International Journal of Dental Hygiene

Official Journal of the International Federation of Dental Hygienists

SYSTEMATIC REVIEW ARTICLE

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Dates:
Accepted 10 January 2014

To cite this article:
Int J Dent Hygiene **13**, 2015; 1–17.
DOI: 10.1111/idh.12072
Sälzer S, Slot DE, Dörfer CE, Van der Weijden GA. Comparison of triclosan and stannous fluoride dentifrices on parameters of gingival inflammation and plaque scores: a systematic review and meta-analysis.

Comparison of triclosan and stannous fluoride dentifrices on parameters of gingival inflammation and plaque scores: *a systematic review and meta-analysis*

Abstract: *Objective:* To systematically review the literature to compare the efficacy of triclosan (Tcs) and stannous fluoride (SnF) dentifrices on parameters of gingivitis and plaque scores. *Materials and Methods:* Medline, EMBASE and Cochrane Central Register of Controlled Trials were searched up to March 2013 to identify appropriate studies. Studies regarding self-performed manual brushing by adults with a minimum 4 weeks of follow-up were included. Primary outcomes were parameters of gingivitis. Secondary outcome was plaque score. *Results:* Of 55 publications, 11 met the eligibility criteria. Additionally, four unpublished papers were added after contacting the manufacturers of the leading brands. In total, 15 studies [10 medium term and five long term (>6 months)] were processed for data analysis. There was no difference in gingival index (or its modification) between the two types of dentifrice [DiffM-0.04, 95% confidence interval CI (−0.11; 0.04); $P = 0.34$]. The change in the average gingival bleeding score was significantly in favour of SnF [DiffM0.02, 95% CI (0.01; 0.02); $P < 0.00001$]. Plaque scores demonstrated a statistical significant difference in favour of Tcs, according to Quigley–Hein Plaque Index (Q&H PI; DiffM-0.29, 95% CI [−0.45; −0.13]; $P = 0.0004$), but there was no difference according to Rustogi Modified Navy Plaque Index (RMNPI) [DiffM-0.09, 95% CI (−0.01; 0.18); $P = 0.07$]. Long-term results supported these findings. *Conclusions:* In the context of inconclusive results for the primary outcome variable of gingival health, it can be concluded that there was a minor and most likely clinically insignificant difference between Tcs- and SnF-containing dentifrices. Meta-analysis of plaque score reduction was also inconclusive; whereas Tcs was more effective when assessed by the Q&H PI, it was not when scored with the RMNPI.

Key words: bleeding; dentifrice; gingivitis; meta-analysis; plaque; stannous fluoride; systematic review; toothpaste; triclosan

Introduction

Although a decline in the prevalence of dental caries over the last several decades has been observed, the prevalence of gingivitis remains high (1). Daily oral hygiene supports the maintenance of healthy marginal periodontal tissues and dental hard tissues. This maintenance contributes to a general feeling of well-being (2). The American Dental Association (ADA) recommends twice daily brushing and once daily flossing as a regimen for

good oral hygiene (3). The success of daily oral care depends on the individual defence mechanism, as well as knowledge, dexterity and discipline (4). A dentifrice is recommended to support the efficacy of tooth cleaning. Dentifrices are ideal vehicles for the carriage of plaque control agents in common usage. Some of their major ingredients include abrasives, detergents, thickeners, sweeteners, humectants, flavours and actives, such as triclosan (Tcs) and stannous fluorides (SnF) or other fluorides (5).

SnF was first added to dentifrice in the 1950s. Because of tooth staining and its taste, it was reformulated in 1997 as stabilized SnF; it still caused stains but was effective. More recently, a dentifrice was introduced into the marketplace (Crest® Pro-Health®; The Procter & Gamble Co., Cincinnati, OH, USA). In addition to 0.45% SnF, it contained sodium hexametaphosphate to facilitate the control of calculus and extrinsic tooth staining (6, 7). Temporarily, the dentifrices Crest® Gum Care (The Procter & Gamble Co.), additionally containing stannous chloride and sodium gluconate, and Crest® Plus Gum Care (The Procter & Gamble Co.) additionally containing an abrasive silica base, were available on the market.

Triclosan (Tcs; 2,4,4′ – trichloro-2′-hydroxy-diphenyl) is a broad-spectrum antimicrobial with anti-inflammatory effects because of its inhibition of the cyclooxygenase/lipoxygenase pathway of arachidonic acid metabolism (8). Because of its low substantivity and moderate effects on plaque formation, zinc citrate was added for a synergistic effect, for example to Mentadent P (Elida Gibbs, London, UK; 0.3% Tcs; 0.75% zinc citrate; 0.8% sodium fluoride). In the early 1990s, Colgate-Palmolive Co. (New York, NY, USA) added a copolymer of polyvinyl-methyl-ether and maleic acid (2.0% PVM/MA copolymer = Gantrez copolymer) to a 0.3% Tcs and 0.243% sodium fluoride dentifrice (Colgate® Total®; Colgate-Palmolive Co.; 9).

The long-term effects of Tcs on gingivitis and plaque reduction, compared with a conventional fluoride dentifrice, were confirmed by a systematic review (10). Similarly, these effects were shown for SnF-containing dentifrice (11). However, to our knowledge, no systematic review has been performed that has directly compared the effectiveness of these two ingredients in dentifrices. Therefore, the aim of this review was to provide, based on the currently available literature, a systematic evaluation of the effectiveness of a Tcs-containing dentifrice, compared with a SnF-containing dentifrice, as an adjunct to toothbrushing with regard to parameters of gingival inflammation and plaque scores.

Materials and methods

Focused PICO question

What are the effects of triclosan-containing dentifrices compared with SnF-containing dentifrices on the parameters of gingivitis and on plaque scores in healthy subjects aged at least 17 years?

Search strategy

Three Internet sources were searched for appropriate papers that would satisfy the study purpose: the National Library of Medicine in Washington, DC (PubMed-MEDLINE), the Cochrane Central Register of Controlled Trials and EMBASE. All databases were searched for studies conducted during or before March 2013. The structured search strategy was designed to include any published paper that compared the effects of Tcs-containing dentifrices and SnF-containing dentifrices on plaque and gingival parameters. For details regarding the search terms used, see Box 1. The reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of this study. In addition, the leading brands of SnF (Procter & Gamble, GABA, New York, NY, USA) and Tcs dentifrices (Colgate-Palmolive Co., Unilever) were contacted with requests to provide their unpublished data as proposed by the Cochrane Handbook (12) and Needleman (13).

Box 1
Search terms used for PubMed-MEDLINE, Cochrane CENTRAL and EMBASE. The search strategy was customized according to each individualized database that was searched. The following terms were used in the search strategy

{<Agent> AND <Intervention> AND <Control>}

{<*Agent*: [MeSh] toothpastes OR [text word] toothpaste OR dentifrice>

AND

<*Intervention*: [MeSh] Triclosan OR [text word] triclosan OR diphenyl ether derivatives OR Colgate total OR Mentadent>

AND

<*Control*: [MeSh] Tin Fluorides OR [text word] stannous fluoride OR tin fluoride OR stannic fluoride OR tin tetrafluoride OR tin difluoride OR inorganic fluoride of tin OR Crest pro-health OR Crest gum care OR Crest plus gum care>}

Eligibility criteria

The following eligibility criteria were applied:

- Randomized, controlled trials (RCTs) or controlled clinical trials (CCTs);
- Manuscripts written in the English, German or Dutch language;
- Studies conducted in humans ≥17 years old with good general health;
- Interventions using triclosan-containing (Tcs) dentifrices;
- Comparisons with stannous fluoride-containing (SnF) dentifrices;
- Only marketed dentifrices;
- Self-performed brushing with a manual toothbrush; and
- Parameters mentioned in studies with a 4-week minimum duration (ADA guidelines on chemotherapeutic products for control of gingivitis (14), that is, plaque, bleeding and gingivitis).

Screening and selection

The papers were independently screened by three reviewers (SS, GAW and DES), first by title and abstract. If the eligibility aspects were present in the title, the paper was selected. If none of the eligibility aspects were mentioned in the title, the abstract was read in detail to screen the article for suitability. After selection, two reviewers (SS and DES) read the full-text papers in detail. Disagreements were resolved by discussion. If disagreement persisted, the judgment of a third reviewer (GAW) was considered decisive.

Heterogeneity assessment

The following factors were used to evaluate the heterogeneity of the different study outcomes:

- Study design;
- Interventions and regimens;
- Clinical indices and
- Funding sources.

