Prevention of root caries: a literature review of primary and secondary preventive agents

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As advances in medicine and dentistry have led to significant improvement of people’s general and oral health, studies have shown that people are not only living longer but also retaining more of their own teeth. The presence of more teeth retained into older ages has inevitably resulted in more dental caries in these older adults, especially root caries. Over the past two decades, studies conducted in nine countries (i.e., the United States, Canada, Brazil, Germany, Finland, Sweden, Japan, India and Sri Lanka) have reported a relatively wide range of root caries prevalence in older adults ranging from 29 to 89%, with most of those studies reporting within the narrower prevalence range of 30–60%. However, even if the prevalence of root caries remains stable in this range for the coming decades, the expected demographic elderly boom will inevitably lead to a large increase in the number of elderly with root caries treatment needs, accompanied by a call for even more effective means of preventing root caries.

A 2004 literature review showed that for the nine studies reporting annual root caries incidence, the estimated mean annual incidence was 23.7% (95% CI = 17.1–30.2%), ranging from 10.1% in Canada to 40.6% in Washington, while for the nine studies reporting on annual root caries increment, the mean was an increment of 0.47 surfaces (CI = 0.34–0.61) per year, ranging from 0.20 surfaces in Canada to 0.98 surfaces in Massachusetts. Two more recent individual studies conducted in the U.S. in 2005 showed similar findings to the prior findings in Massachusetts, with root caries increments of 1.0 and 1.07 surfaces per year. Annual root caries increments of 0.47–1.0 surfaces per year per adult with a prevalence rate of ~45%
suggestions that the prevention of root caries in adults should be a high national oral health priority.

Although a total of 13 literature reviews on chemotherapeutic root caries prevention have been published over the past two decades, they all were limited in scope, for example, none evaluated more than three anti-root caries agents in any one literature review. Further, all of these reviews merely directly reported the differing formats and style of assessments of outcomes by the authors of the reviewed original studies, which made comparative judgments across preventive agents difficult, if not impossible.

This literature review was conducted by the authors at the request of the American Dental Association through its Council on Access, Prevention and Interprofessional Relations’ Elder Care Committee via the ADA Division on Geriatric and Special Needs Populations. The goal of this literature review was two-fold: 1) to conduct a systematic review on the effectiveness of the seven leading preventive agents for root caries, specifically: fluoride, chlorhexidine, xylitol, amorphous calcium phosphate, sealants, saliva stimulators, and silver diamine fluoride (see Table 1 for abbreviation labels) within a single assessment of outcome format to allow direct comparison of effectiveness across agents and 2) to provide recommendations for use of those agents for the general population of healthy older adults as well as specific recommendations for vulnerable older adults.

**Methods**

The following search strategy was used to identify all possible relevant published articles: 1) a search of PubMed/Embase and Cochrane Library electronic databases; 2) a search for additional references from the references section of each relevant, electronically-retrieved article; and 3) a search of the most recent publications in main dental journals to compensate for the delay in transfer of journal publications to electronic data sources. Once all possible relevant published articles were identified via the broad search, the second step (i.e., the “title-and-abstract” review stage) was performed to identify the subset of only the most pertinent articles; this was done by having each reviewer (i.e., the authors) independently screen the initial listing of possible relevant articles using the two following eligibility criteria: 1) the study assessed the effectiveness of at least one of the seven specific agents to prevent or control root caries in older adults; and 2) the study presented meaningfully interpretable original research findings in English-language articles published between January 1979 and July 2010.

The initial broad electronic search identified 387 articles that were possibly relevant, and the second “title-and-abstract” review-stage led to a rejection of 336 (86.8%) of those 387 articles, resulting in the identification of 51 “most pertinent” articles. Subsequently, an additional six references were identified from the references lists in those 51 articles, with one more reference identified by searching main dental journals published from January 2009 to July 2010. Finally, by a “full text” review, this set of 58 “most pertinent” articles was finally reduced to a set of 30 articles (describing 31 studies, as one article presented two separate studies). The electronic search strategies and list of the reviewed journals are presented in Table 2.

