Proven Primary Prevention Strategies for Plaque-Induced Periodontal Disease – An Umbrella Review

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Abstract

Aim: The aim of this umbrella review was to provide a summary of the findings based on the highest level of evidence from published systematic reviews to identify proven, self-administered interventions to prevent periodontal disease.

Methods: A search for systematic reviews and meta-analyses was conducted using the following search terms: systematic review, periodontal disease, periodontitis, gingivitis, and primary prevention. Outcomes included indices for dental plaque (oral biofilm), gingival inflammation, gingival bleeding, and probing pocket depth.

Results: No systematic reviews were found that evaluated the effectiveness of toothbrushing for daily oral hygiene. Methods of mechanical oral biofilm control found to be effective when compared to toothbrushing alone included powered toothbrushes, oral irrigators, and interdental cleaning devices (triangular woodsticks and interdental brushes). Manual tooth brushing and powered tooth brushing were found to be equivalent. Effective topical chemical interventions include chlorhexidine gluconate (CHX), cetylpyridinium chloride (CPC), and essential oils. Other interventions, including sodium benzoate (PLAX), stannous fluoride, hexetidine, hydrogen peroxide, other natural compounds, 0.2% delmopinol, probiotics, anti-inflammatory agents, dietary supplements, anti-oxidants, and smoking cessation are supported only by limited evidence. Triclosan-containing dentifrice adds to the effectiveness of toothbrushing to reduce gingivitis.

Conclusion: Relatively few interventions have been proven to prevent gingivitis and periodontitis.

Keywords: chemical plaque control; evidence-based medicine; gingivitis; mechanical plaque control; oral hygiene

Introduction

Inflammatory periodontal disease is one of the most common afflictions of humans (Eke *et al.*, 2020). The most common inflammatory periodontal diseases are gingivitis and periodontitis. Gingivitis is characterized by gingival inflammation induced by exposure to tooth-associated biofilms. In some patients, gingivitis progresses to periodontitis. Periodontitis is defined by the irreversible destruction of periodontal attachment that results from tooth-born biofilm-induced chronic inflammation (Kinane *et al.*, 2017). Gingivitis is thought to precede periodontitis.

There is substantial evidence supporting a number of interventions as primary prevention strategies for periodontal disease. Most preventive strategies have focused on the elimination/reduction of biofilm, and secondarily on reduction of inflammation or promotion of health-related microbes within the biofilm (Marsh *et al.*, 2011; Kolenbrander *et al.*, 2002; Huang *et al.*, 2011; Hojo *et al.*, 2009). However, the evidence is incomplete for many proposed periodontal disease preventive interventions. The aim of this umbrella review is to provide a summary of the findings based on the highest level of evidence from published systematic reviews to identify proven, self- administered interventions to prevent periodontal disease (Grant and Booth, 2009).

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For the purposes of this review, we made the assumption that the best evidence supporting interventions to prevent diseases such as gingivitis and periodontitis would by now be summarized and evaluated in systematic reviews of randomized controlled trials. Thus, the goal of this study was to evaluate the evidence from published systematic reviews to identify the interventions that have been proven to prevent periodontal disease. This information will assist dental practitioners and the public to identify current best practices for the prevention of periodontal disease.

Materials and Methods

Focused question

The question posed was: "What are the proven self-care interventions that patients can utilize to prevent the onset of periodontal disease?" The literature search included systematic reviews of studies of human adult subjects of either gender presenting with acute and chronic gingivitis. We considered interventions utilizing mechanical plaque control, topical chemicals, and other interventions, conducted at home or administered in a dental office with comparators of placebo rinses, standard mechanical tooth brushing with fluoridated toothpaste, or negative controls. Outcomes considered included statistically significant reductions in dental plaque levels, measures of gingival inflammation such as bleeding on probing, and probing pocket depth levels.

Search strategy

Databases queried included PubMed, EMBASE, and the Cochrane Database of Systematic Reviews for systematic reviews and meta-analyses that met the inclusion criteria. A preliminary search for systematic reviews and meta-analyses was conducted using the following key search terms: systematic review, periodontal disease, periodontitis, gingivitis, and primary prevention. The inclusion and exclusion criteria are presented in Table 1. The search terms appeared as medical subject headings (MeSH) and were combined using Boolean operators (AND, OR: Table 2). The software Endnote, version X8.0.1, was used for managing each stage of the review, with duplicate studies removed. The search was limited to systematic reviews and meta-analyses in English and published after 2000. The searches were conducted in January of 2018.

Quality Assessment and Risk of Bias

The strength of the evidence was judged as low, moderate, or high based on the number of systematic reviews and meta-analyses currently available for an intervention and quality assessment according to the AMSTAR Checklist (Shea *et al.*, 2017). The AMSTAR Checklist served as a questionnaire, with each paper appraised by two independent authors (EIV and FAS), in order to determine the strength of each review. Highly ranked systematic reviews demonstrated low risk of bias, clearly defined inclusion and exclusion criteria, and an appropriate search strategy and data reporting (Aromataris *et al.*, 2015). Moderate-strength evidence was determined for reviews with lack of clarity on risk of bias or consistency of results. Low-strength evidence was determined for reviews containing an overall high risk of bias, along with inconsistent or poor data reporting. To be eligible for inclusion in this investigation (Table 1), studies had to (i) be systematic reviews and meta-analyses of randomized clinical trials (RCTs) or controlled clinical trials (CCTs); (ii) include adult human subjects; (iii) be written in English; (iv) and be published after the year 2000.

Process for Data Extraction and Collection

After two reviewers (EIV and FAS) independently screened titles and abstracts, 382 systematic reviews and meta-analyses were chosen for the second screening. 81 systematic reviews were identified after the second screening process and fully read. Finally, 47 systematic reviews and meta-analyses were selected for inclusion in this umbrella review after qualitative assessment using the AMSTAR Checklist (Shea *et al.*, 2017). The PRISMA statement (Liberati *et al.,* 2009) was also used as a tool to confirm agreement of methods and data reporting in each individual systematic review.

Results

Mechanical Interventions: Powered vs. Manual Tooth-brushing and Professional Plaque Removal

It should be noted that the effectiveness of the mainstay of daily oral hygiene, the toothbrush, seems not to have yet been the subject of well-designed clinical trials. As a result, there are no published systematic reviews that have directly evaluated the effectiveness of the standard toothbrush to prevent periodontitis. A large number of clinical trials have demonstrated that powered tooth brushes are comparable to manual tooth brushes with respect to reducing plaque scores and gingival inflammation (Table 3). Many studies show no conclusive evidence that powered tooth-brushes are superior to manual toothbrushes for preventing gingivitis (Costa *et al.*, 2007; Deery *et al.*, 2004; Robinson *et al.*, 2005; Nagy *et al.*, 2016; Sicilia *et al.*, 2002). Among the different types of powered brushes, rotation oscillation of powered brushes significantly reduce plaque accumulation and gingival inflammation when compared to baseline levels. In addition to evaluating self-performed mechanical plaque control, Needleman *et al.* (2015) determined that there is insufficient evidence to support professional