Quality assessment

Two reviewers (DES, SS) scored the methodological quality of the included studies. This quality was assessed according to the method described by Keukenmeester *et al.* (15). In short, when random allocation, defined eligibility criteria, blinding of examiners, balanced experimental groups, identical treatment between groups (except for the intervention) and follow-up reporting were present, the study was classified as having a low risk of bias. When one of these six criteria was missing, the study was considered to have a moderate risk of bias. When two or more of these criteria were missing, the study was considered to have a high risk of bias, as proposed by Van der Weijden *et al.* (16).

Data extraction

From the collection of papers that met the inclusion criteria, data were extracted with regard to the effectiveness of self-performed toothbrushing with Tcs- versus SnF-containing dentifrices. When intermediate assessments were presented, the baseline and final evaluations were used for this review. Mean values and standard deviations (SDs) were extracted (SS, DES). Some studies provided standard errors (SEs) of the means. When possible, the authors of this review calculated standard deviation based on the sample size ($SE = SD/\sqrt{N}$).

Data analysis

After a preliminary evaluation of the selected papers, considerable heterogeneity was observed regarding the study designs, characteristics, outcome variables and results. Where appropriate, a meta-analysis was performed, and differences in means (DiffMs) were calculated using Review Manager software (RevMan, version 5.1 for Windows, Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011) with either the fixed or 'random effects' model, as appropriate. If there were four or more studies to be analysed, the 'random effects' model was chosen to calculate the weighted average of the treatment effects across the studies (12). If there were fewer than four studies, the 'fixed effects' model was used (17). Not all studies could be included in the quantitative analysis of the total body of evidence. Therefore, data were also summarized using vote counting, and they are presented in a descriptive manner.

To test whether the results of the different studies were homogenous, the studies' heterogeneity was assessed by the chi-squared test and I^2 statistic during the meta-analysis. A chi-squared test resulting in $P < 0.1$ was considered an indication of significant statistical heterogeneity. I^2 yields a quantitative indication of the comparability of studies in a meta-analysis. An I^2 statistic of 0–40% is interpreted as not important, and >40% indicates that moderate to considerable heterogeneity might be present (18).

The ADA's requirements for chemotherapeutic products in the control of gingivitis demand a study period of 6 months to evaluate efficacy (14). Further, they require an evaluation period of at least 4 weeks for adjunctive devices used to control plaque and gingivitis (19). Because of limited available data, the inclusion criterion for this review was set to a minimum duration of 4 weeks. Therefore, a subanalysis was performed for medium-term studies, compared with long-term studies (lasting 6 months; 20).

Additionally, a subanalysis was performed for dentifrices containing Tcs plus copolymer (Colgate® Total®) versus SnF plus hexametaphosphate (Crest® Pro-Health®) in particular because these combinations are found in the two leading products.

The formal testing for publication bias that was proposed by Egger *et al.* (21) could not be used due to insufficient statistical power because <10 studies were included in the meta-analysis (12).

Results

Search and selection results

The PubMed-MEDLINE, EMBASE and Cochrane CENTRAL searches resulted (Fig. 1) in 55 unique papers, which were screened by title and abstract. After full-text reading, four papers were excluded (Table 1 shows the reasons for exclusion). This exclusion resulted in 11 full-text articles, plus an additional four unpublished studies provided by Procter & Gamble Co. Colgate and Unilever could not provide any unpublished work for this review. Additional hand searching of the reference lists of the selected studies yielded no additional papers.

Heterogeneity assessment of the selected studies

Considerable heterogeneity was observed with regard to the study design, evaluation period, professional prophylaxis, additional oral hygiene products used, funding sources and

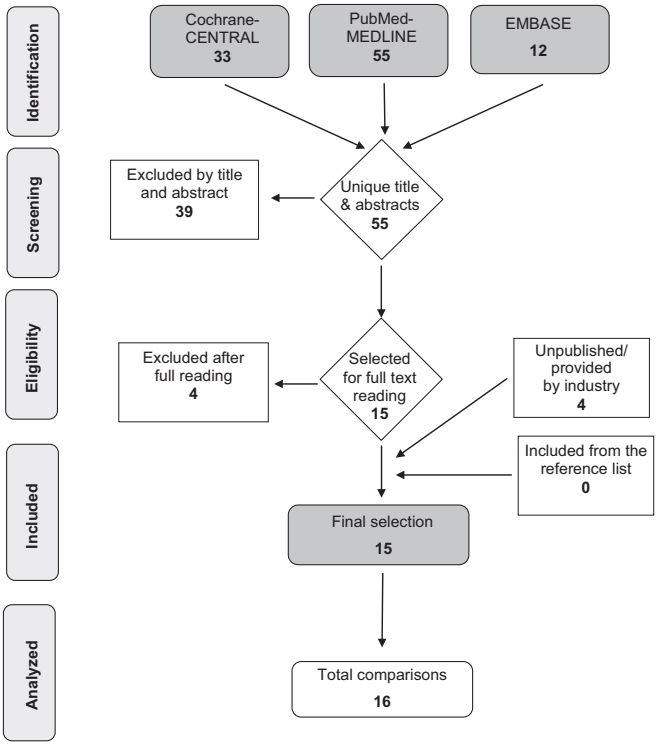

Fig 1. Flowchart of search, selection and analysis process.

clinical indices used. Information regarding the study characteristics, including the study population, is shown in Table 1.

Study design

When considering heterogeneity, the evaluation of balancing and stratifying the participants is a critical feature. Two studies did not mention whether the groups were balanced (22; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review). Some of the studies stratified and balanced their subjects by demographic data (23–25; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011 these unpublished data's are selected for this systematic review). Other studies also stratified groups based on clinical indices, such as gingival index and/or plaque index (23, 26–28). McClanahan balanced the subjects by gender and gingivitis score after a 3-month pretest period. In three other studies, the subjects were balanced only according to their baseline plaque and gingivitis indices (9, 29, 30).

Differences were noted in the oral prophylaxis regimen. Most of the trials did not mention oral prophylaxis before the test period (22–28, 30–32; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011 these unpublished data's are selected for this systematic review). The subjects in the McClanahan study were enrolled in a 3-month pretest period and received oral prophylaxis before and after the pretest. During this pretest period, the subjects were instructed to brush at least twice daily for a minimum 1-min period with a sodium-fluoride-containing dentifrice packaged in a white tube.

The protocols showed further differences. Most of the studies evaluated overnight plaque formation (9, 22, 24, 28, 29; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011 these unpublished data's are selected for this systematic review). In these studies, the subjects were asked to refrain from eating, drinking and smoking for 4 h prior to each study examination. Only small sips of water were allowed. The subjects in two other studies were not allowed to perform oral hygiene or to consume anything at least 4 h prior to their appointments (He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011 these unpublished data's are selected for this systematic review). The remaining studies did not mention any specific requirements.

Interventions and regimens

Most participants in the studies selected for this review were instructed to brush their teeth with either Tcs- or SnF-containing dentifrice twice daily for 1 min. In some studies, the subjects in the test and control groups were given different advice, for example, concerning the duration of brushing (23, 24, 32; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011 these unpublished data's are selected for this systematic review) and the allowance of rinsing after brushing (23, 24; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review).

Within the groups, dentifrices dispensed differed in their additional ingredients. In the Tcs (Colgate® Total®; Mentadent P, Church & Dwight Co. Inc., Princeton, NY, USA) group, all of the dentifrices containing 0.3% Tcs also contained sodium fluoride in various concentrations and additionally contained either a copolymer or zinc citrate.

All dentifrices in the SnF group contained 0.454% SnF and either sodium hexametaphosphate and zinc lactate (Crest® Pro-Health; The Procter & Gamble Co.) or stannous chloride and sodium gluconate (Crest® Gum Care; The Procter & Gamble Co.), as well as a silica abrasive base (Crest® Plus Gum Care; The Procter & Gamble Co.). In a study by He *et al.* (2009, unpublished data is selected for this systematic review), two different SnF- and sodium-hexametaphosphate-containing dentifrices (Experimental L and H) were evaluated. A request for more details revealed that the formulations were only slightly different. Experimental H was not marketed and therefore was not analysed in our study.

