sources of high-quality existing reviews (e.g. The Cochrane Library) should be closely followed to enhance the validity and relevance of future topical fluoride reviews.

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Systematic reviews provide the foundation for better practice and new research in all areas of healthcare and have already answered important questions regarding the effects of fluoride on caries prevention. Consequently, they are becoming more influential as a foundation for preventive practice and policy in dentistry. A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question; it uses explicit, systematic methods that minimize bias, thus providing reliable findings from which conclusions can be drawn [Antman et al., 1992; Oxman and Guyatt, 1993]. It may or may not include a meta-analysis, which is a statistical pooling of results from two or more independent studies. Systematic reviews are still a relatively new kind of research in den-

tistry though [Marinho, 2003], and there is still room for improvement in the *quantity*, in terms of subject areas covered, and *quality* of both the conduct and the reporting of systematic reviews in the field [Glenny et al., 2003; Bader and Ismail, 2004; Richards, 2004; Major et al., 2006].

The various topical fluoride interventions have over six decades of experimental research supporting their value as anticaries measures, and these were the focus of some of the first meta-analyses in dentistry [Stamm et al., 1984; Clark et al., 1985]. Existing systematic reviews of topical fluoride interventions may reflect the available primary research in the field, and their reporting quality may vary. Nevertheless, the breadth of topical fluoride interventions, comparisons, populations, and outcomes covered by published systematic reviews and meta-analyses, and the methodological quality of these reviews, have not been reported previously. Highlighting which direction future reviews in this area should take based on past practice to avoid duplication of effort while advancing knowledge reliably is important, and this should be done in the light of ongoing methodological advancements so as to enhance their validity and applicability.

In 1996, an international group developed a reporting guideline, the QUOROM Statement (Quality Of Reporting Of Meta-analyses), to improve the reporting of systematic reviews and meta-analyses in healthcare research [Moher et al., 1999]. The recent publication of 'Preferred reporting items for systematic reviews and meta-analyses', the PRISMA statement, is an improvement on that guideline [Liberati et al., 2009; Moher et al., 2009]. In addition to the QUOROM items, PRISMA now asks the review authors to make a protocol for the review accessible; to report at least one complete electronic search; to assess risk of bias in and across included studies (along with the selective reporting of outcomes); to report limitations of the review, future research implications and sources of funding. The PRISMA statement has made it clear that the quality and content of systematic reviews is constantly being improved, and has also identified The Cochrane Collaboration as the leader in the field since all these new items are already an essential part of Cochrane reviews. Thus, new reviews incorporating these advancements should have enhanced quality and generate more reliable estimates of treatment effects.

The aim of this paper is to describe the most important features of systematic reviews and meta-analyses on topical fluorides for caries prevention and treatment in terms of content and reporting quality by collating those published up to and including 2009. A comprehensive search

and an appraisal in the light of current reporting guidelines (PRISMA) has enabled us to identify important issues that need consideration by researchers planning a systematic review in this area of dentistry.

Materials and Methods

An electronic search without date or language restrictions was undertaken in December 2009 of: MEDLINE (via OVID including old MEDLINE), The Cochrane Database of Systematic Reviews (CDSR) and The Centre for Reviews and Dissemination (CRD) databases [including DARE (Database of Abstracts of Reviews of Effects), NHSEED (National Health Service Economic Evaluation Database), and HTA (Health Technology Assessment)]. The search terms 'caries AND fluoride' were used in all the searches performed, but a more detailed search strategy was used in MEDLINE (online supplementary material, www.karger.com/doi/10.1159/000322132). This was supplemented by searching the reference lists of the included reviews.

Only completed published intervention systematic reviews and meta-analyses, including any types of study design, assessing the anticaries effects of any topical fluoride therapy (TFT), including toothpaste, mouthrinse, gel, varnish, paint-on solution, whether used alone, or in combination with another TFT, or as part of a larger group of anticaries interventions in any population group were considered relevant for inclusion. Any review that incorporated at least two of the key characteristics of a systematic review outlined in section 1.2.2 of *The Cochrane Handbook of Systematic Reviews of Interventions* [Higgins and Green, 2008] was considered.

For each of the identified reviews included in this study, the following data were then extracted on a standard form: year of publication; whether a clear objective and eligibility criteria (in terms of participants, interventions, comparisons and outcomes – PICOS) were stated in the review; types of intervention(s), comparison(s) and population group(s) addressed; main outcomes addressed; number and types of studies included; methods used for study identification, study selection, quality assessment (risk of bias) and data extraction of included studies; effect measures used; whether a quantitative synthesis was done; statistical methods used in the synthesis (fixed effect or random effects); assessment, exploration and factors explored for heterogeneity; assessment and exploration of publication or reporting bias; whether cost/economic evaluation was reported and in what format. These data were then summarized so as to identify the most important issues in the conduct and reporting of topical fluoride reviews. Search strategy development, study selection and data collection were done by one author (S.I.) in consultation with the other (V.C.C.M.).

