Caries preventive effects of xylitol-based candies and lozenges: a systematic review

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Abstract

Objective: A systematic review of published data was conducted with the aim of assessing the caries preventive effect of consuming xylitol-based candies and lozenges.
Methods: Electronic and hand searches were performed to find clinical trials concerning the consumption of products containing xylitol, published up to November 2009. The studies must have had the following characteristics: a) a comparison of caries progression in subjects who either did or did not consume candies or lozenges containing xylitol during a minimum follow-up period of 1 year; and b) a concurrent comparison of the percentage of caries progression according to the World Health Organization criteria. The caries preventive effect of xylitol was assessed by calculating the prevented fraction.
Results: The initial search identified 127 references. Six studies met the initial eligibility criteria, but three were excluded after thorough analysis. Two more articles were selected after hand searching, but they were excluded due to the presence of chewing gum in the experimental group. Of the three selected studies, two found a lower caries increment in the treatment groups. Although the findings of the analyzed studies suggest that the use of xylitol-based candies and lozenges could favor a reduction in caries increment, in general, their consumption did not seem to be effective on the proximal surfaces. Nevertheless, these findings are not supported by strong evidence.
Conclusion: This research demonstrates the need for well-designed randomized clinical studies with adequate control groups and high compliance by the subjects.

Introduction

Dental caries is a bacterial disease in which diet is a major etiologic factor. Given the dominant role that sugar ingestion plays in the etiology of caries, preventive strategies with the goal of restricting exposure to sugars have been used for generations (1,2). In dentistry, considerable interest has been focused on the search for nonfermentable sugar substitutes, such as xylitol, as a caries preventive measure (3).

The preventive effect of xylitol has not yet been fully explained, but it is probably based on the cycle created in oral bacteria, when the bacteria are forced to reduce the accumulation of intracellular xylitol-5-phosphate by expelling xylitol out of the cell through the cell wall (4).

Xylitol has been recommended by several researchers (5-10) for its positive results in terms of caries preventive effect, demonstrated in various clinical trials using xylitol-containing chewing gum (5-10) and also by a recent systematic review (11). Although these studies have reported a significant decrease in the occurrence of caries associated with the daily use of xylitol-containing chewing gum, some investigators (12-16) have reported that the chewing effect itself increases both saliva stimulation and its buffering capacity, so that it is difficult to separate the effects of xylitol itself from the effects of the saliva stimulation. Thus, a considerable part of the caries preventive effect of xylitol chewing gum has been attributed to the chewing process itself (mechanical effect). Moreover, chewing gum has some unfavorable aspects: In some societies, it is an unacceptable habit, and there are persons who have difficulty with chewing due to dental problems, such as missing teeth (13).

More recently, with a view to eliminating the abovementioned obstacles, researchers have tried to find other ways

of using xylitol to prevent dental decay. Honkala *et al*. (17) suggested that xylitol candies have both strong preventive and clear remineralizing effects on caries. Thus, the aim of this systematic review was to assess the overall caries preventive effect of xylitol candies and lozenges according to explicit and specific selection criteria.

Methods

Sample and study selection criteria

Only controlled clinical trials (CCTs) and randomized controlled clinical trials (RCTs) of at least 1 year's duration and systematic reviews, which tested the efficacy of xylitol candies and lozenges in preventing caries among individuals, were included. To be eligible for this review, the studies must have had the following characteristics: a) the subjects must have consumed candies or lozenges containing xylitol; b) there were no restrictions on study populations; c) the control group included subjects who had not received any kind of intervention or who had received a placebo (e.g., sorbitol), or had received any preventive procedures (such as sealants, supervised tooth brushing with fluoride dentifrices, oral health instructions); and d) the study provided concurrent comparisons of percentages of dental caries increment according to decayed, missing, and filled surfaces (DMFS) scores (World Health Organization criteria) (18). In addition, articles about trials not performed on humans, or if the experimental group was also exposed to products other than candies or lozenges containing xylitol (such as chewing gum and chlorhexidine), were excluded.