Manual toothbrushes were used in all studies except for the study by Biesbrock *et al.* (28). Here, the control group was subdivided into a group using a manual toothbrush with an

Table 1. **Summary and overview of the studies processed for data extraction**

Authors (year)	Study design, duration	Subjects baseline (end) Gender Age in years mean (range)	Gingivitis (periodontitis)	Groups (brand)	Use Instruction Prophylaxis Funding (number of authors related to either one of the products)	Original authors' conclusion
Archila *et al.* (2004)	RCT Parallel Double blind 6 months	199 (186) ♀: 132 ♂: 67 30 (17–65)	Gingivitis? No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Soft-bristled toothbrush 2 day^{-1} for 1 min Instruction: oral?; supervised 2 day^{-1} at the study site for 3 days each week Prophylaxis: at baseline Procter & Gamble (five out of six authors product-related)	The experimental SnF dentifrice over a 6-month period provides a statistically significant benefit in reducing gingivitis compared with a positive control Tcs dentifrice.
Ayad *et al.* (2010)	RCT Parallel Double blind 6 weeks	? (122) ♀: 80 ♂: 42 34.53◊ (18–68◊)	Gingivitis No periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Soft-bristled tooth brush 2 day^{-1} 1 min, Routine oral hygiene procedures allowed Instruction: oral? Prophylaxis: no Colgate-Palmolive (two out of four authors product-related)	Tcs-containing dentifrice provided a greater level of efficacy for the control of gingivitis and supragingival plaque than a dentifrice containing SnF.
Biesbrock *et al.* (2007)	RCT Parallel Single blind 8 weeks	? (89) ♀: ? ♂: ? ? (18–69)	Gingivitis Periodontitis?	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Test: Wave toothbrush, multilevelled (Colgate-Palmolive) Control: CrossAction®, angled (Procter & Gamble) 2 day^{-1} 2 min 'full ribbon of dentifrice' Instruction: written and verbal, supervision at Baseline and 4 weeks visit Prophylaxis: at baseline Procter&Gamble (three out of four authors product-related)	The highest overall plaque score at 8 weeks was found for manual toothbrush + Tcs-containing dentifrice.
Boneta *et al.* (2010)	RCT Parallel Double blind 6 months	121 (109) ♀: 77 ♂: 32 39.50◊ (21–70)	Gingivitis No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Soft-bristled toothbrush 2 day^{-1} for 1 min (no other oral hygiene products allowed) Instruction: oral? Prophylaxis: no Colgate-Palmolive (two out of five authors product-related)	Dentifrice containing Tcs + copolymer provides a significant reduction in established supragingival plaque and gingivitis, As compared to a dentifrice containing SnF + sodium hexametaphosphate when used over a period of six months.

Table 1. **(Continued)**

Authors (year)	**Study design, duration**	**Subjects baseline (end) Gender Age in years mean (range)**	**Gingivitis (periodontitis)**	**Groups (brand)**	**Use Instruction Prophylaxis Funding (number of authors related to either one of the products)**	**Original authors' conclusion**
He *et al.* (2012a)	RCT Parallel Double blind 2 months	150 (150) ♀: 90 ♂: 60 42.4 (18–65)	Gingivitis No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	ADA assigned soft manual toothbrush Test: at least one minute twice daily Control: preferably after every meal or at least twice daily Instruction: Test: verbal and written; supervised at baseline Control: as per manufacturers instruction Prophylaxis: no Procter&Gamble (three out of six authors product-related)	SnF dentifrice provided superior reductions in gingival inflammation and gingival bleeding compared with a Tcs/copolymer dentifrice after two months of toothbrushing.
He *et al.* (2012b)	RCT Parallel Double blind 2 months	200 (196) ♀: 121 ♂: 79 38.1 (19–79)	Gingivitis No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	ADA assigned soft manual toothbrush Test: at least one minute twice daily Control: after every meal and rinse completely after brushing Instruction: oral and written Test: supervised at baseline Prophylaxis: no Procter&Gamble (three out of four authors product-related)	Toothbrushing for 2 months with a SnF dentifrice provides superior reductions in gingival bleeding and inflammation when compared to brushing with a Tcs/copolymer dentifrice.
He *et al.* (2011a) UNPUB†	RCT Parallel Double blind 6 weeks	120 (117) ♀: 89 ♂: 31 38.4 (18–70)	Gingivitis? Periodontitis?	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Oral B Indicator Soft Manual Toothbrush Instruction: oral + written according to each product manufacturer's usage instructions; at baseline demonstration on site Prophylaxis: no Procter&Gamble (four out of six authors product-related)	Both treatment groups demonstrated significant reduction in RMNPI. SnF group demonstrated significantly lower RMNPI.
He *et al.* (2011b) UNPUB†	RCT Parallel Double blind 6 weeks	119 (119) ♀: 67 ♂: 52 30.2 (18–56)	Gingivitis? Periodontitis?	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Oral B Indicator Soft Manual Toothbrush Instruction: oral + written, on site product use baseline + week 3 Test: 1-inch strip, at least one minute twice daily, provided with timer Control: preferably after every meal or at least twice daily Prophylaxis: no Procter&Gamble (?? out of five authors product-related)	Treatment groups demonstrated significant reduction RMNPI. At week 6 SnF group lower but not significant RMNPI compared to Tcs, but not significant.

Table 1. **(Continued)**

Authors (year)	Study design, duration	Subjects baseline (end) Gender Age in years mean (range)	Gingivitis (periodontitis)	Groups (brand)	Use Instruction Prophylaxis Funding (number of authors related to either one of the products)	Original authors' conclusion
He *et al.* (2009) UNPUB†	RCT Parallel Double blind 6 months	205 (190) ♀: 144 ♂: 61 42.1 (18–73)	Gingivitis? Periodontitis?	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®) L: 0.454% SnF (Procter&Gamble) H: 0.454% SnF (Procter&Gamble)	ADA assigned soft manual toothbrush Routine floss permitted Instruction: oral + written; at baseline demonstration on site 1-inch stripe of assigned dentifrice, 1 min, twice daily at same time mornings and evenings Prophylaxis: at baseline Procter&Gamble (?? out of four authors product-related)	For the MGI and GBI, each experimental dentifrice demonstrated effectiveness that was statistically as good as or in some instances statistically superior to Tcs.
He *et al.* (2011c) UNPUB†	RCT Parallel Double blind 2 months	150 (148) ♀: 95 ♂: 55 37.4 (20–69)	Gingivitis No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Gum Care)	ADA assigned soft manual toothbrush Acclimation 4 weeks with Colgate® Total® Routine floss permitted Instruction: oral + written + at baseline demonstration on site; Week 4 telephone compliance recall Test: 1-inch strip, at least one minute twice daily Control: preferably after every meal or at least twice daily Prophylaxis: no Procter&Gamble (?? out of ??? authors product-related)	At month 2 both groups demonstrated significant lower mean GBI and MGI compared with baseline. SnF Group exhibited significant lower mean GBI and MGI relative to Tcs group.
Mankodi *et al.* (2002)	CCT Parallel Double blind 6 months	122 (109) ♀: 66 ♂: 53 34.49◊ (19–56)	Gingivitis? No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Gum Care)	Soft-bristled toothbrush 2/day for 1 min (no other oral hygiene products allowed) Instruction: oral? Prophylaxis: at baseline No sponsoring mentioned (four out of nine authors Colgate-Palmolive-related)	Tcs-containing dentifrice provides a statistically significant, substantive advantage in efficacy for the control of plaque and gingivitis over SnF-containing dentifrice and at the same time better control against extrinsic tooth staining.
McClanahan *et al.* (1997)	RCT Parallel Double blind 6 months	379 (309)◊ ♀: 255◊ ♂: 124◊ 36.07◊ (18–72)	Gingivitis? No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Plus Gum Care)	Own toothbrush; ≥2/day for ≥1 min;, provided with one-minute timers Instruction: oral? Prophylaxis: before and after pretest No sponsoring mentioned (six out of six authors Procter&Gamble related)	Superior clinical efficacy of a SnF dentifrice was shown relative to a Tcs/copolymer dentifrice in the chemotherapeutic control of gingivitis and gingival bleeding.