Results

The searches resulted in 150 citations from MEDLINE, 17 from CDSR, 39 from DARE, 17 from NHSEED, and 7 from HTA databases. These results (230 titles and

abstracts) were read for identifying relevant systematic reviews and meta-analyses of topical fluoride interventions for caries. Reasons for exclusions at this stage were: duplicate citations (n = 64), traditional narrative reviews (n = 46), reviews of non-TFT interventions (n = 42); technology or economic assessments that were not systematic reviews (n = 23).

The remaining 55 papers were then read in full text. Of these, five were protocols of ongoing systematic reviews, six were response publications to already published meta-analyses, three were method papers, and three were commentaries on a TFT systematic review. One did not report the review methodology in sufficient detail while one focused purely on assessment of epidemiological data and did not assess effectiveness of the TFT intervention. These 19 papers were excluded.

Thirty-six papers were included. Two other reviews were identified from the reference lists of the included reviews. Thus a total of 38 systematic reviews addressing effectiveness of some form of TFT for caries were identified. Tables 1 and 2 summarise the data extracted from these reports (general content and methodological features, and features specifically related to data synthesis, respectively). The oldest included review was a meta-analysis from 1984 and the latest from 2009. The greatest number of reviews was published between 2000 and 2004 (fig. 1).

Reporting of Objectives and Eligibility Criteria

Although all publications stated objectives at least in terms of 'intervention for condition', most of these did not provide complete information on eligibility criteria in PICOS format (population, intervention, comparison, outcome, study design), except in Cochrane reviews.

Characteristics of Studies Included – PICOS

Populations. The most covered group was children and/or adolescents from the general population (n = 21, 55%). Three reviews addressed fixed orthodontic appliance wearing patients, two addressed adults, and two covered high caries risk individuals only. Eight did not specify the population group addressed.

Interventions. The topical fluoride intervention most commonly addressed was toothpaste (n = 10, 26%). Varnish was the main intervention of interest in nine reviews, mouthrinses in four, and gels in three. Nine reviews addressed any TFT, while two addressed combinations of TFT. One review specifically addressed silver diamine fluoride – a type of paint-on solution.

Comparisons. The comparison most commonly addressed was intervention (TFT) versus placebo or no treatment (n = 16, 42%). This was followed by comparisons of one concentration of fluoride toothpaste versus another (n = 5), and comparisons of one specific fluoride agent/compound in toothpaste versus another (n = 3). Two reviews addressed comparisons of one type of TFT against another, while 13 (34%) did not specify the comparisons addressed.

Outcomes. Caries increment was the most common outcome measure (n = 31, 81%), followed by caries incidence (n = 4), caries arrest (n = 3) and caries progression (n = 2). Adverse effects and patient-reported outcomes were not measured as a primary/main outcome in any review (although adverse events were mentioned as secondary outcomes in 11 reviews).

Study Design. The most common type of study considered was controlled clinical trial (n = 34, 90%). Four reviews considered various non-RCT designs (prospective controlled studies, uncontrolled longitudinal studies, and even reviews and guidelines) for inclusion and two reviews considered economic evaluations.

Search Methods Used

Six reviews (16%) did not report any search methods (sources, dates, languages, search terms, etc.) for studies, although five of these were published before the first reporting guideline came out in 1999 with clear recommendations on this aspect [Moher et al., 1999]. Only 12 (31%) of the 38 reviews reported a complete search strategy for at least one database – mostly Cochrane reviews, while 17 reported search terms, key words or concepts used for searching.

Seventeen reviews (45%) reported searching multiple databases (more than two) electronically while six reported searching MEDLINE and The Cochrane Library databases, apparently treating The Cochrane Library as one database. Nineteen (50%) reported complementing electronic search with searching one or more other sources (reference/hand/grey literature/authors).

Study Selection and Data Extraction

Three reviews (8%) did not report on the study selection process. Study selection was reported to be performed in duplicate in 27 (71%) reviews. Of these, 20 reviews reported duplicate study selection in the entire sample while seven reported the same in a random one third of the sample. For eight reviews it could not be judged if it was done in duplicate.

Table 1. Details of component studies and methodological features of systematic reviews and meta-analyses of TFT