Search for studies

In the present search of Ovid MEDLINE (1956 to November 2009) and PubMed (1950 to November 2009), a modified version of the strategy employed by the Cochrane Library was used (Table 1). The Ovid MEDLINE and PubMed search strategy was adapted to search ISI WEB of SCIENCE (1945 to November 2009) and Latin American and Caribbean Health Science (LILACS literature) 1982 to November 2009. The Cochrane Library database (accessed in the first week of November 2009) was searched for clinical trials and systematic reviews of the effect of xylitol on caries progression, according to the search strategy of using the descriptors "xylitol" and "dental caries." Hand searching and Related Articles link searches were performed in the selected manuscripts by analyzing their titles and abstracts.

Validity assessment and data extraction

Two examiners (A.G.A and V.S.S.P.) independently evaluated the titles and the abstracts of all clinical trials identified in both the electronic and hand searches. The full report was obtained for all studies that appeared to meet the inclusion criteria, or when there was insufficient information in the title or abstract to allow a clear decision. All full texts were also read by two reviewers (A.G.A and V.S.S.P.). Uncertainties about inclusion were discussed with a third reviewer (L.C.M.), who had read the respective articles.

Table 1 Search Strategy for Systematic Review of Xylitol in the Prevention of Dental Caries

Step	Search terms
#1	Xylitol$
#2	Sugar alcohol$
#3	Sorbitol$
#4	Polymer$
#5	Ribitol$
#6	Polyol$
#7	Inositol$
#8	Sweetening agent$
#9	Sweetener$
#10	Artificial sweetener$
#11	Sugar substitute$
#12	(#1) or (#2) OR (#3) OR (#4) OR (#5) OR (#6) OR (#7) OR (#8) OR (#9) OR (#10) or (#11)
#13	Dental caries$
#14	(#12) and (#13)
#15	(#1) and (#14)
#16	(#1) and (#14) limits: humans, clinical trial

$ – The dollar sign ($) represents zero or one character. Example – Polymer$ matches polymer and polymers.

Data on the following issues were extracted by the authors, with the goal of characterizing the included studies: a) citation and year of publication; b) location of trial; c) sample size; d) study design; e) baseline and follow-up DMFS scores; f) concentration of xylitol, daily dose, and frequency of exposure to xylitol; g) in case of intervention, the type of sweeteners used in the control group; h) study settings (rural, institutionalized, etc.); i) caries-risk status of study groups and method of estimation; j) methods of caries diagnosis; k) supervision and measures of compliance; l) presence of other caries preventive strategies (such as water fluoridation, diet counseling, and patient education); and m) frequency of reported side effects.

Quality assessment

The methodological quality of the studies was assessed by focusing on the following issues adapted from Chambrone *et al*. (19): a) method of randomization; b) allocation concealment; c) initial assembly of comparable or control group; d) calibration of examiners; and e) blinding.

The method of randomization was considered good when random number tables, tossed coin, or shuffled cards were

used; fair when other methods were used, such as alternative assignment (e.g., date of birth, street address); and undetermined when the method of randomization was not described.

Allocation concealment was classified as good when the examiners or subjects were kept unaware of the randomization sequence; fair when other methods were used, such as alternative assignment; and undetermined when the method was not reported.

Classification of initial assembly of comparable or control groups was considered good when the groups contained randomly assigned subjects; fair when the subjects were assigned on the basis of returned permission slip or when schools, classrooms, or households were used as units of randomization instead of the subjects; and undetermined when the groups were not explained. Blinding as regards the type of intervention used in the study, as well as examiner calibration, was assessed as "yes," "no," or "undetermined."

For a study to be considered adequate, it needed to contain at least two items classified as good and the examiners needed to be blinded and calibrated; whereas unclear studies needed to contain at least one item classified as good and their examiners could be either blinded or calibrated or when the study did not meet the requirement of items classified as good, but the examiners were blinded and calibrated; and inadequate when not a single (one) item was considered good, and there was no blinding, even if the examiners were calibrated, or vice versa, considering the last two criteria. The studies classified as inadequate were excluded from the present systematic review.