Table 1. Systematic review entry criteria

Inclusion criteria
1. Humans > 16 years of age with good systemic health
2. At least 16 natural teeth, without orthopedic appliances
3. Gingivitis, defined as bleeding on probing at > 25% of six sites around each tooth
4. Randomized controlled trials (RCTs) or controlled clinical trials (CCTs)
5. Clinical parameters: plaque scores, bleeding scores, gingivitis scores, probing pocket depth
6. Clinical parameters outlined in short-term studies, defined as < 4 weeks
7. Clinical parameters outlined in long-term studies, defined as > 4 weeks
8. Follows guidelines outlined in the PRISMA-P statement
9. Answered "Yes" or "Partial Yes" to each question outlined in the AMSTAR Checklist
10. Reviews written in English , published after year 2000
Exclusion criteria
1. Removable partial dentures
2. Cavitated carious lesions
3. Patients with existing periodontal disease
4. Psychiatric disorders, current use of anti-inflammatory drugs or anti-cholinergic drug

Table 2. Search strategy on periodontal conditions and interventions

Topic	Search Strategy
Periodontal conditions	"Periodontal Diseases" [Mesh] OR "Periodontal Atrophy" [Mesh] OR "Periodontal Ligament" [Mesh] OR "Periodontal Mobility" [Mesh] OR "Periodontal Pocket" [Mesh] OR "Gingivitis" [Mesh] OR "Inflammation" [Mesh] OR "Gingival Diseases" [Mesh] OR "Disease, Gingival" OR "Diseases, Gingival" OR "Gingival Disease" "Hemorrhage" [Mesh] OR "Biofilm" [Mesh] OR "Dental Plaque" [Mesh] OR "Plaque, dental" OR "Tooth Mobility" [Mesh]
Chemical interventions	"Preventive Dentistry" [Mesh] OR "Protective Agents" [Mesh] OR "Mouthwashes" [Mesh]
Mechanical interventions	"Dental prophylaxis" [Mesh] OR "Dental devices, home care" [Mesh] OR "Dentifrices" [Mesh] OR "Oral Hygiene" [Mesh]
Other interventions	"Anti-infective agents" [Mesh] OR "Anti-inflammatory agents" [Mesh] OR "Antioxidants" [Mesh] OR "Diet, food, and nutrition" [Mesh] OR "Dietary supplements" [Mesh] OR "Metalloprotease" [Mesh] OR "metalloproteases" [Mesh] OR "metallopeptidase" [Mesh] OR "metallopeptidases" [Mesh] OR "Micronutrients" [Mesh] OR "Minerals" [Mesh] OR "Phytochemicals" [Mesh] OR "Plant extracts" [Mesh] OR "Toothbrushing" [Mesh] OR "Vaccines" [Mesh] OR "Vitamins" [Mesh]

mechanical plaque removal as a primary intervention to prevent periodontitis, and rather self-performed mechanical plaque control is sufficiently effective to prevent plaque and gingivitis. With regards to manual tooth brushing, Hoogteijling *et al.* (2018) examined whether the shape of tooth brush filaments played a role in plaque control. Tapered toothbrush filaments were compared to end-rounded filaments and no differences were noted between the two filament types with respect to dental plaque removal. However, the tapered filament tooth brush performed significantly better than end-rounded filaments with respect to gingival inflammation.

Interdental Cleaning

A summary of studies evaluating interdental plaque control approaches is provided in Table 4. Kotsakis *et al.* (2018) evaluated the effects of various interdental oral hygiene methods on gingival health, comparing various groups of interdental oral hygiene methods: floss (waxed and un-waxed), automated flosser, toothpick, water jet irrigation device, and interdental brushes. The controls were tooth brushing alone and powered tooth brushing. The results showed that unsupervised flossing did not result in reduction in gingival inflammation.

Table 3. Summary of findings on powered vs. manual tooth-brushing and professional mechanical plaque removal

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Costa *et al*. (2007)	Of 11 RCTs included in the study, 8 were clinically relevant. 8 RCTs on the effectiveness of sonic tooth-brushing compared to manual tooth-brushing.	No conclusive evidence in support of high frequency tooth-brushes over manual in patients with gingivitis.	No meta-analysis of the data due to differences in indices and baseline conditions of patients as well as lacking standardization of the number of analyzed teeth.
Deery *et al*. (2004)	29 RCTs to evaluate the effect of manual versus powered tooth brushing on plaque and gingival health.	Powered brushes reduced plaque and gingivitis at least as effectively as manual brushing. Rotation oscillation powered tooth brushes significantly reduced plaque and gingival inflammation.	Limitations with analyzing brush characteristics such as filament arrangement, size and shape and flexibility, as well as brush head size and shape and other characteristics such as timer.
Robinson *et al*. (2005)	10 RCTs to evaluate the effect of manual versus powered tooth brushing on plaque and gingival health.	Powered tooth brushes with rotation oscillation significantly reduced plaque and gingivitis by 11% and 6% respectively in the short-term (4 week) studies. Data show reduction in gingivitis by 17% in the long-term (> 3 months) studies.	Limitations with analyzing brush characteristics such as filament arrangement, size and shape and flexibility, as well as brush head size and shape and other characteristics such as timer.
Nagy *et al*. (2016)	21 RCTs on the effects of powered toothbrushes compared to manual toothbrushes on removing plaque, reducing gingivitis, and preventing calculus formation.	Plaque reduction was significantly greater in powered brushes with rotation oscillation, side to side sonic, and ultrasonic mode of actions.	No trial fell into the highest quality criteria due to various types of bias and high heterogeneity.
Sicilia *et al*. (2002)	21 RCTs on the effectiveness of power tooth brushes (mostly oscillation rotation mode of action) compared to manualtooth brushing on gingivitis and plaque score.	Not enough evidence to confirm or refute the benefits of powered-driven tooth brushes over manual tooth brushes. Although evidence does support that oscillation rotation powered tooth brushes effectively reduce gingival inflammation.	Variation in indices utilized makes it difficult to perform a statistical analysis. In addition, not all control groups brushed using the Bass technique. Some groups used the Rolling technique. These differences may account for the high heterogeneity.
Needleman *et al*. (2015)	3 RCTs to evaluate the effectiveness of professional mechanical plaque removal (PMPR) on gingival indices (primary), plaque score and probing depths (secondary).	No evidence to support PMPR for primary prevention of periodontal disease. Data show that PMPR combined with OHI reduced plaque scores and gingivitis compared to the control (no treatment). No evidence to support any effects on probing depth.	Professional mechanical plaque removal includes a large variety of procedures, however exclude root planing and root surface debridement, which contributes to data heterogeneity. In addition, risk of bias was determined as unclear to high. Overall, strength of evidence is low due to risk of bias and limited amount of data.

Table 3 continued overleaf...

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van der Weijden and Hioe (2005)	33 RCTs on the quality of self-performed mechanical plaque removal in adults with gingivitis who were provided a single oral hygiene instruction and a prophylaxis. Clinical parameters included gingivitis and plaque score.	The quality of self-performed mechanical plaque removal is not sufficiently effective based on studies of at least 6 months in duration. Adults that were prescribed oral hygiene instruction and a prophylaxis at baseline showed small but significant reduction of gingivitis.	No negative control groups were present in the studies. The control group included standard manual toothbrush and fluoride toothpaste without oral hygiene instruction or prophylaxis. However, the issue with this control group is the possibility of Hawthorne effect.
Hoogteijling *et al.* (2018)	7 RCTs evaluating the effect of manual tooth brushes with tapered filaments compared to end-rounded filaments on plaque and gingivitis.	With respect to plaque reduction, data show inconclusive results for both types of tooth brushes. With regards to gingivitis reduction, tooth brushes with tapered filaments are more effective than end-rounded filaments.	Overall strength of the evidence is strong having overall low risk of bias.