Authors + year of publication	Clear objective + eligibility criteria reported ^a	Population (P), Intervention (I), Comparison (C)	Main outcome(s)	Design of studies included	Search methods (date span = D; language = L; sources = S; terms = T)	Study selection method	Data extraction method	Quality/risk of bias assessment
Rosenblatt et al. [2009]	no	P = NR I = PAFS (SDF) C = FV	caries arrest, caries incidence	CCT	D = 1966–2006 L = NR S = ES (MEDB) + OS T = TO	PR = yes ID = yes	PR = yes ID = yes	PR = yes ID = yes scores used
Azarpazhooh et al. [2008]	no	P = high-risk children/adolescents I = FV C = NR	NR	GL/Rev/SR/ all types of primary studies	D = 2000–2007 L = English S = ES (MEDB) + OS T = SSt	PR = yes ID = yes	PR = yes ID = yes	PR = yes ID = yes scores used
Twetman [2008]	no	P = children (<3 years) I = any caries-preventive inc. any TFT (FTP, FV) C = NR	incidence/% of carious lesions	PCS	D = 1998–2007 L = English S = ES (ML) T = TO	PR = yes ID = yes	PR = NR ID = NR	PR = yes ID = yes as described by Twetman et al. [2003]
Heijnsbroek et al. [2007]	no	P = adults I = TFT (FTP, FMR, FV) C = NR	caries activity/ incidence	RCT, CCT, ULS	D = 1966–2005 L = English S = ES (ML + CL) T = TO	PR = yes ID = yes	PR = yes ID = no	PR = NR ID = NR
Griffin et al. [2007]	no	P = adults I = TFT (FG/FTP/PAFS)/water F C = NR	caries increment (DMFS/T, DFT/S)	RCT/CCT/ longitudinal studies	D = 1966–2004 L = English S = ES (MEDB) T = SSt	PR = yes ID = yes	PR = yes ID = yes on piloted forms	PR = yes ID = NR
Ammari et al. [2007]	no	P = children (<5 years) I = any anticaries agents (PAFS, FTP) C = NR (likely any caries-preventive/PL/NT)	caries increment (dmfs/t, dft/t)	RCT	D = 1966–2003 L = all S = ES (MEDB) + OS T = TO	PR = yes ID = yes	PR = yes ID = yes	PR = yes ID = yes on randomization and blinding
Huiri et al. [2006]	yes	P = <20 years I = FV C = sealants	caries increment DMFS/T	RCT/CCT	D = 1966–2005 L = all S = ES (MEDB) + OS T = SSt	PR = yes ID = yes	PR = yes ID = yes	PR = yes ID = yes on allocation concealment, blinding and follow-up
Benson et al. [2004]	yes	P = FAP I = TFT (FTP/FG/FMR/FV) C = NT/PL/TFT	carious lesion number and severity (any measure)	RCT/CCT	D = 1966–2004 L = all S = ES (MEDB) + OS T = SSt	PR = yes ID = yes	PR = yes ID = yes	PR = yes ID = yes
Chadwick et al. [2005]	no	P = FAP I = TFT (FTP/FG/FMR/PAFS) C = NR	carious lesion severity (DMFS)	CCT/PCS	D = NR L = NR S = ES (MEDB) + OS T = NR	PR = yes ID = yes	PR = yes ID = yes	PR = NR ID = NR
Axelsson et al. [2004]	no	P = NR I = combination of anticaries agents (FTP, FG, FV, FMR) C = Stdd. care/NT/PL	caries increment (dmfs/t DMFS/T)	RCT/CCT	D = 1966–2003 L = Nordic/English/ European languages S = ES (ML) + OS T = TO	PR = yes ID = yes	PR = yes ID = NR	PR = yes ID = yes on randomization, blinding, follow-up and diagnostic criteria

Bader [2004]	no	P = preschool children I = FV C = NT	carries increment	CCT	D = 1966–2001 L = English S = ES (ML + CL) T = TO	PR = yes ID = yes ID = NR	PR = yes ID = NR ID = NR
Petersson et al. [2004]	no	P = any age group I = FV C = PL/NT/TFT (FG/FMR)	carries increment (dmfs/t, DMFS/T)	RCT/CCT	D = 1966–2003 L = Nordic/English/ European languages S = ES (ML + CL) + OS T = TO	PR = yes ID = yes ID = yes	PR = yes ID = yes on randomization, blinding, follow-up and diagnostic criteria
Twetman et al. [2004]	no	P = NR I = FMR C = NR	carries increment (DMFS/T, dmfs/t)	RCT/CCT	D = 1966–2003 L = Nordic/English/ European languages S = ES (ML + CL) + OS T = TO	PR = yes ID = yes ID = NR	PR = yes ID = yes on randomization, blinding, follow-up and diagnostic criteria
Derks et al. [2004]	no	P = FAP I = TFT (FTP/FG)/CHX/bond material/sealant C = NR	incidence/ increment (DMFS/T)	CCT	D = 1970–2002 L = English S = ES (ML + OS) T = SSt	PR = yes ID = yes ID = NR	PR = NR ID = NR
Marinho et al. [2004b]	yes	P = <16 years I = TFT (FTP/FG/FMR/FV) C = another TFT (FTP/FG/FMR/FV)	carries increment (DMFS)	RCT/CCT	D = 1966–2000 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3 ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding domains
Marinho et al. [2004a]	yes	P = <16 years I = combination of 2 TFT (FTP, FG, FMR, FV) C = one TFT (FTP, FG, FMR, FV)	carries increment (DMFS)	RCT/CCT	D = 1966–2000 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3 ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding
Steiner et al. [2004]	no	P = NR I = FTP C = 1,000 × 250 ppm F	carries increment (DFS/DMFS)	RCT/CCT	D = NR L = English S = ES (ML + CL) T = NR	PR = NR ID = NR ID = NR	PR = NR ID = NR
Twetman et al. [2003]	no	P = any age group I = FTP C = PL/NT/one FTP conc. × another conc.	carries increment (DMFS/T, dmfs/t)	RCT/CCT	D = 1966–2003 L = Nordic/English/ European languages S = ES (ML + CL) + OS T = TO	PR = yes ID = yes ID = NR	PR = yes ID = yes on randomization, blinding, follow-up and diagnostic criteria
Ammari et al. [2003]	yes	P = any age group I = FTP C = 1,000 × 500 × 250 ppm F	carries increment (DMFS/T, DFS/T)	RCT	D = 1966–2001 L = English S = ES (MEDB) + OS T = TO	PR = yes ID = yes ID = yes	PR = yes ID = yes scores used
Källestål et al. [2003]	no	P = NR I = any anticaries therapy (FV/FMR) C = NR (any anticaries therapy/PL/NT likely)	costs and caries data (various measures)	economic evaluations/ all types of effectiveness primary studies	D = 1966–2003 L = Nordic/English/ European languages S = ES (ML) + OS T = TO	PR = yes ID = yes ID = NR	PR = yes ID = yes on randomization, blinding, follow-up and diagnostic criteria + Drummonds' checklist
Marinho et al. [2003a]	yes	P = <16 years I = any TFT (FTP, FG, FMR, FV) C = PL/NT	carries increment (DMFS)	RCT/CCT	D = 1966–2000 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3 ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation concealment, blinding domains