Another form was filled out to categorize the risk of bias of each study using the answers "yes," "no," and "undetermined" to the following questions: (on study conduct bias): "Was the sample representative of the entire population?" and "Was the selection of all subjects random?"; (on detection bias): "Were the examiners blinded to assess outcome?" and "Did the study show confounding factors such as the presence of additional caries preventive strategies such as diet counseling and patient education?"; and (on follow-up bias): "Was the frequency of dropouts or exclusion similar between groups?" Each author-reviewer classified the study as A – low risk of bias when the answer was "yes" to all questions; B – moderate risk of bias when the answer was "yes" to at least three questions; C – high risk of bias when the answer was "no" or "undetermined" to two or more questions.

All questions were answered for each selected study, and the evaluation was painstakingly performed by two reviewers (A.G.A and V.S.S.P.), who extracted the data, and these were then cross-checked by a third reviewer (L.C.M.) (20).

Prevented fraction and statistics

The caries preventive effect of xylitol candies and lozenges was expressed by the prevented fraction (PF) (21). The PF is calculated as the difference between the incidence of DMFS in the control group (Ic) and the incidence in the experimental group (Ie), divided by the incidence of DMFS in the control group (Ic) (21-23). PF is therefore defined as

$$PF = (Ic - Ie)/Ic = 1 - Ie/Ic$$

The standard error (SE) of the PF was calculated using the formula,

$$SE(PF) = \sqrt{\left[cv^2(Ie) + cv^2(Ic)\right]} \times Ie/Ic$$

in which cv = coefficient of variation = SD (standard deviation)/PF. The 95 percent confidence interval (95 percent CI) was calculated (23) as

$$PF \pm 2 \times SE$$

The heterogeneity of the studies was evaluated by the Compare 2 statistical test (WinPepi program). *P*-values were obtained by comparing the statistics of the studies using the chi-square test.

Results

Study characteristics

The initial search identified 127 non-duplicate references. Seventy-five studies were identified in PubMed, 14 were provided by ISI WEB of SCIENCE, 12 were identified in the Cochrane Library database, and 26 in LILACS. All studies included in the Ovid MEDLINE were also found in the abovementioned databases, and they were excluded. One additional paper (24) was identified through a Related Articles link. Subsequently, the full texts of six studies (13,15,17,24-26), considered potentially relevant, were evaluated. Of these articles, one (25) did not meet the inclusion criteria and was excluded. Moreover, two systematic reviews (15,26) were also excluded to avoid data repetition once their selected studies have already been included in the present study. Although hand searching allowed two more references to be identified (5,7) at that time, they did not fulfill the inclusion criteria either (Figure 1).

In the selected trials, it was possible to estimate the number of patients at baseline and at the end of the follow-up period (Table 2). Tables 2 and 3 summarize the characteristics of the three selected studies (13,17,24).

Quality assessment of the selected studies

Quality assessment of the included studies (13,17,24) showed that all were categorized as unclear. They presented undetermined (13,17) and fair (24) allocation concealment. The subjects in the control group of the study developed by Honkala *et al*. (17) were assigned on the basis of returned permission

