Timing of first restorations before, during, and after a preventive xylitol trial

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An independent longitudinal retrospective analysis of the timing, number, and cost of tooth restorations was conducted for all subjects ($n = 313$) in the age cohort of a municipal health center, in which two consecutive field trials of up to 3 years on the caries-preventive effect of the use of xylitol chewing gum were conducted (Ylivieska study, 1982–85). A computer program calculated the post-eruptive timing of the first restorations on each permanent tooth surface, and survival analysis methods were applied before, during, and after the trials. The cost of restorations was then calculated. The total number of new restored surfaces was 4.0 per child in the xylitol group and 9.3 in the controls during the decade after onset of the trial. The number of restorations on the occlusal surfaces of the first molars leveled off at 40–50% in the xylitol group and at about 60–70% in the control group. Plateaus for the second molars were at 30–40% and 60–70%, respectively. The time lag for the first restorations was longer in the xylitol group for the proximal and other smooth surfaces. A marked difference in favor of the xylitol group was observed in the proximal surfaces of the upper incisors (for example, the mesial surface of the upper mesial incisor for girls: log-rank chi-square = 11.1, $p < 0.001$). The preventive effect was most pronounced in teeth that had erupted during the trial. This analysis indicated that participation of subjects in the xylitol chewing gum trials resulted in a significant reduction in the number of first restorations and hence in costs during the decade after the onset of gum use. □ *Caries prevention; dental restoration; oral health economics; xylitol*

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The use of xylitol as a caries-preventive measure is based on the knowledge that xylitol is not effectively metabolized by oral microbes to form acids capable of causing demineralization and that its use has been associated with remineralization of enamel caries (1–4). Two consecutive, longitudinal field trials of up to 3 years on the caries-preventive effect of the use of xylitol chewing gum (Ylivieska study) resulted in a significant caries reduction in terms of DMFS values (5, 6). The long-term caries-preventive effects of xylitol gum use were also measured 5 years after termination of the preventive program (7). Results in favor of the xylitol group continued to increase after the program.

Recently, application of Poisson regression models was observed to offer advantages over DMF-based ANOVA analysis of treatment efficacy in the above xylitol trials (8). This reanalysis of xylitol efficacy confirmed the previous findings. Incorporation of xylitol gum into a caries-preventive program resulted in a significant caries reduction. During exploratory analyses two potential xylitol effect modifiers were identified: a period effect and a post-eruptive age effect (8).

To estimate the caries rate, it is important to know the number of tooth surfaces at risk and the time at risk. Without estimation of the time at risk, one cannot calculate disease rate. In the Poisson model the caries rate is estimated for the whole mouth as a function of covariates (such as age and gender) of the patient (8). This requires numerous assumptions of individual variables, such as the distribution of caries increment.

The life-table methods, which take into account the post-eruptive age, have been found to be particularly appropriate for measuring the real time at risk for each individual tooth and calculating the true caries risk (9, 10). Today survival analysis methods have developed, and the life-table methods can be replaced with accurate methods for measuring the prevalence of many diseases. When the survival method is applied individually to each tooth, starting from the time of tooth emergence, the post-eruptive age is known, and no assumptions are needed.

Here a survival analysis method for the post-eruptive timing of all first restorations due to dental caries on each tooth surface before, during, and after the Ylivieska chewing gum trials was applied. Tooth emergence was first determined and considered the zero-point of the analysis separately for each tooth. The irreversible stage of caries attack which requires restoration was then determined as the end-point of the 'survival' of the tooth. Standard patient records of all subjects who attended the Ylivieska xylitol trials and of all other subjects of the same age cohort who were also regularly seen at the public Health Center of Ylivieska were analyzed. The number and cost of the restorations and chewing gum pellets were also calculated.

