

# Meta-analysis on the Effectiveness of Xylitol in Caries Prevention

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**ABSTRACT** **Background:** Oral xylitol products have been labeled as a caries preventive measure; however, their use is still limited. This study aims to summarize the evidence on the effectiveness of xylitol-containing products in dental caries prevention with a focus on dental caries as the primary outcome rather than other pseudo outcomes. **Materials and Methods:** A structured literature search was conducted to identify the studies related to the efficiency of products containing xylitol for the prevention of caries. The literature search was conducted through the following databases: Medline, PubMed (Central), SCOPUS, Web of Science (WoS), Open Grey, and the Cochrane Library and included papers published between 1966 and March 2020. Fixed- and random-effect models were used to obtain pooled estimates through meta-analysis. **Results:** Evidence-based results of this study showed that xylitol is easily available in the form of various products, but clinically tested products are few in markets. The literature review has also concluded that the most effective xylitol product in caries prevention was (100%) xylitol, chewed or consumed three to five times per day, after meals with a total dose of 5–10 g of xylitol per day. Products included xylitol-containing lozenges, candies, and chewing gum, foods based on xylitol, and xylitol-containing toothpaste and mouth rinse. Results showed that xylitol-containing products significantly prevented caries compared with the other (control) non-xylitol products. Pooled estimates using the combined fixed and random effects of standardized mean difference were -0.099 [95% confidence interval (CI): -0.149, -0.049] and -0.089 (95% CI: -2.04, 0.026), respectively. **Conclusion:** This review concluded that xylitol should be part of an overall strategy to decrease and prevent dental caries. Dosage and frequency should be considered strictly when prescribing xylitol as a caries preventive measure.

**KEYWORDS:** Children, dental caries, meta-analysis, prevention, xylitol

## INTRODUCTION

Dental caries is considered to be one of the most widespread chronic diseases. It is five times more common than asthma and their prevalence increases with age.<sup>[1]</sup> Fortunately, dental caries is preventable and several products have been tested and recommended is caries prevention such as fluorides and sealants.<sup>[2]</sup> However, researchers and dental professionals continue to look and investigate for other caries preventive measures such as xylitol.

Xylitol, a naturally occurring substance, was first introduced in Finland during World War II as a sugar substitute. In 1963, the FDA approved the use of xylitol as a nutritional additive. Studies have reported that the consumption of xylitol (5–10 g/day) decreases caries incidence ranging between 30% and 80%.<sup>[3-5]</sup> A recent study that reviewed articles on the role of sugar-free

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chewing gum (SFG) in dental caries also concluded that SFG decreases caries increment in comparison to controls (non-sugar).<sup>[6]</sup> It also reverses carious lesions in children of different ages and children with special healthcare needs.<sup>[7]</sup> One study showed that the timing of xylitol exposure is critical, with researchers concluding that habitual xylitol consumption should start at least 1 year before permanent tooth eruption at 5 years of age.<sup>[4]</sup> For baby teeth, the role of mothers in caries prevention is very important; the use of xylitol by mothers 3 months after giving birth has significantly reduced the transmission of *Streptococcus mutans* to their children. Children in this study were followed up from 0 to 5 years of age, and the caries reduction rate was 70% in comparison to the control groups in which mothers received either topical fluoride or chlorohexidine treatments.<sup>[5]</sup> Furthermore, xylitol has prolonged the suppression of cavity *S. mutans* when combined with commercially available chlorohexidine treatment, suggesting the effective use of xylitol, along with other caries preventive measures, for long-term caries prevention.<sup>[8]</sup>

Although anti- and non-cariogenic properties of xylitol cannot be fully explained, the mechanism of action includes a reduction in *S. mutans* count and reduction of lactic acid production by the bacteria. The short-term consumption of xylitol was found to reduce *S. mutans* levels in both plaque and saliva, with no overall impact on the normal oral flora.<sup>[2,9]</sup>

The safety of xylitol has also been studied extensively. While most studies reported few side effects, these occurred following high ingestion of xylitol, four to five times the recommended dose, reaching 50 g per day, which included stomach disturbance and diarrhea.<sup>[10]</sup> With the appropriate dose and frequency, xylitol was considered completely safe for everyone at a recommended dose of 6 g/day.<sup>[11]</sup>

Multiple oral xylitol products, other than chewing gum, have been circulating in the market including candies, mints, toothpastes, mouth rinses, food ingredients, and gels. This paper summarizes the evidence on the effectiveness of xylitol-containing products in dental caries prevention with a focus on dental caries as the primary outcome rather than other pseudo outcomes.