A detailed Data & Information Abstraction (DIA) Chart was created which consisted of 34 columns with each column representing a specific “characteristic of” or “variable within” that study to be abstracted from each article, noting either “not mentioned” or “mentioned”, giving the details in the latter case. Each author independently reviewed each of the 31 studies using this DIA Chart to ensure consistency of the article reviews.

The inter-reviewer agreement rates during all stages of the evaluation of articles were above 91%. The initial reviews using the DIA Chart revealed a lack of uniformity across the studies as regards a variety of included aspects, including root caries assessment criteria, descriptions of active agents, reporting of fluoride concentration, and reporting of primary and secondary prevention outcomes. In order to achieve a standardized summarization across reviewed articles on these four variables, the following standards were applied across all studies: 1) used a “common-to-all” studies carries outcome assessment criteria of texture (i.e., hardness vs. softness) as the only criteria used to assess effectiveness of tested agents; 2) described active agents based on their chemical composition only; 3) presented fluoride concentration in ppm only; 4) measured the effectiveness of the 1st prevention agents based on

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**Table 1. Abbreviations and brand names of effective agents or combination of agents for 1st and 2nd Root Caries Prevention.**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Chemical Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevident Plus toothpaste</td>
<td>5000 ppm NaF</td>
</tr>
<tr>
<td>Colgate Palmolive Duraphat toothpaste</td>
<td>5000 ppm NaF</td>
</tr>
</tbody>
</table>

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CHX = Chlorhexidine; F = Fluoride; NaF = Sodium Fluoride; SDF = Silver diamine fluoride; SnF2 = Stannous Fluoride; ACP = Amorphous Calcium Phosphate; EC 40 varnish = 40% CHX, sandarac, ethanol; Saforide = 38% SDF; Duraphat varnish = 22, 500 ppm NaF; Colgate toothpaste = 1100 ppm NaF; Dentan rinse = 225 ppm NaF; Colgate Total toothpaste = 1,100 ppm NaF + Triclosan; Enamelon toothpaste = ACP = SnM Ca, SnM PO4, 0.25 mM Fluoride stabilized by NaCl at Ph 7.0; Prevident Plus toothpaste = 5000 ppm NaF.
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Table 2. Detailed search strategy used for literature review of root caries.

<table>
<thead>
<tr>
<th>I. Primary Search conducted with Pubmed using three search structures</th>
</tr>
</thead>
</table>
agents or combination of agents in the Table 3. Thus, the two most effective agents or combination of agents for the 1° prevention of root caries incidence were a 1110 ppm NaF + triclosan toothpaste self-applied daily and a ACP + 250 ppm NaF toothpaste applied daily, both of which nearly doubled the reduction of root caries when compared to an already proven effective root caries prevention products.

As also shown in Table 3, only fluoride in two concentrations and in different routes of administration were found to be effective in the 2° prevention of root caries: a 4,500–5,000 ppm NaF toothpaste gel self-applied daily and a 22,500 ppm NaF varnish professionally applied every 1–3 months (see table 1 for products’ brand names). While the range reported for arrested lesions was similar (52–100% for the self-applied NaF toothpaste and 54–95% for the professionally applied NaF varnish with or without supplementation of NaF toothpastes and rinses), the mean reported arrested lesion rate was higher for the NaF varnish (78% vs. 64%).

One intriguing future line of inquiry into the effectiveness of xylitol is suggested by the findings from a small, early exploratory, nonrandomized clinical trial conducted in Veterans Administration (VA) patients in the U.S. which found that regular use of xylitol gum and/or dragees by subjects over 20 months (as compared to sorbitol use) was protective against the incidence of root caries (Relative Risk = 19, 95% CI 0.06–0.62). However, given the authors’ emphasis on the pilot and very exploratory nature of this study, the findings cannot lead to a direct clinical recommendation at this time, other than for further research into this agent’s effectiveness.26 Another early, small exploratory study was conducted using sealants to treat small and shallow root caries lesions in 22 adults. Although these authors reported favorable results, the very short follow-up seriously limits clinical interpretation of this data.25

### Table 3. Recommendations for Clinicians for use of the most effective root caries preventive agents or combination of agents in general adult population in ascending order of effectiveness.