Table 1 (continued)

Authors + year of publication	Clear objective + eligibility criteria reported ^a	Population (P), Intervention (I), Comparison (C)	Main outcome(s)	Design of studies included	Search methods (date span = D; language = L; sources = S; terms = T)	Study selection method	Data extraction method	Quality/risk of bias assessment
Marinho et al. [2003c]	yes	P = <16 years I = FMR C = PL/NT	caries increment (DMFS)	RCT/CCT	D = 1966–2000 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3	PR = yes ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding domains
Marinho et al. [2003b]	yes	P = <16 years I = FTP C = PL/NT	caries increment (DMFS)	RCT/CCT	D = 1966–2000 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3	PR = yes ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding domains
Marinho et al. [2002b]	yes	P = <16 years I = FG C = PL/NT	caries increment (DMFS)	RCT/CCT	D = 1966–1997 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3	PR = yes ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding domains
Marinho et al. [2002a]	yes	P = <16 years I = FV C = PL/NT	caries increment (DMFS)	RCT/CCT	D = 1966–1997 L = none S = ES (MEDB) + OS T = SSt	PR = yes ID = 1/3	PR = yes ID = 1/3 on piloted forms	PR = yes ID = 1/3 on sequence generation, allocation, blinding domains
Chaves and Vieira-da-Silva [2002]	yes	P = NR I = FTP C = PL/one FTP conc. × another	caries increment	RCT	D = 1980–1998 L = NR S = ES (ML + LILACS) T = TO	PR = yes ID = yes	PR = NR ID = NR	PR = yes ID = yes domain-based criteria by Kay and Locker [1996] + a consensus of experts
Rozier [2001]	no	P = children (primary dentition) I = PACT (FV) C = NR	caries increment	CCT	D = 1966–2001 L = English S = ES (ML) T = TO	PR = yes ID = NR	PR = NR ID = NR	PR = yes ID = NR ordinal scales used
Bader et al. [2001]	yes	P = high-risk individuals I = PACT (PAFS, FV) C = NR	caries increment (DMFS/T)/NNT/% progression/arrest	CCT	D = 1966–1999 L = English S = ES (MEDB) + OS T = TO	PR = yes ID = yes	SA + review	SA + review scores used
Bartizek et al. [2001]	yes	P = children (grade 1–8) I = FTP C = 1,100 × 1,700 × 2,200 × 2,800 ppm F	caries increment (DMFS)	RCT	D = NR L = NR S = NR T = NR	PR = NR ID = NR	PR = NR ID = NR	PR = NR ID = NR
Strohmeier and Brambilla [2001]	yes	P = children (permanent dentition) I = FV C = standard care/PL	caries increment (DMFS/DFS)	RCT	D = 1980–1997 L = NR S = ES (MEDB) T = TO	PR = yes ID = NR	PR = NR ID = NR	PR = NR ID = NR scores used
Van Rijkom et al. [1998]	yes	P = 6–15 years I = FG C = PL/NT	caries increment (DMFS)	RCT	D = 1965–1995 L = English/German S = ES (ML) T = TO	PR = yes ID = yes	PR = NR ID = NR	PR = NR ID = NR