## MATERIALS AND METHODS

### SELECTION CRITERIA

A thorough literature review was performed after conducting an electronic search through Medline, PubMed (Central), Scopus, Web of Science (WoB), Open Grey, and the Cochrane Library (from 1966

to March 2020) to identify studies relevant to the effectiveness of xylitol products in caries prevention. The following keywords were used: “xylitol AND dental caries,” “xylitol AND caries prevention,” and “Xylitol and DMFS.” The search was limited to studies published in the English language and studies performed on humans. Additionally, we reviewed references cited in the retrieved articles, dissertations, reports, and poster presentations in different conferences. A meta-analysis was performed using the identified literature studies with at least 1-year follow-up that reported mean DMFT/DMFS/dfs, SD, and 95% confidence intervals (CIs) as a measure of effectiveness of different xylitol-containing products. The type of studies included were randomized clinical trials (RCTs) and case-control trials (CCT).

### DATA EXTRACTION

Data extraction involved two independent observers who reviewed and categorized the studies according to meta-analysis inclusion criteria. Data extraction was done independently and included the name of the author, publication year, study design, population characteristics, type of xylitol products and total dose/day, years of follow-up, and the outcome measures (mean DMFS, SD, or 95% CIs). Differences between the two observers were resolved by consensus.

Cochrane tool for assessing the risk of bias was used. Both authors (JA and MB) assessed all studies that fulfilled inclusion criteria separately across six fields: detection, performance, selection, attrition, reporting, and other bias. If any disagreement happened, it was resolved through discussion or the input from an optional external reviewer.

### CRITICAL EVALUATION

Critical appraisal of articles was also done by the two observers. The Jaded scale was used to assess the quality of clinical trials.<sup>[12]</sup> Observational studies, on the contrary, were assessed using the U.S. Preventive Health Services Task Force Criteria (good, fair, and poor) scale.<sup>[13]</sup>

### STATISTICAL ANALYSIS

Meta-analysis was performed using Comprehensive Meta-Analysis Software Version 3 with mixed models to get both the fixed- and random-effects estimates in addition to their 95% CIs. The individual and overall prevented fractions of meta-analysis were calculated. Statistical heterogeneity of between-study variability was assessed using  $Q$  statistics and  $I^2$ . We assessed publication bias in three ways. We used the funnel plot as a graphical method to assess the distribution of the

studies, and we used two statistical methods to look for publication bias: the Egger regression test and Kendal correlation. Finally, a Forest plot of all the studies with the final estimates was generated [Figure 1].

## RESULTS

### Search results

We identified 358 studies that measured or reported the effectiveness of xylitol in dental caries prevention. After an initial screening of the articles, 70 studies were not related to xylitol and 116 reviews and reports were excluded. We reviewed the abstracts of the remaining 142 studies, and only 30 met our meta-analysis inclusion criteria [Figure 2]. Figure 1 summarizes the characteristics of all 30 studies included in the meta-analysis procedure.

### CLINICALLY TESTED XYLITOL PRODUCTS

The result of the evidence-based review shows that although there are various forms of xylitol products available in the market, online or supplied through dental offices, the clinically tested products were few. The number of human studies on different xylitol products included 12 studies on xylitol chewing gums (XyliFresh-Leaf B.V., Turku, Finland)/commercially available xylitol pellet gum (Fennobon Oy, Karkkila, Finland) and xylitol stick gum (Koolerz, Hershey Foods, PA, USA), 6 studies on lozenges (Xerodent<sup>®</sup>, Actavis Group, Iceland), 5 studies on candies (XylitolPlus Leaf B.V.), 1 study on xylitol-based foods (Cultor Food Science in Ardsley, NY, USA), 2 studies on gummy bears (Santa Cruz Nutritionals, CA, USA),

5 on different oral hygiene products, and 1 study on the Fall-Asleep Pacifier (FAP) using xylitol tablets.