Table 1. **(Continued)**

Authors (year)	**Study design, duration**	**Subjects baseline (end) Gender Age in years mean (range)**	**Gingivitis (periodontitis)**	**Groups (brand)**	**Use Instruction Prophylaxis Funding (number of authors related to either one of the products)**	**Original authors' conclusion**
Owens *et al.* (1997)	RCT Parallel Double blind 18 weeks	107 (105)◊ ♀: ? ♂: ? ? (18–62)	Gingivitis No untreated periodontitis	Tcs (Colgate® Total®) Tcs (Mentadent P) SnF (Crest® Gum Care)	Multitufted toothbrush; 2/day; no other hygiene products Instruction: oral? Prophylaxis: at baseline No sponsoring mentioned	Small but statistically significant effect for PI was seen at 12 weeks in favour of the Tcs/copolymer dentifrice compared with the SnF dentifrice, This difference had disappeared by the 18-week examination
Sharma *et al.* (2013)	RCT Parallel Double blind 6 weeks	120 (114) ♀: 78 ♂: 42 37.5 (20–82)	Gingivitis? No untreated periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Oral B Indicator Soft Manual Toothbrush Instruction: oral + written, on site product use week 1 + 3 Test: 1-inch strip, at least one minute twice daily Control: after every meal and rinse completely after brushing Prophylaxis: no Procter&Gamble (three out of four authors product-related)	Both treatment groups demonstrated significant reduction in RMNPI. SnF group demonstrated significantly lower RMNPI.
Singh *et al.* (2010)	RCT Parallel Double blind 6 weeks	? (115) ♀: 67 ♂: 48 40.9◊ (19–70◊)	Gingivitis No advanced periodontitis	Tcs (Colgate® Total®) SnF (Crest® Pro-Health®)	Soft-bristled toothbrush; 2/day for 1 min Instruction: oral? Prophylaxis: no Colgate-Palmolive (four out of six authors product-related)	Dentifrice containing Tcs provides a greater level of efficacy for the control of gingivitis and supragingival plaque than does a standard dentifrice SnF.

Dentifrices used in the test group: Colgate® Total® (0.3% Tcs + copolymer + sodium fluoride); Mentadent P (0.3% Tcs + zinc citrate + sodium fluoride) and in the control group: Crest® Pro-Health® (0.454% SnF + sodium hexametaphosphate + zinc lactate); Crest® Gum Care (0.454% SnF + stannous chloride + sodium gluconate); Crest® Plus Gum Care (0.454% SnF + silica abrasive base).

?, Unknown; ◊, Calculated by the authors of this review; RCT, Randomized Controlled Trial; CCT, Controlled Clinical Trial; GBI, Gingival Bleeding Index; MGI, Modified Gingival Index; PI, Plaque Index; RMNPI, Rustogi Modification of the Navy Plaque Index; *, According to manufacturer information control L was marketed as Crest® Pro-Health® and control H was unmarketed, therefore not analysed; †, unpublished data is selected for this systematic review.

angled bristle surface configuration and another using a powered toothbrush, whereas the Tcs group was provided with a manual multilevel toothbrush. For a balanced comparison with the other data, the powered toothbrush data were not entered into the meta-analysis.

Most of the studies did not allow any additional oral hygiene products, whereas one study allowed routine oral hygiene procedures (29). Instructions differed mainly in their procurement. Most of the studies mentioned only verbal instructions and did not mention any monitoring. In some studies, the subjects were supervised at baseline (He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Ohmer B, Widmeyer V, 2009 these unpublished data's are selected for this systematic review) and after 3 or 4 weeks (24, 28; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Ohmer B, Widmeyer V, 2009 these unpublished data's are selected for this systematic review) or twice daily at the study site for 3 days each week (26). In two additional studies, only the subjects in the Tcs group were supervised at baseline (23, 32). Compliance in using the dentifrice was monitored by Mankodi *et al.* (30) when the dentifrices were issued, and the subjects returned their previous tubes. In another study, compliance was monitored by a phone call at week 4. In six studies, the patients in the test and control groups were instructed differently (23, 24, 32; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Ohmer B, Widmeyer V, 2009 these unpublished data's are selected for this systematic review).

Clinical indices

In this review, different indices and their modifications were used and are presented in the online Appendix S3A–D. Plaque was recorded either with the Turesky modification of the Quigley–Hein Plaque Index (Q&H PI; 33) or the Rustogi Modification of the Navy Plaque Index (RMNPI; 34).

For the gingival index, the Löe and Silness Indexes (35) were recorded using the original version or a modified version: the 1967 modification (36), Mandel–Chilton modification (37) or Lobene modification (38). Bleeding was recorded in six studies using the number of sites based on either the Gingival Index grade 2 or 3 or on the gingival bleeding index (GBI) grade 1 or 2. Bleeding was evaluated based on the GBI (39) or as the number of bleeding sites based either on the Gingival Index grade 2 or 3 or on the GBI grade 1 or 2. Six studies presented data on the number of bleeding sites (23, 27, 32, 40; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Ohmer B, Widmeyer V, 2009 these unpublished data's are selected for this systematic review). Following our inquiry, these data were re-analysed, and the percentage of bleeding sites was subsequently provided by the authors to allow for a proper comparison with the data from other studies.

Funding source

Most of the studies mentioned some type of relationship between the authors and the manufacturers of either the test or control dentifrice. Twelve studies were industry funded (nine by Procter & Gamble, three by Colgate-Palmolive). The unpublished studies provided by Procter & Gamble did not mention any sponsoring but were funded by the company. Only the study by Owens (25) did not mention any sponsorship or relationship with either product.

Quality assessment

Quality assessment parameters, including external, internal and statistical validity, are shown in online Appendix S2. Based on a summary of these criteria, the estimated risk of bias was low to moderate.

Study outcomes

Changes within groups

Information regarding the study outcomes within groups is presented in online Appendix S3A–D. A significant change within the groups was observed in most of the studies. In the McClanahan study, the plaque score was compared with the situation after tooth cleaning; therefore, deterioration or increased scores were observed. Both studies that evaluated staining showed increases (27, 30).

Comparison between groups

Table 2 presents a summary of the descriptive data regarding the significant differences between the Tcs and SnF groups. Table 3 details the meta-analysis. For plaque reduction, Tcs was significantly more effective than the SnF group in four studies (9, 22, 29, 30), whereas in four other groups (24, 27, 28; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011, unpublished data is selected for this systematic review), the SnF-containing dentifrice was more effective. Two studies did not show any significant between-group differences (25; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review).

Concerning average bleeding, five studies (23, 26, 27, 32; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review) found a significantly greater reduction in bleeding tendency in the SnF group. A statistically greater reduction in the gingival index for the Tcs group was found in four studies (9, 22, 29, 30), and such a reduction was found in five studies for the SnF group (23, 26, 27, 32; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review).

For the parameters of gingivitis and plaque, a correlation between the outcome and sponsorship was observed.

Table 2. **A summary of statistical analysis outcomes of Triclosan compared with Stannous fluoride-containing dentifrice**

Study	Intervention	Plaque Score	Bleeding Score	Gingival Index	Staining	Control
Archila *et al.* (2004)	Tcs	□	–	–	□	SnF + sodium hexametaphosphate
Ayad *et al.* (2010)		+	□	+	□	
Biesbrock *et al.* (2007)		–	□	o	□	
Boneta *et al.* (2010)		+	□	+	□	
He *et al.* (2012b)		□	–	–	□	
He *et al.* (2012b)		□	–	–	□	
He *et al.* (2011a) UNPUB†		–	□	□	□	
He *et al.* (2011b) UNPUB†		o	□	□	□	
He *et al.* (2009) UNPUB†		□	o	o	□	
Sharma *et al.* (2013)		–	□	□	□	
Singh *et al.* (2010)		+	□	+	□	
He *et al.* (2011c) UNPUB†		□	–	–	□	SnF
Mankodi *et al.* (2002)		+	□	+	+	
McClanahan *et al.* (1997)		–	–	–	+	
Owens *et al.* (1997)		o	□	o	□	SnF + sodium hexametaphosphate
	Tcs*	o	□	o	□	

+, Intervention (Tcs) was significantly more effective; □, No data available; o, No significant difference; –, Intervention was significantly less effective; *, Additionally containing zinkcitrate; †, unpublished data is selected for this systematic review; ▬ Authors related to Procter & Gamble; ▬ Authors related to Colgate.

In contrast, the studies that did not mention any sponsorship or that were unpublished did not favour either of the products.

Both studies evaluating staining demonstrated that tooth discoloration was significantly greater for the SnF group in both studies. In the study by Mankodi *et al.* (30), of the 122 subjects, four participants who had been using an SnF-containing dentifrice dropped out of the study after 3 months due to tooth staining.

Only one study (He T, Barker ML, Ohmer B, Widmeyer V, 2009, unpublished data is selected for this systematic review) did not mention any adverse effects on oral hard or soft tissues, and no study mentioned any product-related reasons for withdrawal, other than staining. In a long-term study by He *et al.*, three of 205 subjects withdrew because of adverse events (one from the Tcs group and two from the SnF group), which were mild but not further specified. Possible/probable treatment-related adverse events were presented by 11% of the subjects in the Colgate® Total® group and 16% of patients in the SnF group. Most of these adverse events (94%) consisted of desquamation of the mucous membranes and hyperesthesia.