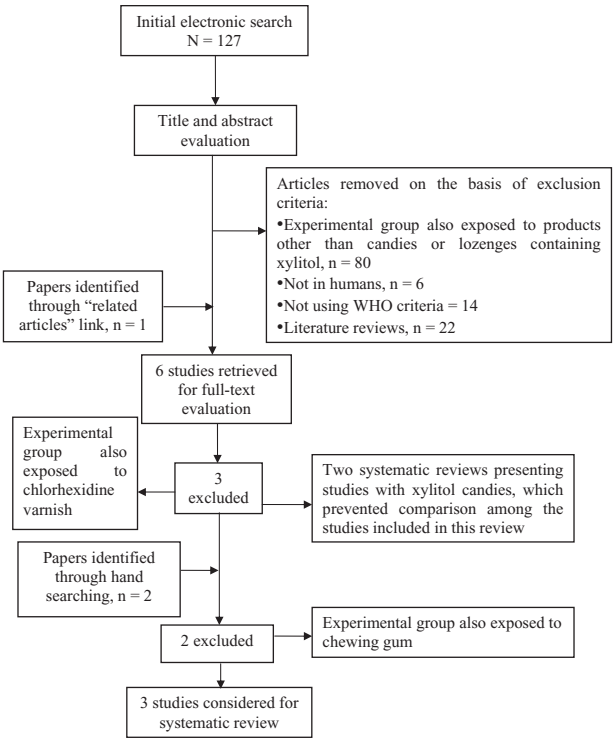

Figure 1 Study selection process for systematic review of the effectiveness of xylitol-based candies and lozenges for managing dental caries.

slips. Whereas the other study developed by Alanen *et al.* (13) showed that although the control and comparable groups were randomly assigned, schools were used as units of randomization instead of the subjects themselves.

The last study (24) (considered as unclear) reported that the control group was formed by those who did not give informed consent to participate in the intervention. Examiner and subject blinding was evident in all selected studies (13,17,24), and so was calibration of the examiners.

Finally, all studies (13,17,24) were considered to have a high risk of bias. Tables 4 and 5 summarize their classification according to quality assessment and risk of bias.

PF

Of three selected studies (13,17,24), two (13,17) found a lower caries increment (PF range 0.37-1.34). On the other hand, Stecksén-Blicks *et al.* (24) found no difference in caries preventive effect between the intervention and control groups (Table 2). The PF and 95 percent CI of the included publications demonstrate their heterogeneity (Table 6).

Data synthesis

In the study developed by Honkala *et al.* (17), a generalized linear model showed that DMFS and DMFT (decayed,

Table 2 Summary of Data Extracted from Selected Studies

Author/year	Country	Study design	Follow-up (years)	Age at baseline (years)		Group intervention/% of xylitol	Baseline sample size (*n*)	Baseline DMFS scores (mean ± SD)	Dropouts (%)	Follow-up DMFS scores (mean ± SD)	Caries increment (mean ± SD)	Statistics
Alanen *et al.* (2000) (13)	Estonia	RCT	3	10	T1	Candies/49% xylitol	125*	2.86 ± 4.03	23.2%	5.36 ± 4.96	2.50 ± 2.34	No statistics
							89†	1.64 ± 2.57	17.9%	3.37 ± 3.41	1.72 ± 2.04	
					T2	Candies/49% xylitol	105*	1.48 ± 2.06	13.3%	3.15 ± 3.80	1.68 ± 2.63	
							93†	1.78 ± 3.08	29.0%	4.50 ± 4.97	2.77 ± 3.05	
					C	–	180	2.18 ± 3.30	18.8%	6.61 ± 6.26	4.42 ± 4.36	
Honkala *et al.* (2006) (17)	Kuwait	CCT	1.5	10-27	T	Candies/49% xylitol	126	8.2 ± 11.1	16.6%	7.1 ± 12.4	–1.2 ± 3.4	Generalized linear model analysis $P < 0.001$
					C	–	50	9.8 ± 9.4	20.0%	13.2 ± 11.3	3.5 ± 4.6	
Stecksén-Blicks *et al.* (2008) (24)	Sweden	RCT	2	10-12	T	Lozenges/42.2% xylitol	56	2.1 ± 1.6‡	28%	4.8 ± 4.9‡	2.7 ± 4.3‡	Analysis of variance NS
					T3	Lozenges/42.2% xylitol + 0.025% sodium fluoride	59	2.9 ± 3.4‡	26%	5.5 ± 5.9‡	2.7 ± 4.4‡	Analysis of variance NS
					C	–	64	2.7 ± 2.3‡	8.6%	4.4 ± 4.6‡	1.7 ± 3.5‡	

* Use of candies stopped after 2 years; † Use of candies stopped after 3 years; ‡ mean values (±SD) of proximal caries.
T, test group; T1, test group with xylitol/maltitol candies; T2, test group with xylitol/polydextrose; T3, test group with xylitol/sodium fluoride; C, control group; NS, not statistically significant.