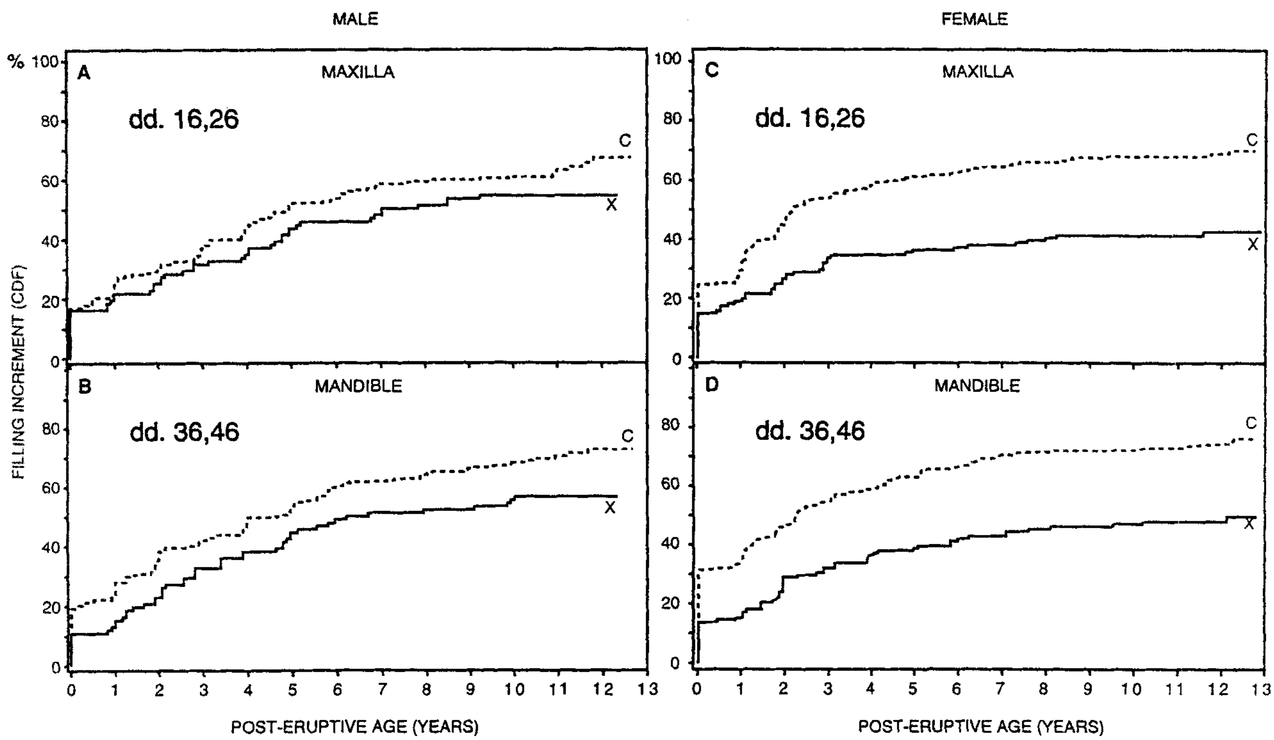

Fig. 1. Annual filling placement rate calculated post-eruptively for occlusal surfaces of first permanent molars in the X group and the C group.

Materials and methods

We reanalyzed the patient records (not the records of the trials) of all subjects born in 1970–71 who were examined and treated at the Ylivieska Health Center. Finnish public dental care provides dental treatment free of charge to all subjects under the age of 19 years. The subjects (n = 313) were the whole age cohort of the Ylivieska health center born in 1970–71, which included the subjects participating in the two xylitol chewing gum trials (5, 6). After registration, subjects who received xylitol chewing gum (3 times per day) for 2 or 3 years in the 1982–85 trials (5, 6) were classified as xylitol (X) subjects (n = 109). All others of the same age cohort formed the control (C) group (n = 204). Owing to the long follow-up time, not all participants in the trials (original study groups: X group, n = 172; C group, n = 152) could be reached.

The time of eruption of each individual tooth (11) and the placement of restorations because of caries (restorations due to, for example, crown fractures were excluded) on each tooth surface up to 18 years of age were recorded annually and analyzed retrospectively. The time lapse between eruption and placement of the first restoration on each tooth surface was determined with a longitudinal system (12, 13).

Number and cost of fillings and chewing gum

All restorations made on the different tooth surfaces at the onset of the trial (1 November 1982) and at the end of the follow-up period (1991) were counted. For the cost analysis the following estimates were used, on the basis of the fees of Finnish private practitioner dentists. A restoration on one surface of a molar or premolar was estimated to cost roughly 150 FIM. An additional restoration on the same tooth was estimated at 50 FIM per surface. The restorations on proximal surfaces of the incisors or canines were considered to cost 200 FIM each. From the information provided by the original trials (5) the reported mean chewing gum consumption was calculated at 2062 pieces per subject during the trials. The retail price in Finland is about 0.3 FIM each.