Volpe et al. [1995]	yes	P = any age group I = FTP C = NaF × SMFP	caries increment (DMFS/T)	RCT/CCT	D = NR L = NR S = NR T = NR	PR = yes ID = NR	PR = NR ID = NR	PR = NR ID = NR
Helfenstein and Steiner [1994]	yes	P = children (permanent) dentition I = FV C = NR (likely NT/PL)	caries increment (DMFT)	CCT	D = 1985–1991 L = NR S = ES (IDL) T = TO	PR = yes ID = NR	PR = yes ID = NR	PR = NR ID = NR
Johnson [1993]	no	P = NR I = FTP C = SMFP × NaF SMFP+NaF × NaF/SMFP	caries increment (DMFS/T)	RCT	D = NR L = NR S = NR T = NR	PR = NR ID = NR	PR = NR ID = NR	PR = NR ID = NR
Stokey et al. [1993]	yes	P = children I = FTP C = PL/NT/SMFP × NaF	caries increment (DMFS)	CCT	D = NR L = NR S = NR T = NR	PR = yes ID = NR	PR = yes ID = NR	PR = yes ID = NR
Beiswanger and Stookey [1989]	no	P = NR I = FTP C = NaF × SMFP	caries increment (DMFS)	CCT	D = NR L = NR S = published literature T = NR	PR = yes ID = NR	PR = NR ID = NR	PR = NR ID = NR
Clark et al. [1985]	no	P = NR I = F supplements/FG/PAFS/FV C = NR (likely NT/PL)	caries increment (DMFS/DMFT/def)	CCT/ community trials	D = NR L = NR S = NR T = NR	PR = yes ID = NR	PR = NR ID = NR	PR = NR ID = NR
Stamm et al. [1984]	no	P = children I = FMR C = PL/NT	caries increment (DMFS)	RCT/ULS/ cost evaluation	D = NR L = NR S = NR T = NR	PR = NR ID = NR	PR = NR ID = NR	PR = NR ID = NR

NR = Not reported; CHX = chlorhexidine; conc. = concentration; FAP = fixed appliance patients; FG = fluoride gel; FMR = fluoride mouthrinse; FTP = fluoride toothpaste; FV = fluoride varnish; NaF = sodium fluoride; NT = no treatment; PAC/T = professionally applied caries therapy; PAFS = professionally applied fluoride solution; SDF = silver diamine fluoride; PL = placebo; SMFP = sodium monofluorophosphate; dmfs/t, DMFS/T = decayed missing filled surfaces/teeth; DFT = decayed and filled teeth; CCT = controlled clinical trial; GL = guidelines; PCS = prospective controlled study; RCT = randomized controlled trial; Rev = review; SR = systematic review; ULS = uncontrolled longitudinal study; CL = Cochrane library; EB = EMBASE; ES = electronic sources; IDL = index to dental literature; MEDB = multiple electronic databases; ML = Medline; OS = other sources; SSt = complete search strategy in at least one database; TO = terms only; ID = independent, duplicate; PR = process reported; SA = single abstraction.

^a No = one or more elements of PICOS missing from the 'Methods' section.

Table 2. Summary of data synthesis features in systematic reviews and meta-analyses of TFT

Authors + year of publication	Studies included	Primary effect measures	Method of quantitative synthesis	Assessment/exploration of heterogeneity	Assess./explo-ration of publication bias	Economic evaluation
Rosenblatt et al. [2009]	2	PF, NNT	NR	NR	NR	NR
Azarpazhooh et al. [2008]	7	NR	NR	NR	NR	NR
Twetman [2008]	22	NR	NR	NR	NR	NR
Heijnsbroek et al. [2007]	6	NR	NR	NR	NR	NR
Griffin et al. [2007]	20	RR, MD	RE MA	χ^2 , I^2 /sensitivity analysis for study design	NR	NR
Ammari et al. [2007]	7	PF	NR	NR	NR	NR
Hiiri et al. [2006]	4	RR	NR	NR	NR	NR
Benson et al. [2004]	15	WMD, Peto's OR	NR	NR	NR	NR
Chadwick et al. [2005]	6	PF	NR	NR	NR	NR
Axelsson et al. [2004]	24	NR	NR	NR	NR	NR
Bader et al. [2004]	6 (FV)	% caries reduction	NR	NR	NR	NR
Petersson et al. [2004]	24	PF	NR (likely done)	NR	NR	NR
Twetman et al. [2004]	25	PF	NR (likely done)	NR/correlation analysis on intervention and population features	NR	NR
Derks et al. [2004]	15	PF	NR	NR	NR	NR
Marinho et al. [2004b]	17 (15 for MA)	PF	RE MA	$\chi^2 + I^2$ tests/RE MR sensitivity subgroup analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Marinho et al. [2004a]	12 (9 for MA)	PF	RE MA	$\chi^2 + I^2$ tests/RE MR sensitivity subgroup analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Steiner et al. [2004]	4	PF	RE + FE MA	Cochran test/NR	NR	NR
Twetman et al. [2003]	54	PF	NR	NR	NR	NR
Ammari et al. [2003]	7 (5 for MA)	WMD	FE MA	NR/sensitivity analysis for intervention feature	funnel plot/NR	NR
Källestål et al. [2003]	17 (2 FV, 3 FMR)	NR	NR	NR	NR	identified + quality-assessed economic evaluations
Marinho [2003a]	144 (133 for MA)	PF	RE MA	$\chi^2 + I^2$ tests/RE MR, sensitivity subgroup analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Marinho [2003c]	36 (34 for MA)	PF	RE MA	$\chi^2 + I^2$ tests/RE MR, sensitivity analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Marinho [2003b]	74 (70 for MA)	PF	RE MA	$\chi^2 + I^2$ tests/RE MR, sensitivity analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR

Table 2 (continued)

Authors + year of publication	Studies included	Primary effect measures	Method of quantitative synthesis	Assessment/exploration of heterogeneity	Assess./explo-ration of pub-lication bias	Economic evaluation
Marinho et al. [2002b]	25 (23 for MA)	PF, SMD	RE MA	$\chi^2 + I^2$ tests/RE MR, sensitivity subgroup analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Marinho et al. [2002a]	9 (7 for MA)	PF, SMD	RE MA	$\chi^2 + I^2$ tests/RE MR, sensitivity analyses on pre-defined and not pre-defined aspects of study quality, and participants, intervention, and outcome-related features	funnel plot/formal tests	NR
Chaves and Vieira-da-Silva [2002]	22	% difference	FE MA	Q test/NR	NR	NR
Rozier [2001]	7 (FV)	PF, NNT	NR	NR	NR	NR
Bader et al. [2001]	27	NR	NR	NR	NR	NR
Bartizek et al. [2001]	6	SMD	MA (type NR)	χ^2 /NR	NR	NR
Strohmenger and Brambilla [2001]	3	WMD	RE MA	Q test/NR	NR	NR
Van Rijkom et al. [1998]	17	PF	MA (type NR)	NR/MR analysis on population and intervention features	funnel plot/NR	reported cost info + NNT
Volpe et al. [1995]	4	WMD	MA (type NR)	NR/subgroup analysis for study design features	NR	NR
Helfenstein and Steiner [1994]	8	PF	RE MA	χ^2 /correlation analysis on aspects of study quality, and participants, intervention, and outcome-related features	NR	NR
Johnson [1993]	10 (9 for MA)	WMD	MA (type NR)	χ^2 /subgroup analysis for study design features	NR	NR
Stookey et al. [1993]	13	WMD	MA (type NR)	χ^2 /subgroup analysis for study design features	NR	NR
Beiswanger and Stookey [1989]	20	% difference	NR (likely done)	NR	NR	NR
Clark et al. [1985]	NR	WMD	RE MA	NR	NR	NR
Stamm et al. [1984]	NR	WMD	MA (type NR)	NR	NR	CEA.

NR = Not reported; OR = odds ratio; MD = mean difference; PF = prevented fraction; RR = risk ratio; SMD = standardized mean difference; WMD = weighted mean difference; FE = fixed effect; MA = meta-analysis; MR = meta-regression; RE = random effect; CEA = cost-effective analysis; USD = US dollar.

For eleven reviews (29%) the data extraction method was not reported and for ten we could not judge whether data extraction was done in duplicate. Duplicate data extraction was clearly reported in 16 (42%) reviews; nine reviews reporting duplicate independent data extraction for the entire sample and seven reporting the same in a random one third of the total sample of studies. One review reported single abstraction of data. Only Cochrane reviews and those from The Swedish Council of Technol-

ogy Assessment in Health Care reported using piloted forms for data extraction.

Methodological Quality Assessment

Thirteen reviews (34%) did not report assessing the quality of included studies. However, an equal number of reviews reported independent duplicate assessment of study quality in the entire sample. Another seven reviews (the series of Cochrane reviews 2002–2004) reported do-

Fig. 1. Frequency of systematic reviews and meta-analyses on topical fluoride by year of publication.

main-based assessment of *risk of bias* in duplicate in a random one third of included studies. Of the rest, one used single assessment and four did not give enough detail to allow judgement of duplicate assessment.

A total of 16 (42%) reviews (including the Cochrane reviews and Swedish Council of Technology Assessment in Health Care series of reviews) reported quality assessment in the domains of allocation concealment and blinding. Four reviews reported using scores for quality assessment – all published after 2000. An assessment of risk of selective outcome reporting bias within studies was not specified by any of the included reviews, reflecting its very recent addition to the risk of bias aspect.

Quantitative Synthesis

Summary effect measures could not be identified for 6 reviews. Prevented fraction was the most common effect measure used ($n = 18$, 47%) followed by weighted mean difference ($n = 7$). Other effect measures used included risk ratio, standardized mean difference, and numbers needed to treat.

Of the 20 (53%) reporting a meta-analysis, 11 reported a random effects meta-analysis and two reported using fixed effect analysis. One reported using both fixed and random effects models while six did not specify the type of meta-analysis performed.