However, interdental brushes and water jets performed better compared to other interdental oral hygiene aids in reducing gingival bleeding. There is strong evidence supporting the use of interdental brushes and water jets as adjuncts to daily brushing to prevent periodontal disease (Chapple *et al.*, 2015; Kotsakis *et al.*, 2018). Poklepovic *et al.* (2013) reported that interdental brushing with conventional toothbrushing significantly reduced plaque score and ginivitis compared to toothbrushing alone, which was consistent across multiple plaque and gingivitis indices that were meta-analyzed in this systematic review.

Husseini *et al.* (2008) evaluated if oral irrigation as an adjunct to tooth brushing is an effective intervention in reducing plaque and gingivitis. The outcomes evaluated were dental plaque, bleeding, gingivitis, and pocket depth. With respect to plaque control and pocket depth, there were no changes between baseline values and values measured at the end of the studies. Thus, adjunctive oral irrigation is not an effective method for reducing plaque and gingivitis when compared to manual tooth brushing alone.

Another interdental cleaning device of interest is the woodstick. Hoenderdos *et al.* (2008) systematically compared the use of triangular woodsticks to tooth brushing alone, interdental brushing, floss (waxed and un-waxed), and dental floss. Woodsticks were found to be an effective tool for patients to use to monitor their gingival health. The authors found that the presence of bleeding after gentle insertion of a woodstick into the gingival sulcus can provide patients with immediate feedback on the status of their gingival health. They suggest that woodsticks should not be recommended for patients as an intervention against periodontal disease, but rather as a self-monitoring device for patients who are interested in observing the status of their gingival health.

Chemical Interventions

Chlorhexidine Gluconate (CHX)

Data from multiple randomized clinical trials show significant reductions in plaque, gingivitis, gingival bleeding, and periodontal pockets following CHX use (Table 5). However, CHX can be used in varying formulations, such as rinse, gel, or spray and in varying concentrations. CHX has been formulated in concentrations ranging from 0.1% - 0.2% to achieve the ideal range of 18-20 mg/dose (Serrano *et al.*, 2015). Overall, the evidence suggest that rinse formulations are more effective anti-plaque agents than gel or spray forms, and concentrations of 0.12% and 0.2% CHX rinses are equally effective anti-plaque agents. No significant differences between various CHX concentrations (0.2% vs. 0.1%/0.12%) were determined and no differences from varying frequency of rinsing (1x/day vs, 2x/day)

Table 4. Interdental plaque removal

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Husseini *et al*. (2008)	7 RCTs evaluating the efficacy of supragingival and subgingival oral irrigation as an adjunct to tooth brushing with respect to plaque and gingivitis.	For plaque, the majority of studies did not present significant data on changes between baseline and end of the study. Pocket depth reduction from baseline was observed in four studies, however none of the results were significant. Oral irrigation is not an effective intervention with respect to reducing dental plaque.	Concerns over supragingival irrigation with respect to introducing bacteremia were considered. More studies are needed in order to assess the risk and benefits of supragingival and subgingival irrigation for patients who are medically compromised.
Kotsakis *et al*. (2018)	22 RCTs evaluating various interdental oral hygiene methods, including interdental oral irrigation, flossing (supervised and unsupervised), interdental brushing, and toothpicks. Clinical parameters included dental plaque and gingival bleeding.	Unsupervised flossing does not yield substantial reduction in gingival inflammation. Among 10 interdental oral hygiene methods, interdental brushes and water jets had the greatest effect in reducing gingival bleeding when compared to flossing. Interdental brushes and toothpicks ranked highest with respect to plaque reduction compared to flossing. Therefore, interdental brushes showed to be more effective with respect to gingival inflammation and plaque parameters when compared to flossing.	Several of the included studies possessed unclear risk of bias. However, clinical parameters for measuring plaque were consistent across most studies and data was overall consistent. Overall the strength of evidence is considered to be high.
Chapple *et al*. (2015)	To systematically review the evidence for the primary prevention of periodontitis by evaluating the efficacy of mechanical self-administered interdental plaque control. Authors also systematically reviewed the evidence for the adjunctive use of chemical and anti-inflammatory agents with respect to plaque and gingival indices.	Data show that interdental brushes significantly improve plaque when compared to manual tooth brushing alone. Other interdental devices such as flossing, oral irrigators, and woodsticks show inconsistent/weak evidence to support their adjunctive use. Weak evidence exists to support the use of non-steroidal anti-inflammatory agents as adjunctive primary prevention therapies.	There was limited information with respect to number of included studies and study design from which data was extracted.
Poklepovic *et al*. (2013)	7 RCTs to evaluate the effects of interdental brushing in addition to tooth brushing as compared to tooth brushing alone or tooth brushing and flossing for the prevention of periodontal disease.	Interdental brushing with conventional toothbrushing found significantly reduced plaque score and ginivitis compared to toothbrushing alone	Overall quality of evidence is considered strong due to consistent data across studies.
Hoenderdos *et al*. (2008)	8 RCTs evaluating the effect that hand-held triangular woodsticks have on plaque reduction and gingival inflammation.	Woodsticks are not effective anti-plaque agents. However, woodsticks showed significant reductions in bleeding score when used as an adjunct to tooth brushing compared to tooth brushing alone.	Overall quality of evidence is considered low. More systematic reviews are warranted to assess whether woodsticks can be recommended to patients for at-home oral hygiene practices.

Table 5. Summary of systematic reviews on chlorhexidine (CHX)-based products and other chemical interventions