<table>
<thead>
<tr>
<th>Agents or combination of agents</th>
<th># &amp; Types of Studies</th>
<th>Strength of Evidence</th>
<th>1° Prevention (% reduction)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1% or 10% or 40% CHX varnish8,20,21 1–3 mo interval</td>
<td>4 RCTs</td>
<td>Moderate strengths, with 4 well done studies</td>
<td>41–57% (vs placebos)</td>
<td>highly effective vs placebo</td>
</tr>
<tr>
<td>22,500 ppm NaF varnish27,29 Every 3 mo</td>
<td>2 RCTs</td>
<td>thin, but strong and consistent</td>
<td>56% – 64% (vs no active agent)</td>
<td>highly effective vs placebo</td>
</tr>
<tr>
<td>1,100 ppm NaF toothpaste3 Daily</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>67% (vs no active agent)</td>
<td>highly effective vs placebo</td>
</tr>
<tr>
<td>38% SDF solution30 Annually</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>72% (vs a near placebo: OHI only)</td>
<td>very highly effective vs a near placebo</td>
</tr>
<tr>
<td>225 ppm NaF rinse10 Daily</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>36% (vs 22,500 ppm NaF varnish)</td>
<td>1/3 more effective vs an agent that was itself highly effective compared to a placebo</td>
</tr>
<tr>
<td>960 ppm SnF2 gel10 Every 3 mo</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>35% (vs 22,500 ppm NaF varnish)</td>
<td>1/3 more effective vs an agent that was itself highly effective compared to a placebo</td>
</tr>
<tr>
<td>1,110 ppm NaF + Triclosan toothpaste18 Daily</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>90% (vs 1,100 ppm NaF toothpaste)</td>
<td>nearly 2-fold the effectiveness vs an agent that was itself highly effective compared to a placebo</td>
</tr>
<tr>
<td>ACP toothpaste + 250 ppm NaF rinse20 Daily</td>
<td>1 RCT</td>
<td>very thin, a single well done study</td>
<td>98% (vs 1,100 ppm NaF toothpaste + 250 ppm NaF rinse)</td>
<td>2-fold the effectiveness vs an agent that was itself highly effective compared to a placebo</td>
</tr>
</tbody>
</table>

### Table 4. Recommendations for Clinicians for use of the most effective root caries preventive agents or combination of agents in vulnerable elderly population in ascending order of effectiveness.

<table>
<thead>
<tr>
<th>Agents or combination of agents</th>
<th># &amp; Types of Studies</th>
<th>Strength of Evidence</th>
<th>2° Prevention (% arrested)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>4,500–5,000 ppm NaF toothpaste/gel11,12,15 Every 3 mo</td>
<td>2 RCTs 1 case-series</td>
<td>a growing and solid body of evidence</td>
<td>52–82% (µ = 67%)</td>
<td>highly effective</td>
</tr>
<tr>
<td>22,500 ppm NaF varnish21,27,29 Every 1–3 mo</td>
<td>3 RCTs 2 case-series</td>
<td>solid and consistent body of evidence</td>
<td>54% – 92% (µ = 80%)</td>
<td>very highly effective</td>
</tr>
</tbody>
</table>

What is recommended for the prevention of root caries in vulnerable elderly

Although the above recommended agents or combination of agents (presented in previous section) were chosen based on their effectiveness in the prevention of root caries, that is, the percent reduction or percent arrested, Table 4 shows the final recommended choices for use with...
particular attention to vulnerable elderly and introduces the consideration of feasibility for use of these effective agents or combination of agents within a vulnerable population, that is, the required frequency of application and the capability of vulnerable elderly to self apply. For the 1° prevention of root caries the recommended “best choice” agent is the 38% SDF solution professionally applied annually. If no professional application is possible, the recommendation for “best alternative” for the 1° prevention of root caries is the use of a self-applied ACP + 250 ppm NaF toothpaste daily. For the 2° prevention of root caries (i.e., arresting lesions), the recommended “best choice” is fluoride in a form of 22,500 ppm NaF varnish professionally applied every 3 months. If no professional application is possible, the recommendation for “best alternative” for the 2° prevention of root caries is the use fluoride, as well, but in a form of a 4,500–5,000 ppm NaF toothpaste/gel self-applied daily.

