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## **Mouthwashes: Implications for Practice**



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#### ABSTRACT

This is the concluding article in the supplement on the role of mouthwashes in oral care, which summarises the current guidelines across the globe regarding their acceptable adjunctive use for managing caries, gingivitis, and periodontal disease. Based on moderate evidence for clinical effectiveness, most current guidelines suggest fluoride mouthwashes for the management of dental caries, and chlorhexidine for the management of periodontal diseases. However there still appears to be gaps in the literature underpinning these recommendations. Importantly, all evidence supports such mouthwash use "adjunctively," alongside mechanical oral hygiene measures. Other antimicrobial mouthwashes such as essential oils and cetylpyridinium chloride may also be clinically effective against plaque and gingivitis, but there is a current lack of robust evidence of natural mouthwashes to recommend their adjunctive use. The authors of the current review are of the view that mouthwashes may not be of much value in those with good periodontal health or low caries risk. The reasons for this are, the potential i) risks of allergic reactions, ii) dysbiosis of the oral microbiota, iii) emergence of antimicrobial resistance, and iv) deleterious effects on the environment. There is, however, much empirical research needed on mouthwashes, particularly in vivo research derived through clinical trials. Thus, dental practitioners need to keep abreast of the evidence base on the current, and the emerging, over-the-counter mouthwashes, and pay heed to the consensus views emanating from systematic reviews, as well as international guidelines on mouthwashes.

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#### Introduction: clinical benefits and mouthwash

In this supplement we discuss a wide range of antimicrobial mouthwashes that are currently used adjunctively to manage oral diseases such as gingivitis, periodontitis, and dental caries. There seems to be general consensus across the board that chlorhexidine, cetylpyridinium chloride, and essential oil mouthwashes display clinical effectiveness by reducing plaque and gingival inflammation (gingivitis).<sup>1,2</sup> This is supported by a plethora of good- and medium-quality publications on these particular agents, with most evidence, available for chlorhexidine. Chlorhexidine might also provide a small clinical benefit when used along with routine oral hygiene

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Zoë L.S. Brookes: http://orcid.org/0000-0002-8096-6256 https://doi.org/10.1016/j.identj.2023.08.013 methods as an *adjunct* to nonsurgical therapy for periodontal disease. However, to date, no mouthwash has been found to be effective for treating periodontal diseases when used *alone*.

Furthermore, there is emerging evidence that frequent use of antimicrobial mouthwashes may cause dysbiosis of the oral microbiome in healthy people, perhaps impacting systemic health. These emerging risks suggest that it may be wise to avoid routine antimicrobial mouthwash use in individuals with good oral health, where there would be no oral health benefits. Therefore, in this concluding document we attempt to summarise the use of mouthwash in the context of current guidelines in different counties.

Whilst evidence is still emerging on the effects of mouthwashes on oral and systemic disease, especially those other than chlorhexidine, it is hoped that some of the concluding remarks will help dental practitioners (dentists, therapists, and hygienists and oral health educators) to make a more informed decision on how they advise patients on the use of mouthwashes for day-to-day management of caries, plaque, gingivitis, and periodontal disease in the face of evolving evidence.

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#### Guidelines: periodontitis and mouthwash

When advising patients on the adjunctive use of mouthwashes, dental practitioners would normally consult their respective national guidelines or consult the best available evidence, depending on the jurisdiction in question. Some countries place a greater emphasis on adhering to guidelines than others, who may prefer to consult the best quality of literature available. However, it must be recognised that, sometimes, the evidence surrounding mouthwashes in particular remains of low quality within the hierarchy of evidence. This partly explains why current mouthwash guidelines differ across the globe and why it is hugely challenging trying to make recommendations in areas where dental research is lacking. Dental practitioners must therefore be able to apply and critically appraise the quality of empirical research and refer to their national guidelines.