Systematic Review	No. studies and Intervention characteristics	Included outcomes	Limitations of data
Elkerbout *et al*. (2018)	10 RCTs on CHX MW as adjunct to oral hygiene. Compared CHX + NaF MW to CHX MW. Control rinse and placebo rinse included.	No significant difference in PI, BS, GI between groups. Both groups showed significant reductions in PI, BS, and GI. Both fluoridated and non-fluoridated CHX MW's are equally effective anti-plaque agents.	Is there enhanced antimicrobial capacity of CHX + NaF compared to CHX? Most participants in studies reported staining as a side effect. CHX + NaF may work synergistically to prevent plaque formation.
James *et al*. (2017)	51 RCTs on long-term adjunctive CHX MW versus mechanical tooth-brushing alone on gingivitis. Control rinse and placebo rinse included.	No difference in CHX concentration (0.2% vs. 0.1%/0.12%) and frequency of rinsing (1x/day vs, 2x/day) at both 4-6 weeks and 6 months. Significant reduction in BS in favor of CHX rinse was observed. Data show significant reduction in plaque in favor of CHX MW.	50 studies had high risk of election, performance, detection, attrition, and reporting bias. Studies from 2012-2015 showed greatest risk of bias. Most studies reported at least one adverse effect e.g. tooth staining, calculus, altered taste.
Supranoto *et al*. (2015)	5 RCTs on effectiveness of long-term adjunctive use of CHX DF/gel compared to CHX MW on PI, BS, GI. Brushing model and non-brushing models were compared over the course of 6 months. CHX DF/gel was compared to triclosan/zinc citrate DF and placebo DF. The effective dose range of CHX DF/gel were used at 15 mg 2X/day, which matched the effective dose range for CHX MW.	3 studies showed significant reductions in PI in favor of CHX. No significant differences were found with respect to BS and GI. CHX and CHX DF/gel are equally effective in reducing plaque when used as adjuncts to tooth-brushing. However, if daily oral hygiene cannot be performed, CHX is more effective than the DF/gel form.	Studies reported significantly more tooth discoloration from CHX than from CHX DF/gel. No significant differences were found between CHX DF and triclosan/zinc citrate DF with respect to plaque inhibition. Some data show better CHX distribution with gel trays for CHX gel as opposed to tooth-brushing with CHX gel. Hawthorne effect in the brushing model is expected.
Slot *et al*. (2014)	16 RCTs evaluating long-term (at least 4 weeks) CHX DF and CHX gel separately. GI, BS, and PI were assessed for both groups. Both groups compared to placebo. Both groups assessed using the brushing model.	Data show significant reduction in PI, GI, and BS in favor of CHX DF (0.4%, 0.6%, 0.8% and 1%) over placebo DF.	Studies on CHX DF reported slightly more tooth discoloration than studies on CHX gel.
Van Leeuwen *et al*. (2011)	18 RCTs on the efficacy of EOMW and CHX MW in reducing PI, GI, and BS. The brushing studies included 5 long term and 1 short-term (3 weeks). The non-brushing/experimental gingivitis studies included 12 short-term studies.	With respect to the long-term studies, data show significant reductions in PI in favor of CHX.	Majority of the studies were non-brushing studies; extrapolation of the findings may not be possible since ths is not a reflection of patients' usual daily oral hygiene routines.
Neely (2012)Y/	19 RCTs on the efficacy of essential oil mouthwash (EOMW) as an anti-plaque agent compared to CHX mouth rinse.	CHX is a more effective anti-plaque agent when compared to EOMW in both short-term and long-term studies. No significance differences were found between CHX and EOMW with respect to gingival index.	

Table 5 continued overleaf...

Table 5 continued

Berchier *et al*. (2010)	10 RCTs on the efficacy of 0.12% CHX MW compared with 0.2% CHX MW on PI, GI, and BS. Meta-analysis on 7 studies calculated the weighted mean differences (WMDs) for plaque using a random effect model. 3 studies comparing the two concentrations provided data on gingival inflammation.	No significant differences were noted between the two concentrations with respect to gingival bleeding. A small but significant difference in favor of 0.2% CHX over 0.12% with respect to PI was noted.	WMD for plaque score is assumed to be inflated due to the nature of the Quigley and Hein Index.
Haas *et al*. (2016)	16 RCTs on the efficacy of essential oil-mouth wash (EOMW) as an adjunct to mechanical oral hygiene (brushing and flossing) compared to mechanical oral hygiene alone and compared to CPC mouth rinse.	With respect to reduction in plaque and gingival inflammation, EOMW is more effective for patients with gingivitis as opposed to mechanical oral hygiene alone or in combination with CPC MW.	High heterogeneity due to differences between studies in the percentage of males, supervision of mouthwashes, and provision of oral hygiene. Hawthorne effect is also a factor. Benefits of EOMW might be over-estimated.
Puig Silla *et al*. (2008)	10 RCTs on the efficacy of 5 different CHX varnishes on PI, GI, BS. The aim is to determine whether CHX varnishes as a long-term adjunct to scaling and root planing can be recommended to patients with chronic gingivitis. Control varnish and placebo were included.	Data show significant differences in PI, GI, and BS in favor of CHX varnish. Not enough data supports the use of CHX varnishes as a long-term adjunct to scaling and root planing.	Not all studies utilized the same varnish and thus have different concentrations of CHX. More RCTs are needed to assess the clinical relevance of CHX varnishes.
Addy *et al*. (2007)	8 RCTs on the effects of 0.2% delmopinol compared to CHX mouth rinses on plaque reduction and inhibition of gingivitis.	0.2% delmopinol are effective in reducing plaque and gingivitis when compared to placebo. Delmopinol does not stain enamel as heavily as CHX.	Study design likely exposed to Hawthorne effect.
Zhang *et al*. (2018)	18 RCTs on the effects of CHX oral sprays on gingival inflammation, plaque reduction, and staining compared to other oral sprays containing CPC, stannous fluoride, and Benzdamine hydrochloride (B-HCl) and to CHX mouth rinse.	11 studies showed up to a 75% reduction in GI scores. No significant GI reduction was found in other oral spays. CHX oral spray showed lower staining outcomes than CHX oral spray when compared to CHX mouth rinse. No differences between CHX spay and rinse with regards to PI.	2 studies were evaluated as having high risk of bias due to incomplete data outcome (attrition bias).
Haps *et al*. (2008)	8 RCTs to evaluate the effects of adjunctive CPC mouth rinse on plaque and gingival inflammation over a period of 4 weeks to 6 months compared to tooth brushing alone and tooth brushing followed by a placebo rinse.	7 out of 8 studies showed positive change in plaque index in favor of CPC mouth rinse compared to tooth brushing followed by placebo rinse. Of 6 studies that measured GI, 3 reported a significance difference in favor of CPC mouth rinse compared to the control. More evidence needed to support the adjunctive use of CPC mouth rinse.	Not enough data available on bleeding score parameters. 2 studies did not compare to a placebo rinse, but reported improvement in plaque scores. Heterogeneity of data across studies is significant.

Table 5 continued overleaf...