Meta-analysis

A meta-analysis was performed to compare the effects of a Tcs-containing dentifrice versus an SnF-containing dentifrice. A summary is presented in Table 3. Further subanalysis was performed to compare medium- and long-term studies, as well as Tcs plus copolymer and SnF plus sodium hexametaphosphate (Colgate® Total® and Crest® Pro-Health®).

Overall analysis

Changes in the average bleeding scores were significantly in favour with the SnF group [DiffM 0.02, 95% CI (0.01; 0.02); $P < 0.00001$]. Assessing the Gingival index and its modifications resulted in a non-significant difference (DiffM −0.04, 95% CI −0.11; 0.04; $P = 0.34$). Focusing on the different modifications of the gingival index, only the Lobene modification was significantly in favour of the SnF group, with a small mean difference in means [DiffM 0.07, 95% CI (0.05; 0.09); $P < 0.00001$].

With regard to plaque scores, seven studies evaluated the Q&H PI, which showed beneficial effects for the Tcs group [DiffM −0.29, 95% CI (−0.45; −0.13); $P = 0.0004$]. In the

Table 3. **Meta-analysis**

Index	Studies	Random/ Fixed	Time of assessment	DiffM	95% CI	Test for overall effect (*P*)	Test for heterogeneity	
							P	I^2 (%)
(A) Overall: triclosan versus stannous fluoride								
GI (total)	Archila *et al.* (2004) Ayad *et al.* (2010) Biesbrock *et al.* (2007) Boneta *et al.* (2010) He *et al.* (2009) He *et al.* (2011a) He *et al.* (2012a) He *et al.* (2012b) Mankodi *et al.* (2002) McClanahan *et al.* (1997) Owens *et al.* (1997) Owens *et al.* (1997)* Singh *et al.* (2010)	Random	Base	0.00	[−0.01; 0.02]	0.61	0.34	10
			End	−0.04	[−0.11; 0.04]	0.34	<0.001	97
Löe-Silness	Archila *et al.* (2004) Ayad *et al.* (2010) Biesbrock *et al.* (2007) Boneta *et al.* (2010) McClanahan *et al.* (1997) Singh *et al.* (2010)	Random	Base	0.03	[0.00; 0.05]	0.02	0.65	0
			End	−0.09	[−0.20; 0.03]	0.13	<0.001	95
Mandel-Chilton Modification	Mankodi *et al.* (2002) Owens *et al.* (1997) Owens *et al.* (1997)*	Random	Base	−0.04	[−0.08; −0.00]	0.05	0.99	0
			End	−0.08	[−0.28; 0.13]	0.45	<0.001	97
Lobene Modified Gingival Index	He *et al.* (2009) He *et al.* (2011b) He *et al.* (2012a) He *et al.* (2012b)	Random	Base	0.00	[−0.01; 0.02]	0.91	0.79	0
			End	0.07	[0.05; 0.09]	<0.001	0.42	0
Average GBI Bleeding	Archila *et al.* (2004) He *et al.* (2009) He *et al.* (2011c) He *et al.* (2012a) He *et al.* (2012b) McClanaham *et al.* (1997)	Random	Base	0.00	[−0.00; 0.01]	0.31	0.92	0
			End	0.02	[0.01; 0.03]	<0.001	0.01	67
			Dif	0.02	[0.01; 0.02]	<0.001	0.26	23
PS Q&H PI (1962)	Ayad *et al.* (2010) Boneta *et al.* (2010) Mankodi *et al.* (2002) McClanahan *et al.* (1997) Owens *et al.* (1997) Owens *et al.* (1997)* Singh *et al.* (2010)	Random	Base	0.03	[−0.01; 0.08]	0.16	0.61	0
			End	−0.29	[−0.45; −0.13]	<0.001	<0.001	90
RMNPI	Biesbrock *et al.* (2007) He *et al.* (2011a,b) He *et al.* (2011c) Sharma *et al.* (2013)	Random	Base	0.00	[−0.01; 0.01]	0.57	0.59	0
			End	0.09	[−0.01; 0.18]	0.07	<0.001	97

Table 3. **(Continued)**

Index	Studies	Random/ Fixed	Time of assessment	DiffM	95% CI	Test for overall effect (*P*)	Test for heterogeneity *P*	Test for heterogeneity I^2 (%)
(B) Subanalysis on study duration analysing long-term studies (>6 months)								
GI (total)	Archila (2004) Boneta (2010) He (2009) Mankodi (2002) McClanahan (1997)	Random	Base	−0.01	[−0.03; 0.02]	0.50	0.38	5
			End	−0.06	[−0.23; 0.10]	0.44	<0.001	97
Average GBI Bleeding	Archila (2004) He (2009) McClanaham (1997)	Random	Base	0.01	[−0.01; 0.02]	0.28	0.77	0
			End	0.02	[−0.00; 0.04]	0.08	0.006	80
			Dif	0.02	[0.01; 0.04]	0.008	0.23	33
PS Q&H PI (1962)	Boneta (2010) Mankodi (2002) McClanahan (1997)	Fixed	Base	−0.04	[−0.12; −0.05]	0.40	0.99	0
			End	−0.26	[−0.34; −0.18]	<0.001	<0.001	93
(C) Subanalysis in BRAND: Colgate® Total® versus Crest® Pro-Health®								
GI (total)	Archila *et al.* (2004) Ayad *et al.* (2010) Biesbrock *et al.* (2007) Boneta *et al.* (2010) He *et al.* (2009) He *et al.* (2012a) He *et al.* (2012b) Singh *et al.* (2010)	Random	Base	0.01	[−0.00; 0.03]	0.12	0.57	0
			End	−0.04	[−0.13; 0.05]	0.41	<0.001	96
Average GBI Bleeding	Archila *et al.* (2004) He *et al.* (2009) He *et al.* (2012a) He *et al.* (2012b)	Random	Base	0.00	[−0.01; 0.01]	0.64	0.91	0
			End	0.02	[0.00; 0.04]	0.02	0.004	78
			Dif	0.02	[0.01; 0.03]	<0.001	0.39	0
PS Q&H PI (1962)	Ayad *et al.* (2010) Boneta *et al.* (2010) Singh *et al.* (2010)	Fixed	Base	0.03	[−0.04; 0.11]	0.36	0.76	0
			End	−0.45	[−0.55; −0.35]	<0.001	0.28	21
RMNPI	Biesbrock *et al.* (2007) He *et al.* (2011a,b) He *et al.* (2011c) Sharma *et al.* (2013)	Random	Base	0.00	[−0.01; 0.01]	0.57	0.59	0
			End	0.09	[−0.01; 0.18]	0.07	<0.001	97

DiffM, difference in means; CI, confidence interval; GI, gingival index; GBI, gingival bleeding index; PS, plaque scores; *, Additionally containing zinkcitrate Base, baseline investigation; End, end of investigation; Dif, difference between baseline and end of investigation.

four studies that assessed RMNPI scores, no statistically significant differences were observed [DiffM −0.09, 95% CI (−0.01; 0.18); $P = 0.07$]. Heterogeneity was significant for all plaque and gingivitis parameters, except for the Lobene Modified gingival index.

Subanalysis of study duration

The long-term data (duration ≥6 months) supported the findings of the primary meta-analysis. As for the overall analysis, a minor but statistically significant difference was found in the change in average bleeding sites [DiffM 0.02, 95% CI (−0.01; 0.03); $P < 0.001$]. The gingival index and its modifications were consistently not different between the groups [DiffM −0.06, 95% CI (−0.23; 0.10); $P = 0.44$].

The Q&H PI outcome was significantly in favour with the Tcs group [DiffM −0.26, 95% CI (−0.34; −0.18); $P < 0.00001$]. No studies evaluating plaque according to the RMNPI were included in this subanalysis.

Subanalysis of two specific formulations

Comparing the change in average bleeding with Colgate® Total® and Crest® Pro-Health® in a subanalysis, a significant

Table 4. **GRADE evidence profile of the difference between Tcs and SnF-containing dentifrices in relation to the indices evaluated**

Outcome	Gingival Index	Bleeding score	Plaque score
Risk of bias	Moderate	Moderate	Moderate
Consistency	Inconsistent	Consistent	Inconsistent
Directness	Possibly generalizable	Generalizable	Possibly generalizable
Precision	Moderate	Good	Moderate
Publication bias/Limitation	Possible	Possible	Possible
Strength of recommendation	**Weak**	**Moderate**	**Weak**

difference in favour with SnF was demonstrated [DiffM 0.02, 95% CI (0.01; 0.03); $P < 0.00001$]. As for the overall analysis, the gingival index did not show a difference for the subanalysis of brands [DiffM −0.04, 95% CI (−0.13; 0.05); $P = 0.41$]. The Q&H PI outcome was significantly in favour of Tcs [DiffM −0.45, 95% CI (−0.55; −0.35); $P < 0.00001$]. The data with regard to the RMNPI did not change because the studies included in the overall analysis and in the subanalyses were identical.