Assessment of heterogeneity was reported by 17 of those reporting a meta-analysis (85%); χ^2 and I^2 statistics were the most commonly used tests ($n = 12$) to assess heterogeneity. Fourteen reviews (70%) reported additional analyses for exploration of heterogeneity between stud-

ies. Cochrane reviews pre-specified the aspects to be assessed in these additional meta-regression, subgroup or sensitivity analyses, and reported any post-hoc decision for further analyses undertaken. These reviews explored heterogeneity through regression analysis on aspects of study quality, baseline caries level, additional fluoride exposure, F^- concentration, frequency of TFT use, and mode and form of TFT use. Another eight reviews used sensitivity or subgroup analyses for the aspects of study quality or study design, with five of these published before 2000.

Nine reviews (24%) explored publication bias by observing funnel plot asymmetry, and seven of these (all Cochrane reviews) used formal tests for its assessment. One review reported carrying out supplemental analysis including studies published later, one assumed publication bias to be nonexistent, and two just mentioned publication bias in the text.

Only three (8%) reviews addressed economic data. Of these, one identified economic evaluations on fluoride mouthrinses and varnishes and quality-assessed/graded them, another, assessing fluoride gels, reported numbers needed to treat as a measure of resource intensiveness, and one reported a cost-effectiveness analysis of mouthrinse studies.

Discussion

This study is the first to provide a comprehensive assessment of the content and reporting quality of systematic reviews and meta-analyses on TFT for dental caries. We included 38 reviews published from 1984 to 2009. This is a relatively large number of systematic reviews/meta-analyses identified in one particular area of dentistry. This may be partly explained by the fact that two of the first meta-analyses in dentistry appeared exactly on this topic as early as in the mid-1980s [Stamm et al., 1984; Clark et al., 1985], and also by the large amount of experimental evidence published over five decades. In addition, we were deliberately inclusive in classifying a publication as a systematic review in order to get a broader perspective on the development of evidence synthesis in this particular area. The highest number of publications between 2000 and 2004 were associated with the publication of a series of Cochrane reviews and systematic reviews from the Swedish Council of Technology Assessment in Health Care assessing the effectiveness of fluoride toothpastes, mouthrinses, gels and varnishes.

This study identified some key issues in the published TFT systematic reviews. We found that in terms of content (PICOS), children and adolescents, fluoride toothpastes, no treatment/placebo comparisons, and the outcome of caries increment have been addressed repeatedly. Some important population groups (e.g. adults), TFT interventions (e.g. paint-on solutions), comparisons (e.g. of various application features), and outcomes (e.g. adverse effects, economic) have not been addressed sufficiently though, or have not been covered at all. Some Cochrane reviews that could be identified as protocols at the time of the search, and have now been published, are likely to narrow some of the existing gaps, such as those related to the assessment of direct comparisons of toothpaste application features (fluoride concentration) [Walsh et al., 2010] and of adverse effects (fluorosis) [Wong et al., 2010].

We had expected that the dissemination of methods for conducting systematic reviews from the mid 1990s [CRD, 1996; Clarke and Oxman, 2002], and the publication of reporting guidelines for systematic reviews since 1999 [Moher et al., 1999] would result in an overall improved reporting quality in the TFT systematic reviews that followed. Higher quality reviews that were published post QUOROM have been reported in other healthcare areas [Delaney et al., 2005; Al Faleh and Al-Omran, 2009]. This appears to be the case for TFT systematic reviews as well, where the reviews published after QUOROM were of better overall reporting quality than those published before it. There remains room for improvement though. Even very recently published reviews did not adopt the clear structured format (PICOS) advised by the guidelines. Reporting of search methods was also found to be largely inadequate, particularly the complete reporting of a search strategy which was rare outside of Cochrane reviews. In addition, searching multiple sources for studies was reported by only half of the reviews even if pre-QUOROM publications are disregarded.

Published reviews sometimes reported searching the Cochrane Library without specifying the databases searched within it. The Cochrane Library includes specific databases for searching various types of studies such as Cochrane and non-Cochrane systematic reviews, controlled trials, methods studies, economic evaluations, and health technology assessments. It should be specified which of these were used to locate studies. Nevertheless, methods used for 'selection of studies' were found to be more in line with the current reporting guidelines – done in duplicate – and reported in more detail than they were for data extraction, although both aspects are advised to be equally explicitly reported.

Another important finding was that the quality/risk of bias assessment in most reviews did not meet current reporting guidelines, except in Cochrane reviews. For example, the use of summary scores for risk of bias assessment, even though guidelines are explicitly discouraging this approach now [Higgins and Altman, 2008; Liberati et al., 2009]. The assessment of risk of bias in included studies according to the latest PRISMA recommendations is a major development that should be widely adopted.