The review of the literature has also concluded that the most effective xylitol product in caries prevention was the xylitol (100%), chewed or consumed three to five times per day, after meals with a total dose of 5–10 g/day. Frequencies less than three times a day (less than 3.44g/day) did not show any caries preventive benefit. Doses up to 15.6 g/day were like 11.7 g/day in caries prevention.

### XYLITOL VS. SUGAR ALCOHOLS

While comparing xylitol with other sugar alcohols, the risk of developing caries in the xylitol group was lower than sorbitol and mannitol or even when xylitol was mixed with other sugar alcohols. This can be explained because of the different chemical natures of sugar alcohols. Sorbitol is a hexanol type of polyol and cariogenic bacteria prefer the six-carbon structure as an energy source.

### XYLITOL PRODUCTS COMPARED

In a 3-year randomized clinical trial, children 10–12 years of age were randomized into three groups consuming either candies or chewing gum or a control group with no xylitol product. Both xylitol candies and chewing gum showed a significant reduction in caries from 35% to 60%. The results of this study suggested that xylitol candies were equally effective as xylitol chewing gum in caries prevention. It also recommended that the most effective way to distribute and promote

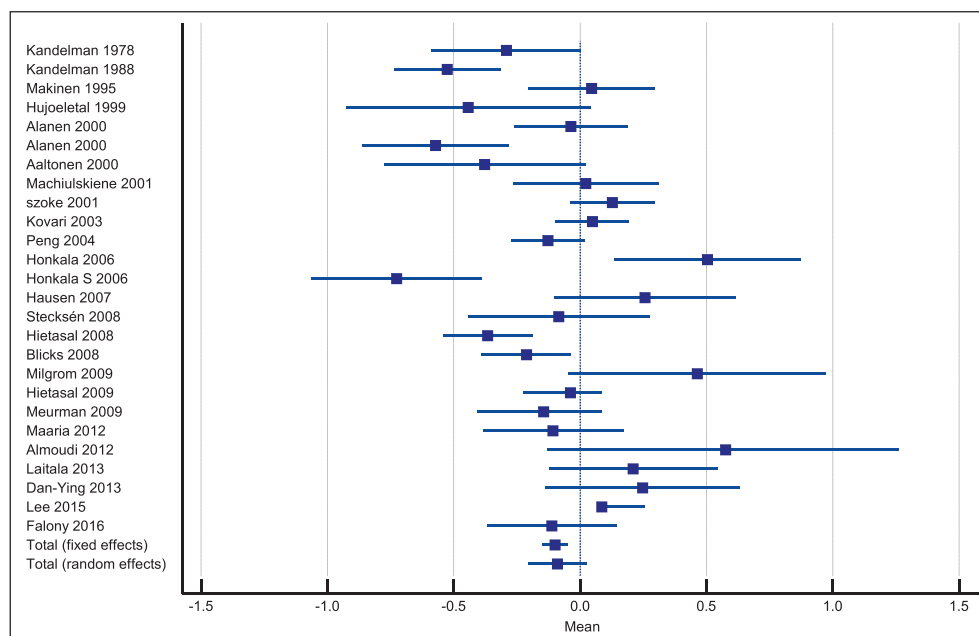
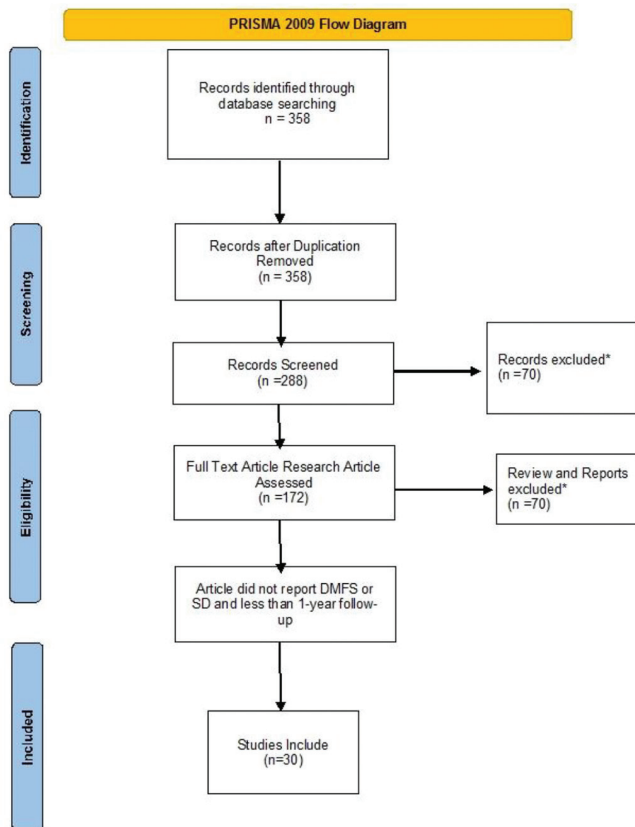
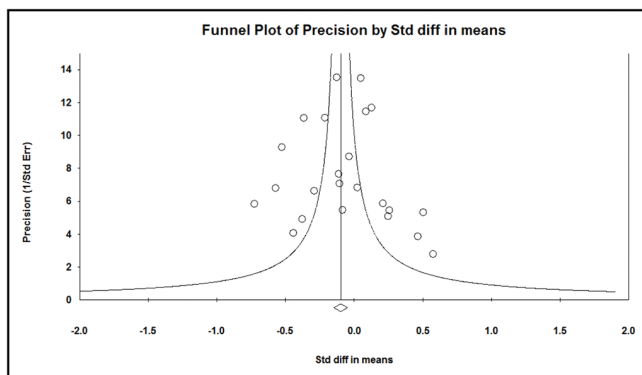