Table 5 continued

Serrano *et al.* (2015)	65 RCTs to evaluate the effectiveness of chemical anti-plaque agents in the management of gingival inflammation assessed by gingival and bleeding indices.	Overall, the tested chemical anti-plaque agents show clinical improvements beyond those obtained with mechanical oral hygiene instruction and self-administered mechanical plaque removal alone.	There was limiting blinding of evaluators and/or patients. Overall evidence is considered moderately strong.
Herrera (2009)	8 RCTs evaluating whether the use of a CPC-containing mouth rinse as an adjunct to tooth brushing is more effective than tooth brushing alone in preventing plaque accumulation and gingivitis. Clinical parameters included plaque, bleeding, gingivitis or pocket depth.	CPC is recommended as an adjunct to tooth brushing for primary prevention of periodontal disease.	Evidence to support the use of CPC as an adjunctive anti-plaque rinse is moderately strong due to significant data heterogeneity.
Angelillo *et al.* (2002)	19 RCTs evaluating the effectiveness of PLAX, a pre-brushing rinse, in reducing plaque and gingivitis.	With respect to gingivitis, there was significant reduction in gingival inflammation from baseline in favor of PLAX pre-rinsing.	Moderately strong evidence supports the adjunctive use of PLAX pre-brushing mouth rinse due to significant data heterogeneity.
Afennich *et al.* (2011)	5 RCTs to evaluate the effectiveness of hexetidine-containing mouthwash as a monotherapy or as an adjunct to daily oral hygiene for the prevention of dental plaque accumulation and gingivitis.	0.14% hexetidine is not currently recommended as an adjunct to routine oral hygiene.	Included studies contained high risk of bias and results across studies showed high data heterogeneity.
Hossainian *et al.* (2011)	10 RCTs evaluate the effects of fluoridated hydrogen peroxide (H_2O_2) mouthwashes as an adjunct to tooth brushing in dental plaque reduction and gingival inflammation. To evaluate fluoridated H_2O_2 against CHX using same parameters.	H_2O_2 is significantly less effective than CHX in reducing plaque accumulation and gingival inflammation.	There is currently little evidence supporting the use of fluoridated hydrogen peroxide as an adjunct to tooth brushing. More randomized controlled trials are warranted to lend power to future systematic reviews.
Mathur *et al.* (2018)	9 RCTs evaluating the effects of green tea-based mouthwashes on dental plaque and gingival inflammation in India.	There is inconclusive evidence with respect to the adjunctive use of green-tea based mouth washes.	High data heterogeneity and inconsistent results across studies included in this systematic review. Also, there is unclear risk of bias in most of the studies.
Chen *et al.* (2014)	11 RCTs evaluating the effectiveness of mouth rinses containing various plant extracts with respect to plaque reduction and gingivitis reduction.	Evidence in support of the adjunctive use of mouth rinses containing natural compounds is not sufficient.	Some of the included studied possessed low quality evidence. Furthermore, more randomized controlled trials are warranted to lend power to future systematic reviews.

at both 4-6 weeks and 6 months (James *et al.*, 2017; Berchier *et al.*, 2010). CHX mouth rinses are more effective anti-plaque and anti-gingivitis interventions than CHX dentifrices and gels (Supranoto *et al.*, 2015). However, CHX dentifrices or gels are effective in reducing plaque and gingival indices when compared to a placebo dentifrice (Slot *et al.*, 2014). With respect to in-office procedures, CHX varnishes were also explored as a potential primary prevention strategy. Puig Silla *et al.* (2008) found there were significant differences in plaque and gingival bleeding indices in favor of CHX varnish compared to the placebo group. However, more clinical trials are indicated to substantiate these results.

Cetylpyridinium chloride

The evidence supporting cetylpyridinium chloride (CPC), a quaternary ammonium compound, as an effective adjunct is moderately strong, with significant reductions noted in plaque levels and gingival inflammation compared to baseline values over durations ranging from a period of 7 days to over 6 months of adjunctive rinsing. The systematic review conducted by Zhang *et al.* (2018), noted that 0.05% CPC mouth rinse was associated with significant reduction in dental plaque compared to the control after 7 days of use. Haps *et al.* (2008) also evaluated the effects of adjunctive CPC mouth rinse on plaque and gingival inflammation over a period of > 4 weeks to > 6 months compared to tooth brushing alone and tooth brushing followed by a placebo rinse. On the contrary, they concluded that there is insufficient evidence to support daily adjunctive use of CPC mouth rinse due to the presence of publication bias in the reviewed clinical trials. Herrera *et al.* (2009) determined that CPC-containing mouth rinses are excellent adjuncts for tooth brushing in preventing plaque accumulation and gingivitis. Overall, the data show that CPC mouth rinse has a small but significant additional benefit in preventing plaque accumulation and gingivitis and can be recommended as an adjunct to tooth brushing for both high (>0.1%) and low (>0.07%) concentrations (Serrano *et al.*, 2015).

PLAX

The effectiveness of a sodium benzoate mouth rinse (PLAX) in various formulations, including triclosan plus copolymer of methoxyethylene and maleic acid or with increased concentrations of sodium lauryl sulfate has been evaluated (Angelillo *et al.*, 2002). A meta-analysis evaluating PLAX as an adjunct to self-performed oral hygiene revealed that the use of sodium benzoate significantly reduced plaque levels at 3-4 weeks, however no differences were noted between intervention and comparison groups after 6, 12, and 24-weeks. PLAX formulated with triclosan performed better than PLAX without triclosan. Interestingly, the results showed that rinsing after brushing had no significant effect on plaque reduction. However, when PLAX was used as a pre-brushing rinse, significant reduction in plaque levels were observed after a single exposure, suggesting that the beneficial effects of rinsing with PLAX are masked by dentifrice. More trials are needed to evaluate the inhibitory effects of PLAX on plaque growth as a pre-brushing rinse to reduce gingival inflammation in the long-term.

Stannous Fluoride

The effect of stannous fluoride (SF) mouth rinse on reducing dental plaque and gingival inflammation has been evaluated (Zhang *et al.,* 2018). The quality of the evidence is low due to a lack of systematic reviews. However, the available data show that stannous fluoride mouth rinse is less effective than CHX mouth rinse with respect to plaque indices and that both fluoridated and non-fluoridated CHX mouth washes are equally effective in reducing plaque and gingivitis. Therefore, either formulation of CHX can be recommended to patients for reducing gingival inflammation (Elkerbout *et al.*, 2018).

Hexetidine

There is insufficient evidence supporting the adjunctive use of hexetidine mouth rinse, despite having demonstrated beneficial anti-microbial properties as reviewed by Zhang *et al.* (2018) and Afennich *et al.* (2011) evaluated the effect of hexetidine mouth rinse on plaque inhibition over short-term durations (< 4 weeks) and long-term (> 6 months). Various concentrations of hexetidine mouth rinses (0.1%, 0.14%, and 0.2%) were studied and data show 0.14% had the greatest significance on plaque reduction in the short-term studies. However, the substantivity of hexetidine appears less than that of CHX gluconate, resulting in insignificant differences in the numbers of salivary bacteria after a hexetidine rinse when compared to a CHX rinse (Afennich *et al.*, 2011).

Hydrogen peroxide

Hossainian *et al.* (2011) evaluated the effects of fluoridated hydrogen peroxide (H_2O_2) mouthwashes compared to CHX mouth wash using plaque and gingivitis indices, and concluded that H_2O_2 is significantly less effective than CHX mouth wash in reducing plaque levels and gingival inflammation. Most of the studies evaluated the short-term effects (less than 3 weeks) of H_2O_2 and therefore it is unknown whether H_2O_2 mouth wash has long-term clinical benefits. Thus, H_2O_2 remains unproven for primary prevention of gingival inflammation.

Essential Oils, Herbal Extracts, Green Tea, and Other Natural Compounds

Neely (2012) reviewed essential oil mouth wash (EOMW) compared to CHX mouth wash on plaque and gingival outcomes. The CHX mouth wash performed significantly superior to EOMW as an anti-plaque agent in the short-term studies (< 4 weeks), but no significant differences were found between test and control groups with respect to gingival indices. after 4 weeks. Haas *et al.* (2016) compared adjunctive rinsing with essential oil to brushing alone and determined that adjunctive rinsing with EOMW is more effective in reducing gingivitis and plaque compared to mechanical plaque control alone. Furthermore, adjunctive rinsing with EOMW resulted in significant reductions in plaque and gingival inflammation when compared to adjunctive rinsing with cetylpyridinium chloride (CPC) mouth rinse. The evidence suggests that EOMWs can be recommended as a first-choice daily adjunct to tooth brushing over CPC mouth rinse (Van Leeuwen *et al.*, 2011).