The use of quantitative synthesis, meta-analysis, was reported in half of the reviews with reporting of the methods of synthesis variable across them. Although heterogeneity was also formally assessed in nearly half of the reviews, its presence was usually not adequately explored by means of subgroup, sensitivity, or meta-regression analyses. The exceptions were, again, Cochrane reviews, which predefined and detailed the analyses and the investigations of potential reasons for heterogeneity between studies to be undertaken, and reported any post-hoc decisions on analyses or deviations from protocol with reasons for doing so. In line with a previous study assessing systematic reviews in health care [Moher et al., 2007], assessment of publication bias was also a relatively rare feature in the reviews despite its known importance in affecting reviews' findings. However, a note of caution would be always required in assessing and interpreting heterogeneity and publication bias; there will often be insufficient data for these investigations to be done reliably using statistical methods, and they would be of questionable value when based on very few studies [Higgins et al., 2002; Sterne et al., 2008]. In addition, explorations of heterogeneity that are devised after heterogeneity is identified can at best lead to the generation of hypotheses [Deeks, 2008].

We found that economic evaluations in TFT systematic reviews have been uncommon so far. Current methodological developments from the Cochrane and the Campbell Collaboration (www.campbellcollaboration.org) support the introduction of economic evaluations in systematic reviews, and these have the potential to enhance the applicability of new TFT review's findings, since such evaluations are becoming increasingly important for decision makers to help identify more cost-effective treatments.

Our findings were consistent with those from previous studies of this nature in that the Cochrane reviews performed better than others in reporting quality [Moja et al., 2005; Jørgensen et al., 2006, 2008; Moher et al., 2007; Mrkobrada et al., 2008; Lundh et al., 2009]. Our broad

inclusion criteria for systematic reviews may be considered a reason for the low review quality observed generally. However, in a recent study of similar nature, restricting inclusion to reviews clearly labelled as systematic reviews did not result in improved overall quality, nor did it explain the differences in quality between Cochrane and non-Cochrane systematic reviews [Lundh et al., 2009].

The suboptimal reporting outside of Cochrane reviews may indicate a low level of awareness regarding existing reporting guidelines for systematic reviews among authors and dental journals, which is understandable considering that these involve relatively new methodology. However, although information on the endorsement by journals of reporting guidelines for systematic reviews (QUOROM/PRISMA) is not available (www.prisma-statement.org), the list of around 350 scientific journals officially endorsing the reporting guideline for clinical trials – CONSORT (CONsolidated Standards Of Reporting Trials) included only nine dental journals in early 2010 (www.consort-statement.org). Recent studies suggest that endorsement of reporting guidelines by journals can lead to improved overall quality [Moher et al., 2001, 2007; Plint et al., 2006; Mrkobrada et al., 2008; Alvarez et al., 2009]. With this regard, it has also been suggested that directing continuing education efforts towards journal editors may improve the quality of published research faster than other interventions [Sørensen and Rothman, 2010]. Thus, the endorsement of PRISMA by dental journals may be the simplest way to ensure up-to-the-mark reporting of systematic reviews and meta-analyses in dentistry.

As regards potential limitations of our study, it should be noted that we restricted our search to MEDLINE and certain dedicated databases of systematic reviews. We may have missed out on publications not covered by these and available from other sources. In addition, selection of included studies, and data extraction were done by one author with a second author consulted at each stage and consensus achieved. These were not undertaken independently, which may have allowed some degree of bias. Finally, it should be pointed out that we essentially assessed included reviews for reporting quality with regard to adherence to reporting guidelines. We did not use a review quality assessment tool such as AMSTAR [Shea et al., 2007, 2009] or OQAQ [Oxman and Guyatt, 1991] for their appraisal, although most aspects assessed would also be covered by these tools.

In summary, we have identified some content and reporting quality issues for consideration in future topical fluoride reviews.

In terms of reporting quality, complete reporting of objectives and eligibility criteria (in PICOS format), and of the search strategy, assessment of risk of bias, exploration of heterogeneity, and explicit reporting of the review process – what was and was not done in the review – are important issues in current publications that should be addressed more thoroughly in future reviews. We found the methods and reporting in the Cochrane topical fluoride reviews to be superior to others in general, and in line with PRISMA recommendations. Therefore, future systematic reviews on topical fluorides will benefit from following the PRISMA statement.

In terms of content, these are assessments of interventions and of direct comparisons of application features within interventions, population groups, and outcomes not covered to date or sufficiently. In addition, the relative economic value of topical fluoride therapies should also be assessed more widely. The CDSR in The Cochrane Library provides a registry of systematic reviews, making complete and ongoing Cochrane reviews an essential reference resource when undertaking a new systematic review, as they provide an indication of content areas already covered so that effort is not duplicated. An initiative to develop an international registry for prospective registration of protocols for all systematic reviews is now underway [Booth et al., 2010] and will be invaluable in assisting those planning new reviews and updating existing ones.

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Disclosure Statement

V.C.C.M. is an editor of the Cochrane Oral Health Group and the lead author in a series of Cochrane Topical fluoride reviews. S.I. and R.E.C. are review authors with the same group. None of the authors have any financial conflict of interests to declare.

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