Figure 1: Forest plot of xylitol studies included in the meta-analysis



**Figure 2:** Number of studies retrieved following our search criteria



**Figure 3:** Funnel plot of xylitol studies included in meta-analysis and the pooled results

the use of xylitol was through a school-based delivery system. No other comparisons between xylitol products were identified.

#### **XYLITOL VS. PREVENTIVE MEASURES**

Alanen *et al.* compared the effectiveness of xylitol chewing gum to occlusal sealants in schoolchildren. After 5 years of follow-up, xylitol chewing gum was found to be equally effective to sealants with no statistical difference in caries reduction between the two groups. In a 2-year randomized clinical trial, the use of xylitol lozenges in schoolchildren aged 10–12 was compared

with fluoride varnish for the prevention of approximal caries. The results also showed no differences in caries reduction between the two interventions. The results of these two studies suggest the equal effectiveness of xylitol to sealants and fluoride varnish in caries prevention.

#### **META-ANALYSIS RESULTS**

A total of 30 studies met our inclusion criteria—at least 1-year follow-up studies that reported the mean DMFS, SD, and 95% CIs—and were included in the meta-analysis. Study designs included 19 clinical trials,<sup>[9,14-30]</sup> 7 case-control trials,<sup>[7,31-34]</sup> and 4 cohorts.<sup>[3,4,32,35]</sup> Most of the studies that were included in the meta-analysis were recent studies: 23 were published between the years of 2000 and 2019,<sup>[7,14,17-30,34]</sup> 2 studies in the 1990s,<sup>[3,4]</sup> 2 studies in the 1980s,<sup>[10,32]</sup> and 3 studies in the 1970s.<sup>[11,31,36]</sup> Xylitol products that were tested in the studies included 19 studies on chewing gum, 6 studies on candies, 4 on lozenges, and only 1 study on the Fall-Asleep Pacifier using xylitol tablets. The follow-up years ranged between 1 and 5 years. Additionally, there was a wide range of study populations, 10 studies originated from Finland,<sup>[3,4,14,16,25,27,30-32,37]</sup> 2 studies in Estonia,<sup>[19,20]</sup> 3 studies in Kuwait,<sup>[7,34]</sup> 2 studies in China,<sup>[23,33]</sup> 2 studies in Denmark,<sup>[22,28]</sup> 3 studies in USA,<sup>[21,29,32]</sup> and 1 study each in Canada,<sup>[36]</sup> Hungary,<sup>[15]</sup> Sweden,<sup>[9]</sup> India, Lithuania,<sup>[18]</sup> and Norway.<sup>[24]</sup> The Jaded scale for the clinical trials ranged between 1 and 5. All the studies except for one had a score of 1.5 or higher which indicates an overall good quality of clinical trials. The observational studies, in contrast, had an overall fair quality.