A number of herbal extracts have been evaluated as adjuncts to oral hygiene to prevent gingival inflammation. Casarin *et al.* (2018) evaluated the effect of *Melaleuca alternifolia* essential oils compared to a control intervention (i.e. CHX, Fluoridated toothpaste), using plaque and gingival (bleeding and inflammatory) as outcomes. The duration of studies ranged from 5 days to 6 months. Overall, the quality of the evidence was found to be low due to limitations in experimental design. However, the evidence is promising for 2.5% and 5% gel formulations of *Melaleuca alternifolia* used as adjuncts to scaling and root planing.

Keukenmeester *et al.* (2014) conducted a systematic review on the effects of chewing gum containing CHX or other ingredients such as eucalyptus, acacia, funoran, pycnogenol, mastic, and magnolia. The majority of chewing gums were able to reduce plaque scores and gingival inflammation compared to baseline values over a duration of at least 6 months. The active ingredients with the greatest effect on gingival inflammation was CHX. Other additives such as magnolia and eucalyptus showed modest effects. However, the quality of the evidence supporting such chewing gums for primary prevention is low due to lack of statistical power.

Mathur *et al.* (2018) evaluated the effect of green tea-based mouthwashes on dental plaque and gingival inflammation in India. Green tea mouth wash was compared to CHX mouth wash or a placebo mouth rinse over a duration of 1 to 6 weeks. The quality of evidence suggesting anti-plaque and gingival benefits of green-tea mouth wash was found to be low.

There are many other natural compounds that could prove to prevent gingivitis and prevent the onset of periodontal disease that should be explored through future clinical trials (Chen *et al.*, 2014).

0.2% Delmopinol

Addy *et al.* (2007) conducted a meta-analysis on the effects of 0.2% delmopinol, a third-generation anti-plaque mouth rinse, to prevent gingivits (e.g. reduce inflammation and bleeding). The results found delmopinol to be effective in reducing plaque and gingivitis when compared to the placebo rinse. The overall quality of evidence was low due to lack of well-powered studies that could be included in the analysis.

Triclosan

Zhang *et al.* (2018) evaluated the effects of 0.15% triclosan (TRN) mouth rinse with regards to plaque and gingival bleeding indices. Results show an overall reduction in plaque scores and gingival bleeding scores in the TRN mouth rinse group compared to the placebo group. With respect to triclosan/zinc citrate rinse, significant differences were found with respect to bleeding on probing only. Currently, TRN mouth rinse is not supported by enough evidence to be recommended to patients with gingivitis.

Triclosan Dentifrice

Several systematic reviewers evaluated the efficacy of fluoridated toothpaste containing the anti-microbial agent, triclosan (5-chloro-2-(2,4 dichlorophenoxy) phenol), over 6 months or more and found that this agent significantly reduced supragingival plaque, gingival bleeding, and gingival inflammation (van der Weijden *et al.*, 2005) (Table 6). Furthermore, no differences were found between triclosan with the addition of polyvinyl-methyl ether maleic acid copolymer versus zinc citrate in reducing gingival inflammation (Hioe *et al.*, 2005). Significant reductions in plaque score compared to baseline levels after a duration of at least 6 months were found in favor of fluoridated toothpastes with triclosan/copolymer. Overall, the data show that both triclosan/copolymer and triclosan/zinc citrate dentifrices are excellent mechanical plaque control agents (Salzer *et al.*, 2015; Riley *et al.*, 2013; Trombelli *et al.*, 2013). It must be noted that the use of triclosan containing dentifrices has been curtailed over the past few years due to safety concerns.

Other Interventions

Probiotics

Probiotics are live microorganisms that are used to promote health benefits. Currently, evidence in favor of probiotics as a preventive strategy is promising but not yet proven (Table 7). Significant reductions in gingival inflammation and probing pocket depths were observed mainly with the use of lactobacilli (LB) with a total dose average of 1.26×10^{12} CFU/ml administered in milk-based and non-milk vehicles (Yanine *et al.*, 2013; Gruner *et al.*, 2016). Additional large scale trials are required for every probiotic strain considered before probiotics can be accepted as validated interventions to prevent periodontal diseases.

Table 6. Summary of findings on triclosan (Tcs)-containing dentifrices and stannous fluoride dentifrices

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Salzer *et al*. (2015)	11 RCTs on the efficacy of long-term use of Tcs/copolymer DF with respect to GI, PI, and BS. Control DF was SnF. Chemical rinses were excluded.	Data show significant differences in BS in favor of SnF DF. No significant differences in GI were found between the groups. Data show significant reductions in plaque score with respect to Tcs.	Different indices and their modifications were used with respect to plaque and gingival inflammation. This led to significant heterogeneity for all plaque and gingivitis indices. Hawthorne effect suspected for experimental durations under 6 months.
Riley and Lamont (2013)	30 RCTs on the effects of Tcs/copolymer fluoride toothpastes compared to fluoride toothpastes for long-term plaque and gingivitis control in adults.	Use of Tcs/copolymer toothpaste for 6-7 months reduced plaque by 22% compared to control. After 6-9 months of use tcs/copolymer toothpaste reduced gingival inflammation by 22% and bleeding by 48%.	Characteristics of the trial designs are questionable due to poor reporting of locations and settings of experiments in half of the included studies.
Trombelli and Farina (2013)	4 RCTs on the efficacy of Tcs/copolymer tooth paste compared to a control fluoride dentifrice over a 6-month period of plaque and gingivitis control in adults.	Data show that 0.3% Tcs/2% copolymer/.243% NaF dentifrice formulation showed decreases in plaque deposits, peri-implant mucosal inflammation, and peri-implant probing depths.	Heterogeneity in the formulations of the tested products complicates the results in the studies.
Hioe and van der Weijden (2005)	18 RCTs on the effect of Tcs/copolymer or Tcs/zinc citrate compared to fluoride-containing dentifrice on supragingival plaque, gingival inflammation, and gingival bleeding. Studies were conducted over 6-12 months.	Plaque control was significantly improved compared with a control fluoride dentifrice. Significant reductions in gingival inflammation and bleeding score were found in favor of Tcs/zinc citrate.	Measurements for each clinical parameter (gingivitis and plaque) were taken as baseline values and compared to end-trial values. No incremental data was included for the 6-12-months.

Anti-inflammatory Agents

Zhang *et al.* (2018) evaluated the anti-inflammatory effects of benzydamine-HCl (B-HCl), a non-steroidal anti-inflammatory agent. Insufficient evidence is currently available to support the use of mouth rinses containing B-HCl as a primary prevention strategy. Polak *et al.* (2015) evaluated the effect of NSAIDs (non-steroidal anti-inflammatory drugs) as a monotherapy (without mechanical debridement) and as an adjunctive therapy (with mechanical debridement) compared to mechanical debridement alone. Patients with chronic gingivitis who were treated with Flurbiprofen and Naproxen showed significant reductions in gingival inflammation indices compared to the placebo group. However, more studies are needed to better understand the long-term effects of NSAIDs as a solo treatment and as an adjunct to mechanical plaque control before they can be recommended as an oral hygiene intervention. There is overall weak evidence in support of adjunctive therapy using non-steroidal anti inflammatory agents (Chapple *et al.,* 2015) (Table 8).