Table 3 Characteristics of Included Studies

Author/year	Study settings	Daily dose/ frequency of xylitol exposure	Caries-risk status of study groups/ method of estimation	Methods of caries diagnosis	Measures of compliance	Confounding factors	Frequency of reported side effects
Alanen *et al.* (2000) (13)	Community intervention	2 candies in the morning, 3 candies after lunch and 3 candies before the children left school	All levels of caries, but the schools were clustered (as a result the study had 3 control school classes/method not reported)	Clinical exam in dental office	Not mentioned	Participants were given no additional prevention outside routine local measures†‡	4 children had tired of regular use
Honkala *et al.* (2006) (17)	Community intervention	1 Xylitol candy/3 times every school day	High risk of caries/ method not reported	Clinical exam in the classrooms	Monthly discussions with nurses (who distributed the candies)	Health education, supervised toothbrushing†‡ sealant application, and restorative care†‡	Not described in article
Stecksén-Blicks *et al.* (2008) (24)	Not institutionalized	2 tablets/3 times a day	High risk of caries/ computerized risk assessment was based on caries prevalence combined with clinical data on oral hygiene, dietary, and fluoride habits	Clinical exam including bitewings*	Children were classified as having good, fair, or poor compliance according to returned tablets during entire study period	Health education and fluoride varnish application (2 or 3 times/year)†‡	No side effects or adverse events were reported by participating subjects or their parents, among those who completed the study

* Only proximal caries were evaluated; † xylitol group; ‡ control group.

missing and filled teeth) indices in the control group after a 1.5-year intervention differed statistically to a highly significant extent from the xylitol group ($P < 0.001$), whereas Stecksén-Blicks *et al*. (24) found no statistically significant differences between xylitol and lozenge users and control groups ($P > 0.05$), considering the 2-year incidence of proximal enamel lesions and total proximal DMFS scores.

Alanen *et al.* (13) did not carry out any statistical tests between the xylitol groups, but they did report the lowest 3-year increment in caries in all xylitol groups when compared with the control group (Table 2).

Discussion

Xylitol, a five-carbon sugar alcohol, has the ability to decrease the volume and acidity of plaque (27). At present, there are over 300 dental and oral biologic studies dealing with xylitol. Most of them have presented favorable caries preventive results – reduction in plaque volume and *Streptococcus mutans* counts – mainly associated with the use of xylitol chewing gum (5-10). Clinical trials with the aim of measuring the caries preventive effect of polyol-sweetened gums have used a control group, in which a gum without any polyols is tested. Nevertheless, it has been shown that such a control gum is as effective as a xylitol-sweetened gum, indicating that the caries preventive effect of chewing sugar-free gums could be related to the chewing process itself, rather than being an effect of the polyols (14). Therefore, the development of studies (13,17,24) with the goal of evaluating the effect of xylitol used in products other than gum is highly justified.

In the present research, among all the evaluated studies (Figure 1), one (25) did not meet the inclusion criteria and was excluded because the experimental group was also exposed to chlorhexidine varnish. Another two studies (15,26) were excluded because, although both were systematic reviews about the effect of xylitol and dietary changes on the prevention of dental caries (including studies with xylitol candies or lozenges), their data have nevertheless been included in the present work.

The present review included RCTs and a CCT that evaluated experimental groups exposed to candies or lozenges containing xylitol that also benefited from other preventive strategies for ethical reasons. Therefore, this systematic review ended up analyzing only three studies. In two of them (17,24), the groups were offered sealant application and restorative care. Although the main aim of controlled trials is to find out how effective the intervention applied in the studied disease would be when compared with a control group that would not receive any kind of intervention, it is considered unethical not to offer the control groups any treatment, particularly when treatments for the disease are available. Thus, all the results presented herein take into account the presence of possible confounding factors.