Within Europe, the EFP S3 level clinical practice guidelines regarding treatment of stages I through III periodontitis address whether adjunctive use of chlorhexidine mouthwash can improve the clinical outcome of nonsurgical therapy, involving professional mechanical plaque removal.<sup>3,4</sup>

A systematic review determined that slightly higher pocket depth reduction during stage I through III was achieved when chlorhexidine mouthwash was used in conjunction with scaling and root planing (SRP) than SRP alone.<sup>5</sup> Thus, the consensus recommendation within current EFP S3 guidelines is that dental practitioners should use "chlorhexidine mouth rinses for a limited period of time, in periodontitis therapy, as adjuncts to mechanical debridement, in specific cases."<sup>3,4</sup> However, there was no recommendation for any other type of mouthwash for gingivitis. We remind the clinician that the key words in these current guidelines are *adjunctive* use and *limited period of time* and that there is no recommendation that chlorhexidine would be effective when used alone without mechanical plaque control via tooth brushing and subgingival instrumentation.

The British expert group interpretation of these European guidelines mirror the adjunctive use for mechanical debridement in specific cases.<sup>6</sup> European guidelines further point out that chlorhexidine use must be weighed against the side effects of chlorhexidine, such as tooth staining and altered taste, and suggest that use should be no longer than 2 weeks to minimise these.<sup>3,4</sup> There have also been fatal allergic reactions to the use of chlorhexidine mouthwash; these are extremely rare and anecdotal but have been reported in the literature nonetheless.<sup>7</sup>

The Australian Therapeutic Guidelines also present independent information on best practice and is a distillation of current best evidence interpreted by experts.<sup>8</sup> These guidelines are written principally for prescribers to provide clear, practical, succinct, and up-to-date therapeutic information for a range of diseases. The 3rd edition of the Oral and Dental version of the latter publication states that a mouthwash is usually not required as part of a standard oral hygiene routine and should not be used as a substitute for proper mechanical teeth cleaning. However, similar to European guidelines, they indicate that chlorhexidine containing mouthwashes can be used for a short duration in addition to mechanical tooth cleaning. Specifically, the publication clearly iterates that although the use of antiseptic mouthwashes in periodontal disease is controversial, they are only effective against supragingival plaque and are not effective beyond the gingival crevice or periodontal pocket. These guidelines recommend that patients should be informed that the principal treatment for chronic periodontal disease is professional intervention with debridement of involved teeth and meticulous oral hygiene. Nevertheless, these guidelines state that, in some circumstances, such as for short-term use in patients with gingivitis or necrotising gingivitis, when inflammation restricts normal tooth brushing, the use of an antiseptic mouthwash can be beneficial.<sup>8</sup>

The Australian guidelines further elaborate on the use of chlorhexidine mouthwash that is available as both 0.12% and 0.2% concentrations; they state that its use can cause a burning sensation, altered taste, and increased calculus formation. It can also cause brown discolouration of the teeth, tongue, buccal cavity, and margins of dental restorations, supporting recommendations for short-term use, for periods of up to 2 weeks, to minimise adverse effects. The guidelines also points out, as stated above,<sup>7</sup> that chlorhexidine allergy may be rarely severe so as to be life-threatening and as such recommend that if a patient reports a history of allergy to chlorhexidine, it must be avoided via all routes of administration, including topical application.<sup>8</sup> Finally, the Australian Therapeutic Guidelines<sup>6</sup> state that alcohol-containing mouthwashes may be associated with oral cancer and should be avoided if possible. In addition, patients with oral mucosal disease and dry mouth should avoid alcohol-containing mouthwashes because they cause profound drying of the oral mucosa.<sup>8</sup>

As opposed to the European and Australian guidelines, the American Dental Association has a dichotomous approach to the mouthwash use as either cosmetic or therapeutic, based on either the presence or absence of a chemically active ingredient.<sup>9</sup> Cosmetic mouthwashes are those that lack bactericidal or bacteriostatic properties, including those for temporary masking of symptoms such as bad breath. These products are typically sold OTC and do not require a prescription for purchase; they include some of the aforementioned "natural" mouthwashes. Essential oil–containing antimicrobial mouthwashes recognised as being clinically effective against plaque and gingivitis<sup>10</sup> are, however, available OTC. Therapeutic mouthwashes, on the contrary, contain active ingredients such as cetylpyridinium chloride, chlorhexidine, fluoride, or hydrogen peroxide and are antimicrobial. They must all be dispensed by prescription, are indicated for shortterm use, and are designed to treat a specific condition. The prescriptive use relates to active ingredients in these mouthwashes being effective at reducing plaque and gingivitis when combined with daily brushing and flossing.<sup>9</sup> However, antimicrobial mouthwashes are not recommended for children younger than 6 years of age due to risk of swallowing.