Dietary Supplements and Anti-oxidants

Currently, there is insufficient evidence to support the claim that mineral supplementation or dietary lipids improves periodontal health (Table 8). The overall evidence is weak due to a lack of randomized trials and inconsistent measures of clinical outcomes (Varela-Lopez *et al.*, 2016a; Varela-López *et al.*, 2016b). Kulkarni *et al.* (2014) explored the efficacies of nutritional supplementation and anti-oxidants on managing gingivitis and preventing periodontal disease. The results found that multi-vitamin nutritional supplementation significantly improved gingival index and probing pocket depth. However, the strength of the evidence is considered weak since most studies used small group sizes.

Smoking Cessation and Health Education Interventions

Evidence suggests that tobacco smoking interferes with periodontal therapy (Table 9). As a result, it is important to consider the evidence in support of smoking

Table 7. Summary of findings on probiotics and other nutritional intervention strategies

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Yanine *et al*. (2013)	4 RCTs on the effects of probiotics on the prevention of periodontal disease compared to a placebo control group. Some of the included probiotics were Lactobacillus rhamnosus, Lacrobacillus salivarius, Lacrobacillus acidophilus, Bifidobacterium, Lactobacillus reuteri and Lactobacillus casei.	Primary outcome was probing depth. Secondary outcomes included plaque index, gingival inflammation, and bleeding on probing. Insufficient evidence to support the use of probiotics for the treatment of gingivitis.	Two of the four articles included in the review were categorized as having high risk of randomization bias and the other two as low risk of bias, in accordance with the Cochrane Collaboration tool. Sources of bias could be attributed to funding from private laboratories, short follow-up period, and the risk of experimentally inducing gingivitis in participating patients. Quality assessment was accomplished using the Cochrane Handbook for clinical studies.
Casarin et al. (2018)	25 RCTs on the effect of Melaleuca alternifolia essential oils compared to a control intervention control (i.e. CHX, Fluoridated toothpaste). Primary outcomes included dental plaque, gingival inflammation, and the bleeding on probing, and probing pocket depth in adult patients who have gingivitis. Some studies assessed supragingival and subgingival microbiota.	Most studies were determined to have low to moderate quality of evidence. Bactericidal and bacteriostatic effects of M. alternifolia are similarly effective as CHX. M. alternifolia showed no significant reductions in plaque score, but showed a significant reduction in gingival inflammation with 2.5% gel having the greatest number of improved bleeding and gingival scores. Significant reduction in probing depth from baseline was seen with 5% gel in adjunct with SRP.	The formulations of M. alternifolia varied across studies. Formulations included toothpaste (.5%), gel (2.5% and 5%), and solutions (0.2%, 0.34%, 1.5%). Duration ranged from 5 days to 6 months, all of which likely contributes to heterogeneity of data. The presence of methodological differences between studies resulted in the inability to perform a meta-analysis.
Varela-Lopez *et al*. (2016)	17 human RCTs on the effect of minerals on the onset and progression of periodontal disease. 9 different minerals were analyzed: calcium, magnesium, phosphorus, iron, potassium, copper, zinc, selenium, and manganese.	Overall, little evidence exists to support that mineral supplementation improves periodontal health.	Wide variability exists across studies, particularly in the evaluation methods of periodontal health. The overall evidence is weak due to lack of studies and inconsistent measures of clinical outcomes.
Varela-López *et al*. (2016)	6 RCTs on the short-term and long-term effects of dietary intake of lipids on periodontal health. Clinical parameters included plaque index, bleeding on probing, probing pocket depth, gingival index, and salivary RANKL and MMP-8.	Subjects treated with borage oil showed significant improvement in gingival inflammation compared to the placebo. Small improvements noted with fish oil with respect to probing pocket depth, however not significant. No changes were noted in GCF or Beta-glucuronidase levels.	Overall evidence is considered weak. It was not disclosed in the included studies which subjects had chronic periodontal disease at baseline compared to subjects with gingivitis. Conclusions cannot be drawn from this review with regards to use of dietary lipids in the primary prevention of periodontal disease.

Table 7 continued overleaf...

Table 7 continued

Kulkarni *et al.* (2014)	6 RCTS and 17 systematic reviews were included in this review. The studies were conducted to explore the efficacies of nutritional supplementation and anti-oxidants on managing gingivitis and preventing periodontal disease.	Data show that multi-vitamin nutritional supplementation significantly improved gingival index and probing pocket depth. Data show zinc is an effective anti-plaque agent.	There is weak evidence to support the use of dietary nutrients to control gingivitis and prevent the onset of periodontal disease. There is very weak evidence to support the use of anti-oxidants such as carotenoids, vitamin E, Vitamin C, glutathione, iron and copper to prevent periodontal disease.
Gruner *et al.* (2016)	50 RCTs evaluating whether probiotics are an effective adjunct to oral hygiene and whether using bacterial number measurements as a surrogate for periodontal disease is an effective clinical outcome measurement.	There is currently insufficient evidence supporting the use of probiotics to prevent periodontal disease. Little validity exists for using bacterial number measurements as surrogate for periodontal disease.	8 studies had high risk of bias, 34 studies had unclear risk of bias, and 8 studies had low risk of bias. Heterogeneity was high and publication bias suspected for all outcomes either statistically or graphically.

Table 8. Summary of findings on anti-inflammatory agents, metallopeptidases, and other drugs

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Polak *et al.* (2015)	14 RCTs on whether anti-inflammatory agents are effective in treating gingivitis both as a monotherapy (without mechanical debridement) and as adjunctive therapy (with mechanical debridement). Clinical parameters included gingival inflammation by gingival index, sulcus bleeding, and bleeding on probing. The control was mechanical debridement alone.	Patients with gingivitis who were treated with Flurbiprofen showed an approximate 90% reduction in gingival inflammation compared to the placebo group. No significant differences in plaque score were found between groups. Naproxen as an adjunctive therapy led to significant reductions in gingival inflammation.	More studies needed on the effects of NSAIDs as a solo treatment and as an adjunct to tooth-brushing with respect to gingival inflammation. Many studies involved the use of natural products, most of which were applied topically. Most agents showed reduction in gingival inflammation, however more clinical trials need to be conducted to further investigate their potential use as primary interventions.
Keukenmeester *et al.* (2014)	14 RCTs on the effects of medicated sugar-free chewing gum on clinical parameters including plaque score and gingivitis. Active ingredients in the medicated chewing gum include CHX, eucalyptus, acacia, funoran, Pycnogenol, mastic, and magnolia.	The majority of chewing gums containing antimicrobial activity or herbal extracts showed reductions in plaque scores and gingival inflammation. The active ingredients with the greatest effect on gingival inflammation included magnolia, eucalyptus and CHX. Stain effects of CHX-chewing gum were significantly lower compared to CHX mouthwash.	Lack of statistical power limited the authors' ability to do a meta-analysis and assess for publication bias (less than 10 studies were included in the meta-analysis).