Research gap analysis: the next needed steps in research

Tables 3 and 4 clearly show which agents or combination of agents are most effective, as well as “the depth” of the evidence attesting to that level of effectiveness. For the 1° prevention of root caries, there are eight identified effective agents or combination of agents (with six of them found to be “highly effective”), but for all but two of those eight, the “depth” only amounts to a single clinical study. Perhaps the common term used for this situation is to declare those agents or combination of agents as “promising”. The most studied 1° preventive agent, CHX varnish, has replicated findings across four clinical studies, but is the least effective of the eight listed 1° prevention agents or combination of agents. The only other 1° prevention agent with more than a single study as evidence, NaF varnish, is supported by the evidence from three of the clinical studies. The best alternative to NaF varnish, an ACP + 250 ppm NaF toothpaste self-applied daily, is nearly as effective in arresting root caries lesions, and has well supported evidence from six clinical studies. The research gap analysis for 2° preventive agents suggests priority should be placed on identifying new agents or improved regimens of existing agents that would achieve even higher rates of arresting root caries lesions, with application modes that would heighten feasibility for use with the vulnerable elderly.

Conclusions

For the 1° prevention of root caries the recommended “best choice” is the 38% SDF solution professionally applied
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annually. If no professional application is possible, the recommendation for “best alternative” for the 1° prevention of root caries is the use of a self-applied ACP + 250 ppm NaF toothpaste daily. For the 2° prevention of root caries (i.e., arresting lesions), the recommended “best choice” is the 22,500 ppm NaF varnish professionally applied every 3 months. If no professionally application is possible, the recommendation for “best alternative” for the 2° prevention of root caries is the use of a self-applied 4,500–5,000 ppm NaF toothpaste/gel daily.

Our review identified eight agents or combination of agents (six for primary prevention and two for secondary prevention) that were found to be highly effective in prevention of root caries in older adults. However, for the primary prevention studies, the “depth” of evidence is “thin”, since all six of the most effective primary prevention agents or combination of agents were each tested only in a single study.

The supportive evidence was stronger for the secondary preventive agents or combination of agents as each of them was tested in multiple studies, specifically three studies for NaF varnish and five studies for NaF toothpaste. The most plausible explanation of why primary prevention agents or combination of agents are less extensively tested is most likely related to the fact that primary prevention studies—as compared to secondary prevention studies—are more expensive, more time consuming, and require larger sample sizes both in order to compensate for attrition and to find statistically significant differences.

For 1° preventive agents or combination of agents for root caries, clearly there is an immediate and urgent need for clinical trials to replicate the “promising” findings for any and all of 1° prevention agents or combination of agents found to be effective, as all are supported only by a single study. Highest priority should be placed on conducting replication clinical trials on the most effective of the already identified and once-tested 1° prevention agents or combination of agents: silver diamine fluoride, which is professionally applied annually, making it very feasible for use with the elderly in general and with vulnerable elderly in particular. The second priority should be to develop new 1° preventive agents or combination of agents that are either professionally applied at long intervals or that require minimal dexterity and strength so that they have heightened feasibility for use with the vulnerable elderly. For the 2° preventive agents or combination of agents, the most urgent clinical research need is to replicate identified positive findings by conducting studies using more diverse, and larger, subject samples. Also, future studies should be conducted to identify a “universal” agent(s) or combination of agents that will be simultaneously effective as a 1° and 2° preventive agent, i.e., capable at the same time to prevent occurrence of new root caries on previously sound root surfaces as well as arrest progression of already existing root caries lesions.

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Conflicts of Interest

None of the four authors has a Conflict of Interest, either financial or personal.

Author Contributions

The lead author (RG) conducted the highly detailed, multi-stage analyses of research design and findings from the 31 selected articles, constructed the series of charts and tables that culminated in the two final summary Tables in this article, and largely wrote the first draft of the manuscript. The Corresponding Author (RVK) guided and collaborated with RG in the decision-making to create and analyze the series of highly detailed, multi-stage charts and tables, wrote sections of the first draft, and edited several versions of the manuscript. The two librarian co-authors (BJF and RM) planned and conducted the literature search, contributed to the writing of methods section of the manuscript on the literature search strategy, and participated in the editing of the final manuscript.

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