Grading the 'body of evidence'

Table 4 shows a summary of the various aspects that were used to rate the quality of the evidence and the strength of the recommendations according to GRADE (41).

The data were generally estimated to have a moderate risk of bias and possible publication bias. The data for the gingival index and plaque scores were inconsistent. These findings led to the conclusion that the strength of recommendation was considered to be 'weak' for the gingival index and the plaque scores and to be 'moderate' for bleeding. As the results were inconclusive for the different parameters evaluated, the recommendation to prefer either Tcs- or SnF-containing dentifrice was considered 'weak'.

Discussion

Colgate® Total® and Crest® Pro-Health® are the only two dentifrices with antiplaque and antigingivitis properties accepted by the ADA (42). This systematic review was conducted to compare the effectiveness of a Tcs-containing dentifrice and SnF-containing dentifrices with regard to gingivitis and plaque scores based on the currently available literature. The efficacy of the separate therapeutic agents was already proven to be superior compared with a control based on earlier systematic reviews (10, 11, 20, 43). The present study was a systematic review of head-to-head comparisons. The determination of the therapeutic relevance of the clinical effects of SnF versus Tcs formulations for the reduction in gingivitis is more relevant in a direct comparison of the products.

Study characteristics: study quality assessment

All studies included in this review were RCTs. Nonetheless, further data analysis revealed differences in the quality of the study designs, for example, in the balancing of groups, percentage of dropouts and reported loss to follow-up. In the study by Biesbrock (28), the conditions were different, apart from the dentifrice intervention, as different types of manual toothbrushes were used (angled in the SnF group and waved in the Tcs group), which might have led to additional differences in outcomes. Slot *et al.* (44) have shown that the effect of mechanical brushing is diverse and depends on the toothbrush type used. Chemical plaque inhibition could provide an additional benefit with respect to plaque reduction.

Furthermore, different instructions given to each group in some studies might have influenced the results (23, 24, 32; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011; He T, Barker ML, Miner M, White DJ, Sharma N, Quaqish J, 2011; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011 these unpublished data's are selected for this systematic review). Furthermore, the study duration varied considerably between studies. Therefore, a subanalysis of long-term (≥6 months) studies was performed. Further differences were noted in the statistics, for example, per protocol or intention-to-treat analyses. None of the studies provided information regarding allocation concealment or sample size calculation. Assessing quality is important in interpreting differences in outcomes and in limiting bias in systematic reviews. As all studies provided information on sample size, outcomes and standard errors/deviations, a meta-analysis could be performed, but the studies were separately analysed based on the index used.

No significant differences between groups were observed at baseline. Therefore, the differences revealed in the meta-analysis at the end of the study demonstrated true differences in outcomes of the investigated products. Heterogeneity was significant for all the plaque indices and for the gingivitis index, with I^2 showing values of 90–97%.

Further bias might have been related to the funding by industry. Only one study (25) did not mention a relationship between the authors and manufacturers. Correlations between funding by industry and study outcomes have been frequently observed in the literature (45–47), but this correlation has not been generally observed (48). In this review, the studies that did not show any between-group differences were either not related to the industry or were unpublished. Moreover, Khan *et al.* (48) demonstrated that studies funded by the industry were more likely not to be published. The clinical investigation of the included studies was performed either at a university setting or a research centre. Whether this introduced a publication bias could not be assessed.

Compliance

The compliance of the given protocols should be considered as an important factor in the study outcomes. Only a few stud-

ies mentioned that compliance was evaluated. Although Mankodi *et al.* (30) monitored the use of dentifrice by evaluating the returned tubes, they did not mention any outcomes related to compliance. Other studies randomly controlled compliance through monitoring at certain time intervals (24, 40, 49; He J, Eynon H, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review). However, once again, none of the studies mentioned compliance outcomes.

Considering compliance, the Hawthorne effect plays a role in evaluating prospective studies. The subjects are likely to having changed their behaviour in the regarded studies. These behavioural changes are most obvious at the beginnings of the studies (16). Note that in an attempt to reduce the Hawthorne effect, a pretest was performed in the McClanahan study (27). During this 3-month period, the subjects were provided with a sodium fluoride dentifrice packaged in uniquely labelled, identical white tubes, which mimicked the appearance of the tubes that were subsequently used for the test products during the treatment phase of the study. The Hawthorne effect might possibly have abated in the five long-term studies.

Only five studies (9, 25, 27, 29; He T, Rooney J, Barker ML, Widmeyer V, Miner M, 2011, unpublished data is selected for this systematic review) evaluated a negative control group provided with a sodium-fluoride-containing dentifrice in their study designs. A missing negative control arm might have biased the analysis because an improvement might have been observed as well in a negative control group. This fact is most likely due to the Hawthorne effect. As we evaluated head-to-head comparisons, this effect should have had a similar influence on both of the evaluated groups. Nevertheless, a true estimate of the antigingivitis and antiplaque effects cannot be obtained without a negative control group. The ADA guidelines (14) on chemotherapeutic products for the control of gingivitis (mentioned earlier) also consider antigingivitis agents compared with a negative control.

Formulations

The higher substantivity of a dentifrice aligns with the longer effectiveness of the active ingredients. Therefore, the properties of the active ingredient and its substantivity should be considered as discriminating factors.

Sodium hexametaphosphate seems to influence the properties of SnF-containing dentifrices with regard to substantivity, staining and calculus formation (50). Sodium hexametaphosphate is supposed to provide stronger attraction to calcium hydroxyapatite in enamel and dentin, thereby resulting in greater substantivity and an increase calcium hydroxyapatite's potential to prevent crystallization on the enamel surface (i.e. calculus prevention) and stain-chromogen adsorption (50).

The improved efficacy and enhanced substantivity when PVM/MA is added to a Tcs-containing dentifrice have been demonstrated by several studies (51–53). This copolymer, when combined with Tcs, ensures the delivery and retention of the Tcs on the enamel and epithelial cells (51, 54).

In combination with zinc citrate, Tcs does not seem to be as effective as when is formulated with Gantrez. Its effect versus a control was shown to be non-significant (20). Subsequently, a subanalysis of Tcs plus copolymer-containing dentifrices was performed in the meta-analysis.

Tcs was clinically proved to reduce plaque and gingivitis in an adult population. It is a bisphenolic antibacterial agent, which has low toxicity and a broad spectrum of activity, being effective against both Gram-positive and Gram-negative bacteria (55). According to Fine *et al.* (56), the antimicrobial effects of Tcs seem to be greater than those of SnF-containing dentifrices. Fine *et al.* compared the reduction in six microbial groups from four sites (i.e. plaque, saliva, the tongue and the buccal mucosa) after brushing with a Tcs-, SnF- or sodium-fluoride-containing dentifrice for 2 weeks. They found a sustained and significantly greater reduction in all of the microbial groups evaluated in all four oral environments. This finding is also reflected in the meta-analysis of this review, in which the effect on plaque score was greater with Tcs dentifrices.

Efficacy data

According to the acceptance program guidelines for chemotherapeutic products for the control of gingivitis, published by the ADA and the Council on Dental Therapeutics (14), a tested product should demonstrate a ≥15% reduction in gingivitis in terms of efficacy, compared with a control product. Therefore, the minor but significant difference in bleeding index of 0.02 seemed to be clinically negligible.

The two different indices used in the selected studies to evaluate the level of plaque accumulation demonstrated inconclusive results. The Q&H PI outcome was significantly in favour with Tcs. This finding corroborates the findings of Barnes *et al.*, in whose 24-h plaque study the changes in the Modified Gingival Margin Plaque Index were smaller in the Colgate® Total® group, compared with the Crest® Pro-Health® group (57). Despite these findings, the RMNPI outcome did not demonstrate any difference between Tcs and SnF. Different outcomes, depending on the index, were supported by Biesbrock *et al.* (49), who found numerically higher values for the Q&H PI, compared with the RMNPI. This difference was also discussed by Slot *et al.* (44). A full explanation for this finding could not be provided. Whether the indices analysed in this systematic review are sensitive enough cannot be stated based on this systematic review, but all of them are however commonly used in dentistry for this particular purpose.