Table 4 Classification of Selected Studies according to Quality Assessment

Author/year	Method of randomization	Allocation concealment	Initial assembly of groups	Blinding	Calibration of examiners	Classification
Alanen *et al*. (2000) (13)	Undetermined	Undetermined	Fair	Yes	Yes	Unclear
Honkala *et al*. (2006) (17)	Undetermined	Undetermined	Undetermined	Yes	Yes	Unclear
Stecksén-Blicks *et al*. (2008) (24)	Fair	Fair	Fair	Yes	Yes	Unclear

All the selected studies (13,17,24) were classified as unclear, according to our quality criteria, mainly because they did not present randomly assigned subjects, showing a high risk of bias. Moreover, the lack of homogeneity of the selected studies (Table 6) demonstrated that there were genuine differences underlying the results. However, since systematic reviews bring together studies that are diverse both clinically and methodologically, heterogeneity of results is to be expected (28).

In the two researches classified as presenting a high risk of bias (13,17), a reduction in caries indices in the xylitol groups compared with a control group was clearly recognized (Table 2), even when sealants were offered to the control group (18). However, regarding the results of caries increment after a 3-year follow-up period reported by Alanen *et al.* (13), further questions should be answered about the optimal timing and length of xylitol use. According to the article, the consumption of xylitol candy for 3 years did not improve the results of caries increment compared with a 2-year period of consumption (Table 2). The authors added that this occurred because of the slow progression of dental decay (13). Nevertheless, these same authors reported the lowest 3-year increment of caries in all xylitol groups compared with the control group.

It is also important to stress that the study of Honkala *et al.* (17) was conducted in physically disabled subjects with a very wide age range (10-27 years), who were practically unable to perform normal oral hygiene.

In the third study (24) selected for this systematic review, the results showed no statistically significant differences between the xylitol lozenges and control groups ($P > 0.05$), considering the 2-year incidence of the total proximal DMFS scores, even when sodium fluoride was added to the contents

Table 5 Classification of Selected Studies according to Risk of Bias

Author/year	Was sample representative of entire population?	Was selection of all subjects random?	Were examiners blinded to assess outcome?	Did study show confounding factors?	Was frequency of dropouts similar between groups?	Classification
Alanen *et al*. (2000) (13)	Yes	No	Undetermined	No	Yes	High risk of bias
Honkala *et al*. (2006) (17)	Undetermined	No	Undetermined	Yes	Yes	High risk of bias
Stecksén-Blicks *et al*. (2008) (24)	Yes	No	Yes	Yes	No	High risk of bias

Table 6 Summary of Prevented Fraction including 95% Confidence Intervals (CI) according to Caries Increment of Experimental Groups, and Heterogeneity Test

Author/year	Experimental groups	Caries increment (mean ± SD)	Quantified prevented fraction	95% CI	Heterogeneity test
Alanen *et al*. (2000) (13)	A1	2.50 ± 2.34	0.43	0.43; 0.44	$P < 0.001$
	A2	1.72 ± 2.04	0.61	0.60; 0.61	
	A3	1.68 ± 2.63	0.62	0.61; 0.62	
	A4	2.77 ± 3.05	0.37	0.37; 0.38	
Honkala *et al*. (2006) (17)	H	–1.2 ± 3.4	1.34	1.34; 1.35	
Stecksén-Blicks *et al*. (2008) (24)	SB1	2.7 ± 4.4	–0.59	–0.59; –0.58	
	SB2	2.7 ± 4.3	–0.59	–0.59; –0.58	

P-values are obtained by comparing the statistics of the studies using chi square test.
A1, Alanen *et al*. (13) – test group with xylitol/maltitol candies (treatment stopped after 2 years); A2, Alanen *et al*. (13) – test group with xylitol/maltitol candies (treatment stopped after 3 years); A3, Alanen *et al*. (13) – test group with xylitol/polydextrose candies (treatment stopped after 2 years); A4, Alanen *et al*. (13) – test group with xylitol/polydextrose candies (treatment stopped after 3 years); H, Honkala *et al*. (17) – test group with xylitol; SB1, Steckesén-Blicks *et al*. (2008) – test group with xylitol/sodium fluoride; SB2, Steckesén-Blicks *et al*. (24) – test group with xylitol.