Thus, the current consensus is that clinicians should consider alongside national guidelines and best evidence on effectiveness and balance this against the adverse effects of mouthwashes such as oral microbiome dysbiosis and emergence of bacterial resistance, systemic health issues, and the environmental contamination. Mouthwash use for each patient needs to be considered on a case-by-case basis, asking "do the oral health benefits outweigh the risks?" Whether the mouthwash is obtained OTC by the patient or prescribed therapeutically by a dental practitioner, a combination of treating a more serious oral disease alongside a low risk of adverse outcomes associated with use makes the recommendation of an adjunctive mouthwash more likely, even if it confers only a small clinical benefit.

Even so, with a wide range of antimicrobial mouthwashes available, there is still a lot of empirical research urgently required to determine the most effective mouthwashes for reducing oral disease, whilst mitigating adverse effects. In the authors opinion, the goal would be to find a "balance," reducing pathogenic bacteria possibly associated with disease whilst maintaining commensal bacteria associated with health. The strongest evidence so far on adverse effects has been acquired through randomised controlled trials in humans, although in many areas not enough original research yet exists for a systematic review: for example, the effects of chlorhexidine on cardiovascular health, including the "enterosalivary" pathway. If this mechanism is fully proven, in the future patients with periodontitis may have to avoid certain mouthwashes if they are at risk of cardiovascular disease. Conversely, there are strong links emerging for periodontal disease being causative of cardiovascular disease which would favour the use of mouthwashes: If more targeted adjunctive use of specific antimicrobial mouthwashes could improve periodontal disease, again no matter how small, this in turn could be of benefit to cardiovascular health.

Given the limited effectiveness on periodontal disease when used alone, it may be that future work continues to assess the effectiveness of mouthwashes at the earlier stages of periodontal disease, namely gingivitis, particularly in populations at high risk for periodontal disease later in life. Gingivitis implies a stage of gum disease where pocketing depths are less, inflammatory changes often reversible, and pathogenic supragingival bacteria more "reachable" by antimicrobials. Indeed, a Cochrane Review has demonstrated that chlorhexidine used as an adjunctive to mechanical cleaning in patients with mild gingival inflammation reduced plaque and gingivitis, although this was not considered to be clinically relevant.<sup>8</sup> At that time, more than 6 years ago, there was insufficient evidence for the effectiveness of chlorhexidine mouthwash use for moderate or severe gingival inflammation.<sup>11</sup>

The most current publication of the National Health Service (NHS) of the United Kingdom, the "Delivering Better Health" (DBOH) toolkit, states that there is high-certainty evidence for the use of chlorhexidine mouthwash to reduce dental plaque and gingivitis,<sup>12</sup> whilst pointing out its limitations<sup>11,12</sup> and the need for much more clinical research investigating the effects of antimicrobial mouthwashes on gingivitis in different population groups. Indeed, determining more specific uses of their existing products could be an exciting area of future mouthwash research for drug manufacturers who produce them, in turn future-proofing products with this more targeted use, as our understanding of the oral microbiome in both health and disease continues to grow.

#### Caries

In reviewing the clinical effectiveness of sodium fluoride in dental health care products, including mouthwashes, its anticariogenic effects can be supported by evidence of increased remineralisation properties.<sup>13</sup> However, there appears to be a current lack of high-quality evidence linking fluoride mouthwash effectiveness to a bactericidal action in vivo or changes in the overall oral microbiota. Most of the evidence supporting fluoride effectiveness has also been acquired from studies involving children and adolescents,<sup>14</sup> and more research is needed in adults as well as those with root caries. Interestingly, a Cochrane Review, including the use of fluoride mouthwashes in orthodontic patients wearing fixed braces, showed no additional effects against demineralisation.<sup>15</sup>

NHS Public Health guidance in England (DBOH) recommends daily use of 0.05% w/v (230 ppm) fluoride mouthwash as good practice to mitigate caries in children from age 8 years onwards, in patients who are at a higher risk and likely susceptible to the development of dental caries.<sup>12</sup> The fluoride mouthrinse is more effective when used at an other time than brushing. The same advice is often provided for adults who are at a higher risk for dental caries. However, fluoride mouthwash is not recommended in either children or adults with lower risk of dental caries. This guidance also favours 230 ppm daily, rather than 900 ppm daily, for effectively reducing caries within in the permanent dentition or adolescents and children.<sup>12</sup> However, the aforementioned NHS guidance recognises the limited evidence on the effects of fluoride mouthwashes on prevention of caries in the primary dentition. Across the globe, therefore, clinical studies on the effectiveness on fluoride mouthwashes on caries in human volunteers are still needed in a range of populations.