Table 9. Summary of findings on smoking cessation and oral health promotion

Systematic Review	Intervention characteristics	Included outcomes	Limitations of data
Leite *et al*. (2018)	21 longitudinal RCTs included in meta-analysis on the efficacy of smoking cessation on the incidence of periodontal disease. Follow-up periods ranged from 2 years to 38 years across studies. Assessment for periodontal disease included partial and full-mouth radiographic assessment (to measure alveolar and clinical attachment levels) and clinical examination (to measure probing depth at worst site per tooth).	Adjusted results (for participation rate and other compounding variables) showed that tobacco smoking increased the risk of periodontitis by 85% (risk ratio = 1.85, 95% confidence = 1.5, 3.3).	More future studies are needed in order to quantify dose-dependent effects of tobacco smoking on gingival inflammation. Radiographic signs of bone loss can over-estimate clinical attachment and therefore many studies may have reported inflated values.
Fiorini *et al*. (2014)	2 RCTs on the effects of smoking cessation on periodontal pocket depth and risk of tooth loss. Smoking cessation intervention and non-surgical periodontal treatment were simultaneously implemented across all subjects. Periodontal pockets were evaluated after a 1 year follow-up.	Periodontal pocket reduction was significantly higher after 1 year for quitters compared to smokers. Data show that quitters had a significantly lower risk for tooth loss compared to smokers. After a 10-year follow up, the risk of tooth loss equaled that of never-smokers.	Meta-analysis was not performed due to heterogeneity of the studies, small sample size, and high drop-out rate. The systematic review included 5 studies in total, 3 of which were epidemiologic and therefore do not satisfy our inclusion criteria. The review did not include clinical studies that evaluated the effect of smoking cessation on periodontal health alone, which likely accounts for data heterogeneity.
Hausen (2005)	13 RCTs to evaluate whether oral health promotion improves oral hygiene and gingival health. The primary clinical outcomes were reductions in dental plaque levels and/or gingivitis. The intervention was health education/health promotion interventions in clinical or workplace settings.	Some evidence suggests that health promotion has a positive effect on oral hygiene and gingival health in the short term. However, the beneficial effects remain unclear over the long-term.	Design quality across studies varied. Some studies did not include a control group. There was no clear indication that any particular type or style of educational approach was more effective than the other.

cessation as a primary prevention of periodontal disease. More studies are needed in the future in order to quantify dose-dependent effects of tobacco smoking on gingival inflammation (Leite *et al.*, 2018). Fiorini *et al.* (2014) found that periodontal pocket reduction was significantly greater after 1 year for subjects who quit smoking compared to subjects who continued smoking. The evidence shows that those who quit smoking have a significantly lower risk for tooth loss compared to smokers. After a 10-year follow up, the risk of tooth loss equaled that of individuals who had never smoked. With respect to health education interventions, some evidence suggests that health promotion improves patient oral hygiene in the short term (Hausen, 2005) . However, it is unclear whether these changes can be sustained in the long-term and therefore additional studies with longer follow-up periods are needed.

Discussion

It is well established that inflammatory periodontal diseases (gingivitis and periodontitis), amongst the most common diseases of humans, result from extended exposure of the periodontium to tooth-borne biofilms known as dental plaque (Eke *et al.,* 2020; Lasserre *et al.*, 2018). The primary prevention of periodontal diseases requires daily removal of plaque by use of oral hygiene procedures, most often including mechanical tooth brushing (using manual or powered toothbrushes) and interdental cleaning. The mainstay of interdental cleaning for most people is flossing. Interestingly, many studies comparing flossing to interdental brushes show that interdental brushing are more effective in plaque removal compared to flossing. However, for patients with non-receded interdental papillae, flossing is encouraged over interdental brushing (Kotsakis *et al.*, 2018; Poklepovic *et al.*, 2013). In general, flossing or interdental brushing should be part of daily self-performed oral hygiene.

Apart from mechanical plaque control measures, mouth rinses containing antiseptics such as chlorhexidine gluconate (CHX), essential oils (Listerine) or cetylpyridinium chloride (CPC)- should be used as adjuncts to help patients manage dental plaque formation to prevent gingivitis. The evidence is strong favoring the use of CHX mouth rinse to reverse gingivitis (Supranoto *et al.,* 2015; Berchier *et al.,* 2010; Elkerbout *et al.,* 2018). However, CHX mouth rinse possesses several adverse effects, such as staining and altered sensation of taste, that on occasion limits its use in certain patients. Thus, other chemical interventions should be considered for at-home use. There is strong evidence supporting the adjunctive use of essential oil mouth rinses and cetylpyridinium chloride-containing mouth rinses for adjunctive therapy in patients with significant levels of plaque and/ or chronic gingivitis. While several herbal extract-based rinses show promise for anti-plaque and anti-gingivitis effects, additional clinical trials are required to prove their efficacy.

The efficacy of triclosan-containing rinses and dentifrice are supported by strong data (Trombelli and Farina, 2013; Hioe and van der Weijden, 2005; Salzer *et al.,* 2015; Angelillo *et al.,* 2002; Riley and Lamont, 2013). The systematic reviews included in this umbrella review conclude that triclosan has significant gingival and anti-plaque benefits. However, their use have diminished in recent years due to public health concerns (Weatherly *et al.*, 2017). Triclosan-containing soaps were recently banned by the Federal Drug Administration in 2016 due to concerns pertaining to its potential role in various types of cancer as well as in developmental and reproductive defects (Weatherly and Gosse, 2017). Triclosan is easily absorbed by human skin and oral mucosa. Also, triclosan has recently been removed from the most popular toothpaste in the United States. It thus appears that triclosan use will diminish for plaque control over the foreseeable future.

Other interventions that have received attention to prevent periodontal disease include probiotics, anti-inflammatory agents, anti-oxidants and other topically applied natural products. There is promising evidence to support future use of these products, however no clinical recommendations supporting their use can be made at this time. It is important to consider behavioral modifications as primary prevention strategies such as smoking cessation as there is strong evidence that smoking cessation interrupts periodontal disease progression and should be clinically recommended to patients with a poor periodontal prognosis.

A number of limitations have been identified for many studies that restrict application of findings in clinical practice. These limitations include the inadvertent increased attention to oral hygiene technique in control groups (Hawthorne effect), variation in gingival and plaque indices, the potential for reporting and publication biases, and the paucity of well-designed clinical trials. Variations in plaque and gingival indices used makes it difficult to compare results between studies, which was pointed out by most of the systematic reviews that were included in this umbrella review. Variations in techniques between trials (for example variation in brushing technique; e.g. Bass technique vs the Rolling technique) were also identified as limiting factors of the included trials. All of these variations contribute to the great data heterogeneity that was observed across most studies.

We conclude that only a few interventions presently in routine use have been proven to prevent gingivitis and periodontitis. These include methods of mechanical biofilm control, such as the use powered toothbrushes, oral irrigators, and interdental cleaning devices. No differences were found between manual tooth brushing and powered tooth brushing. Topical chemical interventions proven to prevent periodontal inflammation include chlorhexidine gluconate (CHX), cetylpyridinium chloride (CPC), and essential oils. Many other promising interventions are presently under investigation.

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