Adverse events

Staining is a known complication with SnF-containing dentifrices (11). Adding hexametaphosphate to the SnF dentifrice formulation appears to reduce this risk. He *et al.* (31) demonstrated, in a randomized, CCT, no statistically significant differences in the Lobene Staining Index over 5 weeks between Colgate® Total and SnF-containing dentifrices. This finding correlated with Schiff *et al.*, who found only a minor increase

after 6 months (58). Two of the included studies showed less staining with Tcs, compared with SnF-containing dentifrices. In contrast, we found less staining for the Tcs-containing dentifrice in both studies that investigated staining (27, 30). These conflicting outcomes might find their origin in the duration of these two studies because the observation periods were ≥6 months. In a study by Paraskevas (59), 301 subjects, using either amine fluoride/SnF dentifrice and mouth rinse or a regular sodium fluoride dentifrice, demonstrated a significantly greater increase in staining for the SnF group. In this study, five subjects in this group discontinued the study because they felt that the staining was interfering with their social lives. Another 15 dropped out from either of the groups for unknown reasons. According to a systematic review of Tcs-containing dentifrices, the dropouts ranged from 1% to 13% and were all non-product-related; no adverse events were reported (43).

The environmental and health effects of Tcs have been widely discussed (60, 61). However, there has been no evidence that Tcs is hazardous to humans. Some animal studies have demonstrated an alteration in hormone regulation. Furthermore, Tcs might influence bacterial resistance. Tcs is included in many products in addition to dentifrices, such as soaps, deodorants, toys and kitchen utensils (60, 61). As only small amounts of dentifrices containing 0.3% Tcs are used, the total amount of Tcs used in dentifrices is comparatively low. Nevertheless, because of the above-mentioned concerns, SnF-containing dentifrices might be privileged in case of similar clinical results.

Limitations

*Although the major databases were used for the literature search, papers might have been missed because they were either not listed in these sources or because they were published in languages other than English, Dutch or German.

*The four manuscripts with unpublished data that were supplied by the manufacturer did not face a peer-review process, which could introduce a bias. However, a detailed quality assessment (online Appendix S2) of all included studies has been performed.

*This review was also intended to address the parameters of gingivitis in some studies; specifically, it was not clear whether the selected subjects were true gingivitis patients. The inclusion criteria ranged from the absence of the description to the lack of advanced or untreated periodontitis. This limitation hampers any extrapolation to subjects with only gingivitis.

*Various toothbrush types were used in the studies included and therefore evaluation of the added benefit of the toothpaste between studies might be influenced by this diversity.

Recommendation for further research:

This review assessed the added effect of SnF and Triclosan over the effect of mechanical toothbrushing alone. Future studies should address standardization of toothbrushing techniques and the quality of the toothbrush itself.

Conclusion

In the context of the inconclusive results for the primary outcome variable of gingival health, it can be concluded that there was a minor and, most likely, clinically insignificant difference between Tcs- and SnF-containing dentifrices.

The meta-analysis of plaque reduction was also inconclusive; whereas Tcs was more effective as assessed according to the Q&H PI, the plaque scores did not substantiate this finding when scored according to the RMNPI.

Acknowledgements

The authors gratefully acknowledge the support of Joost Bouwman, head librarian of the ACTA, and Stephen Siegel from the *Journal of Clinical Dentistry*, who helped retrieve full-text papers. The authors would also like to thank Paula Koenigs from the Procter & Gamble Company, who responded to a request to provide additional unpublished data. The authors also acknowledge support from Christian Andres Schneider and Christian Flörke, who were of great help in screening and selecting the literature. Furthermore, the authors thank Prof. J. C. Gunsolley (Department of Periodontology, Virginia Commonwealth University, Richmond, Virginia, USA) for his comments and suggestions.

Conflict of interest

The authors declare that they have no conflict of interest.

Source of funding

This study was initiated and self-funded by the authors and their institutions. Dörfer, Slot and Van der Weijden have formerly received either external advisor fees, lecturer fees or research grants from either Procter & Gamble, Colgate/GABA or Unilever.

References

♦ Indicates studies selected for this systematic review.

1 Micheelis WSU. Vierte Deutsche Mundgesundheitsstudie (DMS IV). In: Ärzte-Verlag D, ed. *IDZ Materialreihe*. Köln, Institut der Deutschen Zahnärzte, 2006.

2 Dörfer CE, Staehle HJ. Strategien der häuslichen Plaquekontrolle. *Zahnmedizin Up2date* 2010; **3**: 229–254.

3 ADA. *Toothbrushes*. 2010.

4 Kenney EB, Saxe SR, Lenox JA *et al*. The relationship of manual dexterity and knowledge to performance of oral hygiene. *J Periodontal Res* 1976; **11**: 67–73.

5 Sheen S, Pontefract H, Moran J. The benefits of toothpaste–real or imagined? The effectiveness of toothpaste in the control of plaque, gingivitis, periodontitis, calculus and oral malodour. *Dent Update* 2001; **28**: 144–147.

6 Liu H, Segreto VA, Baker RA, Vastola KA, Ramsey LL, Gerlach RW. Anticalculus efficacy and safety of a novel whitening dentifrice containing sodium hexametaphosphate: a controlled six-month clinical trial. *J Clin Dent* 2002; **13**: 25–28.

7 Baig A, He T. A novel dentifrice technology for advanced oral health protection: a review of technical and clinical data. *Compend Contin Educ Dent* 2005; **26**: 4–11.

8 Gaffar A, Scherl D, Afflitto J, Coleman EJ. The effect of triclosan on mediators of gingival inflammation. *J Clin Periodontol* 1995; **22**: 480–484.

9 ♦ Singh S, Chaknis P, DeVizio W, Petrone M, Panagakos FS, Proskin HM. A clinical investigation of the efficacy of three commercially available dentifrices for controlling established gingivitis and supragingival plaque. *J Clin Dent* 2010; **21**: 105–110.

10 Hioe KP, van der Weijden GA. The effectiveness of self-performed mechanical plaque control with triclosan containing dentifrices. *Int J Dent Hyg* 2005; **3**: 192–204.

11 Paraskevas S, van der Weijden GA. A review of the effects of stannous fluoride on gingivitis. *J Clin Periodontol* 2006; **33**: 1–13.

12 Higgins JPT, Green S. *Handbook for Systematic Reviews of Interventions; Version 5.1.0 2009*. Available at: http://cochrane-handbook.org (accessed 28 October 2013).

13 Needleman IG. A guide to systematic reviews. *J Clin Periodontol* 2002; **29** (Suppl. 3): 6–9.

14 ADA. *Chemotherapeutic Products for Control of Gingivitis*. Acceptance Program Guidelines; 2008. p. Web site.

15 Keukenmeester RS, Slot DE, Rosema NA, Van der Weijden GA. Determination of a comfortable volume of mouthwash for rinsing. *Int J Dent Hyg* 2012; **10**: 169–174.

16 Van der Weijden GA. Models for assessing powered toothbrushes. *Adv Dent Res* 2002; **16**: 17–20.

17 Poklepovic T, Sambunjak D, Johnson TM *et al*. Interdental brushing for the management of periodontal diseases and dental caries in adults. *Cochrane Database Syst Rev* 2012; (12): CD009857.

18 Van Strydonck DA, Slot DE, Van der Velden U, Van der Weijden F. Effect of a chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review. *J Clin Periodontol* 2012; **39**: 1042–1055.

19 ADA. *Adjunctive Dental Therapies for the Reduction of Plaque and Gingivitis*. Acceptance Program Guidelines 2011.

20 Gunsolley JC. A meta-analysis of six-month studies of antiplaque and antigingivitis agents. *J Am Dent Assoc* 2006; **137**: 1649–1657.

21 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629–634.

22 ♦ Boneta AE, Aguilar MM, Romeu FL, Stewart B, DeVizio W, Proskin HM. Comparative investigation of the efficacy of triclosan/copolymer/sodium fluoride and stannous fluoride/sodium hexametaphosphate/zinc lactate dentifrices for the control of established supragingival plaque and gingivitis in a six-month clinical study. *J Clin Dent* 2010; **21**: 117–123.

23 ♦ He T, Barker ML, Goyal CR, Biesbrock AR. Anti-gingivitis effects of a novel 0.454% stabilized stannous fluoride dentifrice relative to apositive control. *Am J Dent* 2012; **25**: 136–140.

24 ♦ Sharma N, He T, Barker ML, Biesbrock AR. Plaque control evaluation of a stabilized stannous fluoride dentifrice compared to a triclosan dentifrice in a six-week trial. *J Clin Dent* 2013; **24**: 31–36.

25 ♦ Owens J, Addy M, Faulkner J. An 18-week home-use study comparing the oral hygiene and gingival health benefits of triclosan and fluoride toothpastes. *J Clin Periodontol* 1997; **24**: 626–631.