#### Summary and recommendations for clinicians

Taken together, this supplement summarises the database on the most used antimicrobial mouthwashes, such as chlorhexidine and essential oil formulations. These formulations are still widely used by virtue of the strong evidence of their effective bactericidal and/or bacteriostatic action, particularly in vitro. Most effective antimicrobial mouthwashes therefore seem to also "kill" bacteria in the oral cavity, due to fatal destruction of the bacterial cell membranes. There has also been a study on the virucidal effects of mouthwashes, including COVID-19 and other emerging respiratory pathogens, but the antiviral effects of mouthwashes in vivo remain uncertain. Clinically, there is evidence that alongside oral hygiene measures and professional mechanical plaque removal, antimicrobial mouthwashes effectively reduce bacterial plaque and gingivitis. A corollary of this is that mouthwashes have similar effectiveness in mitigating periodontitis, but there are limited quantitative and qualitative data in this regard. Hence, this supplement reinforces the current informed opinion that most antimicrobial mouthwashes are of limited use as sole agents to manage periodontal diseases.

Fluoride mouthwashes are recommended for prevention of caries, primarily due to their salutary effects on tooth remineralisation rather than their antimicrobial effect, and recommended for use as adjunctive agents in individuals prone to high caries risk. Antimicrobial mouthwashes may further play an adjunctive role in the management of halitosis either in masking malodour or addressing the underlying bacterial cause, although there are limited clinical trials. There is a resurgence of interest in the role of mouthwashes in perioperative dental care and health care in general, but considering the gaps in the literature reported here, antimicrobial mouthwash recommendations remain challenging. There is also a lack of high-quality evidence for many of the emerging natural products. Thus, based on guidelines across the globe and reviewing the current best evidence, these are the final recommendations of this supplement, which also incorporates national guidelines where possible:

- Per the findings of the extant systematic reviews, mouthwashes can reduce supragingival plaque and gingival inflammation (gingivitis) when used adjunctively alongside self-care and professional oral hygiene care.
- Per the guidelines pertaining to management of periodontal diseases, we prudently advise that mouthwashes should be used for a short term (up to 2-4 weeks) to manage mild to moderate periodontal disease (no evidence was available for severe periodontal disease) and only as an adjunct to oral hygiene measures and professional mechanical plaque removal in specific cases. Be aware that the clinical benefits of this approach may be minimal and there is a dearth of studies supporting this approach.
- If asked to advise on which antimicrobial mouthwash is "best" for "gum disease," explain that there is most evidence supporting the use of chlorhexidine- and essential oil-containing products. There is a necessity to do more research on these products, and hence the "best" product can not be nominated.
- Support the appropriate use of fluoride mouthwashes for adjunctive self-care, at some other time than tooth brushing, considering that its effectiveness on caries prevention is supported by moderate evidence.
- If you are consulted about mouthwash use for the management of halitosis and in tooth-whitening, understand there is a currently lack of in vivo clinical trials to inform the evidence.
- Avoid strongly advocating the use of mouthwashes in patients with good periodontal health or low caries risk, due to the potential risks of allergic reaction and oral microbiome dysbiosis, which may also be associated with compromised systemic health, antimicrobial resistance, and deleterious effects on the environment; these could outweigh any benefits of use in this group.
- Do not advocate the use of natural or alternative mouthwashes available in health food stores, explaining that, although there is no evidence of harmful effects with many of the products, there is also no evidence of their beneficial effects for alleviating periodontal disease; more evidence is needed on their effectiveness, mechanisms, and adverse effects to support their use.

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#### **Conflict of interest**

None disclosed.

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