of the xylitol lozenges. In this study, the level of compliance, which was evaluated according to an explicit and specific criterion by the authors, was crossed with the caries increment results. By means of this analysis, the children with poor compliance, who could be looked upon as an almost nontreated reference group (24), showed, on average, more new lesions than those with better compliance. However, this difference was not statistically significant. It is important to note that, in this study, the percentage of children with high compliance was very low, which could also have influenced the results. Moreover, this study (24) included only poorly motivated subjects assessed as being at high risk of caries, which probably explains the above-mentioned low compliance.

Moreover, the authors of the Stecksén-Blicks study (24) evaluated only the caries preventive effect of xylitol on proximal surfaces, their results indicating that xylitol might not be effective in caries prevention on those surfaces. This could also be due to the difficulty of xylitol's gaining access to the dental plaque on proximal surfaces. According to Thylstrup and Fejerskov (29), the effect of preventive procedures, such as cleansing solutions, fluoride, and toothbrushing, is more evident on smooth surfaces than on proximal surfaces, where access to the dental plaque is more difficult. Since xylitol has the ability to decrease the volume and acidity of plaque (24), the results found by Stecksén-Blicks *et al*. (24) are easily explained. Vanderas and Skamnakis (30), in a systematic review, suggested that further researches are needed to evaluate the effectiveness of various preventive measures on proximal caries progression.

Another explanation for the mentioned outcomes (24) was found in the daily dose of xylitol. Studies (31,32) have demonstrated that more beneficial results are achieved with daily doses of around 6 g. Stecksén-Blicks *et al*. (24) proposed a daily dose of 2.5 g xylitol; however, some researchers (13,33) found significantly favorable results after a daily intake of less than 6 g.

Considering the different outcomes presented by the three selected studies, another important topic to be discussed is the discrepancy between caries-risk status and baseline caries profile for subjects included in those studies. This discrepancy occurred mainly between Honkala *et al*. (17) and the other selected studies (13,24), as shown by their baseline DMFS scores. Therefore, this factor should be considered as a further contributor to the heterogeneity among the selected studies (13,17,24), previously discussed.

Making an allowance for this systematic review, gray literature was not consulted during the authors' search, and therefore, the possibility of publication bias in the present study is worth mentioning, particularly because, often, only significant studies are published. On the other hand, a positive aspect is that the authors do not have any commercial or associated interest that represents a conflict of interest in connection with this review.

In the present study, the caries preventive effect of xylitol candies and lozenges was expressed by the PF (21,34). In contrast to absolute reductions, the PF is assumed to be less sensitive to experimental circumstances, such as the age range of the study population and duration of the study (21). However, PF values have already been used in other systematic reviews to show that the number of cases of disease could be lowered by protective exposure or intervention, as demonstrated by Lötters and Burdof (21), who evaluated whether primary interventions, such as educational programs (exposure factor), reduced the musculoskeletal symptoms (disease). In the present systematic review, despite the results found by Stecksén-Blicks *et al.* (24), which demonstrated unfavorable results (PF = −0.59), the other two studies found lower caries increment in the experimental groups when compared with the controls (PF range, 0.37-1.34).

The findings of the analyzed studies suggest that although the use of xylitol-based candies and lozenges could reduce caries incidence in a wide segment of the population, their use did not seem to be effective on proximal surfaces. However, the current data should be interpreted with caution because they are based on results retrieved from only three studies, all of which were classified as "unclear." Moreover, the present study did not show homogeneity of the selected studies. To reduce bias and improve the quality of the evidence, CONSORT guidelines (http://www.consort-statement.org) should be incorporated in future clinical trials.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Studies excluded and main reason for rejection (in chronological order).

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