26 ♦ Archila L, Bartizek RD, Winston JL, Biesbrock AR, McClanahan SF, He T. The comparative efficacy of stabilized stannous fluoride/sodium hexametaphosphate dentifrice and sodium fluoride/triclosan/copolymer dentifrice for the control of gingivitis: a 6-month randomized clinical study. *J Periodontol* 2004; **75**: 1592–1599.

27 ♦ McClanahan SF, Beiswanger BB, Bartizek RD, Lanzalaco AC, Bacca L, White DJ. A comparison of stabilized stannous fluoride dentifrice and triclosan/copolymer dentifrice for efficacy in the reduction of gingivitis and gingival bleeding: six-month clinical results. *J Clin Dent* 1997; **8**: 39–45.

28 ♦ Biesbrock AR, Bartizek RD, Gerlach RW, Terezhalmy GT. Oral hygiene regimens, plaque control, and gingival health: a two-month clinical trial with antimicrobial agents. *J Clin Dent* 2007; **18**: 101–105.

29 ♦ Ayad F, Stewart B, Zhang YP, Proskin HM. A comparison of the efficacy of a triclosan/copolymer/sodium fluoride dentifrice, a stannous fluoride/sodium hexametaphosphate/zinc lactate dentifrice, and a sodium fluoride dentifrice for the control of established supragingival plaque and gingivitis: a six-week clinical study. *J Clin Dent* 2010; **21**: 111–116.

30 ♦ Mankodi S, Lopez M, Smith I *et al*. Comparison of two dentifrices with respect to efficacy for the control of plaque and gingivitis, and with respect to extrinsic tooth staining: a six-month clinical study on adults. *J Clin Dent* 2002; **13**: 228–233.

31 ♦ He T, Dunavent JM, Fiedler SK, Baker RA. A randomized clinical study to assess the extrinsic staining profiles of stannous- and triclosan-containing dentifrices. *Am J Dent* 2010; **23** Spec No B: 22B–26B.

32 ♦ He T, Barker M, Biesbrock A, Sharma N, Qaqish J, Goyal C. Assessment of the effects of a stannous fluoride dentifrice on gingivitis in a two-month positive-controlled clinical study. *J Clin Dent* 2012; **23**: 80–85.

33 Turesky S, Gilmore ND, Glickman I. Reduced plaque formation by the chloromethyl analogue of victamine C. *J Periodontol* 1970; **41**: 41–43.

34 Rustogi KN, Curtis JP, Volpe AR, Kemp JH, McCool JJ, Korn LR. Refinement of the Modified Navy Plaque Index to increase plaque scoring efficiency in gumline and interproximal tooth areas. *J Clin Dent* 1992; **3**: C9–C12.

35 Löe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol Scand* 1963; **21**: 533–551.

36 Löe H. The gingival index, the plaque index and the retention index systems. *J Periodontol* 1967; **38**: S10–S16.

37 Talbott K, Mandel ID, Chilton NW. Reduction of baseline gingivitis scores with repeated prophylaxes. *J Prev Dent* 1977; **4**: 28–29.

38 Lobene RR, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. *Clin Prev Dent* 1986; **8**: 3–6.

39 Saxton CA, van der Ouderaa FJ. The effect of a dentifrice containing zinc citrate and Triclosan on developing gingivitis. *J Periodontal Res* 1989; **24**: 75–80.

40 Archila L, He T, Winston JL, Biesbrock AR, McClanahan SF, Bartizek RD. Antigingivitis efficacy of a stabilized stannous fluoride/sodium hexametaphosphate dentifrice in subjects previously nonresponsive to a triclosan/copolymer dentifrice. *Compend Contin Educ Dent* 2005; **26**: 12–18.

41 Guyatt GH, Oxman AD, Vist GE *et al*. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**: 924–926.

42 ADA. *Toothpastes with At Least These Attributes: Plaque/Gingivitis Control*.
43 Davies RM, Ellwood RP, Davies GM. The effectiveness of a toothpaste containing triclosan and polyvinyl-methyl ether maleic acid copolymer in improving plaque control and gingival health: a systematic review. *J Clin Periodontol* 2004; **31**: 1029–1033.
44 Slot DE, Wiggelinkhuizen L, Rosema NA, Van der Weijden GA. The efficacy of manual toothbrushes following a brushing exercise: a systematic review. *Int J Dent Hyg* 2012; **10**: 187–197.
45 Momeni A, Becker A, Bannasch H, Antes G, Blumle A, Stark GB. Association between research sponsorship and study outcome in plastic surgery literature. *Ann Plast Surg* 2009; **63**: 661–664.
46 Bhandari M, Busse JW, Jackowski D *et al*. Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. *CMAJ* 2004; **170**: 477–480.
47 Popelut A, Valet F, Fromentin O, Thomas A, Bouchard P. Relationship between sponsorship and failure rate of dental implants: a systematic approach. *PLoS One* 2010; **5**: e10274.
48 Khan NA, Lombeida JI, Singh M, Spencer HJ, Torralba KD. Association of industry funding with the outcome and quality of randomized controlled trials of drug therapy for rheumatoid arthritis. *Arthritis Rheum* 2012; **64**: 2059–2067.
49 Biesbrock AR, Bartizek RD, Walters PA. Improved plaque removal efficacy with a new manual toothbrush. *J Contemp Dent Pract* 2008; **9**: 1–8.
50 White DJ. A new and improved "dual action" whitening dentifrice technology–sodium hexametaphosphate. *J Clin Dent* 2002; **13**: 1–5.
51 Gaffar A, Nabi N, Kashuba B *et al*. Antiplaque effects of dentifrices containing triclosan/copolymer/NaF system versus triclosan dentifrices without the copolymer. *Am J Dent* 1990; **3** Spec No: S7–S14.
52 Palomo F, Wantland L, Sanchez A, Volpe AR, McCool J, DeVizio W. The effect of three commercially available dentifrices containing triclosan on supragingival plaque formation and gingivitis: a six month clinical study. *Int Dent J* 1994; **44**: 75–81.
53 Renvert S, Birkhed D. Comparison between 3 triclosan dentifrices on plaque, gingivitis and salivary microflora. *J Clin Periodontol* 1995; **22**: 63–70.
54 Nabi N, Mukerjee C, Schmid R, Gaffar A. In vitro and in vivo studies on triclosan/PVM/MA copolymer/NaF combination as an anti-plaque agent. *Am J Dent* 1989; **2** Spec No: 197–206.
55 Lindhe J. Triclosan/copolymer/fluoride dentifrices: a new technology for the prevention of plaque, calculus, gingivitis and caries. *Am J Dent* 1990; **3** Spec No: 53–54.
56 Fine DH, Sreenivasan PK, McKiernan M, Tischio-Bereski D, Furgang D. Whole mouth antimicrobial effects after oral hygiene: comparison of three dentifrice formulations. *J Clin Periodontol* 2012; **39**: 1056–1064.
57 Barnes VM, Richter R, DeVizio W. Comparison of the short-term antiplaque/antibacterial efficacy of two commercial dentifrices. *J Clin Dent* 2010; **21**: 101–104.
58 Schiff T, Saletta L, Baker RA, He T, Winston JL. Anticalculus efficacy and safety of a stabilized stannous fluoride/sodium hexametaphosphate dentifrice. *Compend Contin Educ Dent* 2005; **26**: 29–34.
59 Paraskevas S, Versteeg PA, Timmerman MF, Van der Velden U, Van der Weijden GA. The effect of a dentifrice and mouth rinse combination containing amine fluoride/stannous fluoride on plaque and gingivitis: a 6-month field study. *J Clin Periodontol* 2005; **32**: 757–764.
60 FDA. *Triclosan: What Consumers Should Know*. In: Administration USFaD, ed. 2012.
61 SCCP SCoCP-. Opinion on triclosan – COLIPA P32. 2009.

Supporting information

Additional supporting information may be found in the online version of this article.

Appendix S1. Overview of excluded studies and reasons for rejection

Appendix S2. Quality assessment of the studies analysed

Appendix S3. (A) Extracted data from included studies showing gingival index means and standard deviation as well as statistical analysis within groups. (B) Extracted data from included studies showing bleeding index means and standard deviation as well as statistical analysis within groups. (C) Extracted data from included studies showing plaque score means and standard deviation as well as statistical analysis within groups. (D) Extracted data from included studies showing staining index means and standard deviation as well as statistical analysis within groups

Appendix S4. Funnel plot of the Gingival Index

Appendix S5. Forrest plot of the Gingival Index at baseline and end