When we assessed heterogeneity, we found that the  $I^2$  statistic score was 95.8%, suggesting a high degree of variability between studies. Looking at the  $Q$  statistics, this high level of heterogeneity was related to 4 of the 30 included studies, which highly contributed to this heterogeneity. We decided to remove those, which reduced the  $I^2$  significantly to 79%, a heterogeneity score suggesting a moderate level of study variability. An Egger test and a Kendal correlation (Tau,  $-0.114$ ) showed that no publication bias was found in the studies selected, with a  $P$ -value of 0.675 and 0.404, respectively. This confirms the results from the funnel plot in Figure 3, which showed a normal distribution of studies included in the meta-analysis.

Meta-analysis results showed that xylitol products had significantly prevented and reduced the DMFS score using the combined fixed effect with a standardized mean difference of  $-0.099$  and 95% CI ( $-0.149, -0.049$ ) and the combined random effect with a standardized

mean difference of  $-0.089$  and 95% CI ( $-2.04, 0.026$ ). This suggests that caries risk in the xylitol group was less than the caries risk in the control group and the difference was statistically significant. The prevented fraction of the studies ranged between 5% and 75% with an overall preventive fraction of 17%.

## DISCUSSION

The evidenced-based systematic review and meta-analysis results provide good evidence for the effectiveness of different xylitol products in dental caries prevention. The pooled result of the meta-analysis has favored the preventive effect of xylitol in comparison to the control with an overall preventive fraction of 17%.

Deshpande and Jaded have also supported the preventive effect of sugar alcohol in dental caries prevention with an overall preventive fraction of 58% with the use of xylitol chewing gum. Our results showed a lower preventive fraction in comparison to this study. This could be explained by the fact that chewing gum increases the effectiveness of xylitol by two-folds due to salivary secretion.<sup>[21]</sup> In our meta-analysis, there was a wide range of products including lozenges, candies, FAP, and confectionary in which salivary stimulation might not be an additive factor.

The consistency of the findings also supports the low prevented fraction of xylitol with only 10 of the 31 studies showing statistical significance [see Figure 3]. The xylitol forms that showed a statistical significance included confectionary, lozenges, candies, and 2 studies on chewing gum.

As the bacterial count is considered a poor predictor for dental caries measurement, we chose our primary outcome measure of mean DMFS.<sup>[7,26,27]</sup> This has affected the total number of studies that were included in the meta-analysis. In contrast, a recent review found out xylitol has less effect on reducing dental caries and there is very low evidence that xylitol had preventive property.<sup>[38]</sup>

Other limitations include a limited number of studies on different xylitol products in which we had to consider a wide study population of toddlers, children, and adults. Moreover, xylitol has never been studied as a standalone product and can never be tested because it is not possible to eliminate normal preventive measures. For this reason, xylitol should always be recommended alongside fluorides, chlorhexidines, and sealants.

## CONCLUSION

We conclude that xylitol should be part of an overall strategy to decrease and prevent dental caries. Practitioners should consider product, dose, and

frequency when prescribing xylitol as a caries preventive measure. Frequencies less than three times a day (less than 3.44 g/day) did not show any caries preventive benefit. In an era of evidence-based dentistry, efforts are still needed to test the effectiveness of different xylitol products in caries prevention such as candies, gummy bears, and oral syrup.

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Nil.

## CONFLICTS OF INTEREST

There are no conflicts of interest.

## AUTHORS CONTRIBUTIONS

Jehan ALHumaid: Conceptualization, methodology, software, writing—original draft preparation, final draft review. Mohamed Bamashmous: Methodology, software, writing—original draft preparation, supervision, writing—reviewing and editing.

## ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

As this research is a systematic review, ethical approval was not applied.

## PATIENT DECLARATION OF CONSENT

Patients were not involved in this research, all data was gathered from previously published studies.

## DATA AVAILABILITY STATEMENT

AlHumaid, Jehan (2021): Meta-analysis on the Effectiveness of Xylitol in Caries Prevention. figshare. Dataset. <https://doi.org/10.6084/m9.figshare.18517490.v1>.

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