Treatment of data and statistical analysis

The age of each subject was entered into the computer with an accuracy of 1 day, and the date of examination with an accuracy of 1 month. For the analysis the timing of the examination, the timing of dental eruption, and the timing of the placement of the first restoration on each tooth surface due to caries were

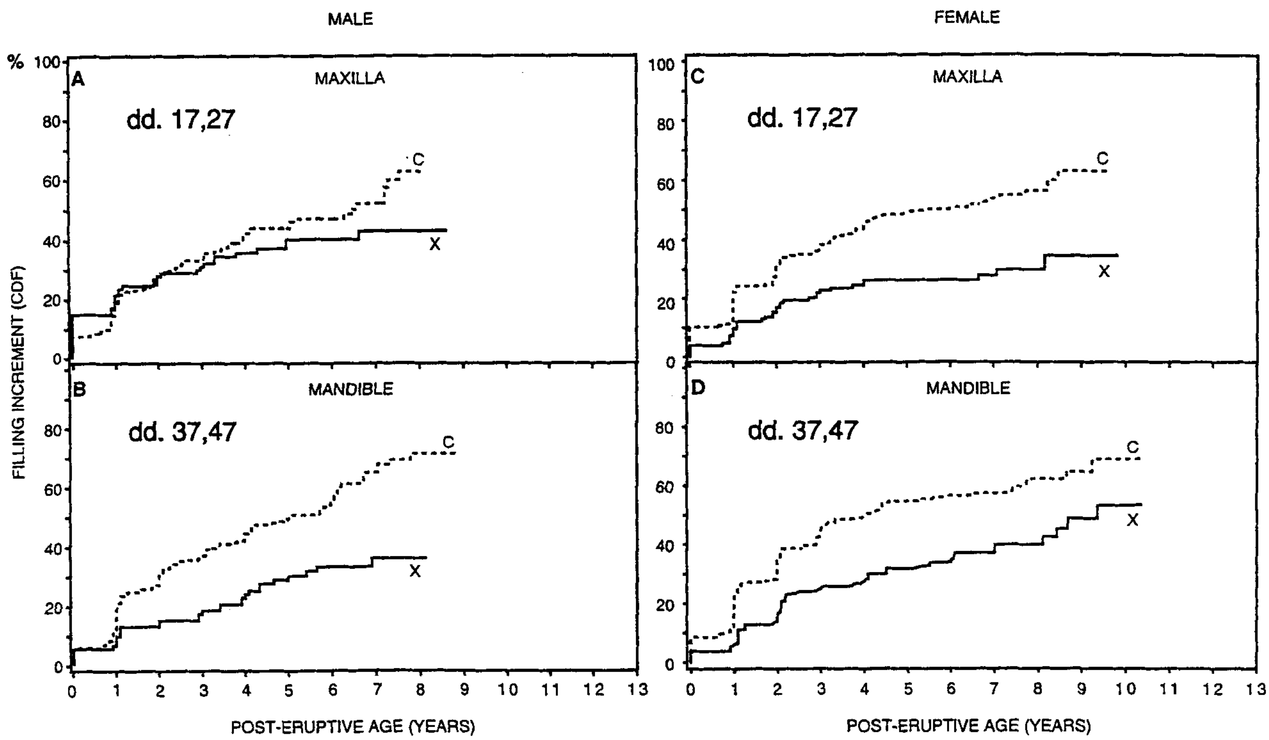

Fig. 2. Annual filling placement rate calculated post-eruptively for occlusal surfaces of second permanent molars in the X group and the C group.

recorded. A computer program was designed to process all the material electronically. The SAS statistical software program (14) and the CIA program (15) were used for the statistical analyses. Confidence intervals (CI) were used when comparing differences at a specific time.

The main task in this study was to determine the time needed for an event to occur. When analyzing time (for example, the time between tooth eruption and the placement of the first filling), possibly with censoring (no event is recorded or a patient may drop out), it is useful to apply the methods of survival analysis. From a practical point of view the cumulative distribution function (CDF) was estimated for each tooth and tooth surface, using the product-limit method, also called the Kaplan–Meier method (16). The CDF curves were compared by means of the log-rank test and the Wilcoxon test. To avoid pseudoreplication of the *n* value, only the teeth on the right side of each individual mouth were chosen for the statistical tests.

Results

The filling increment curves (expressed as CDF curves) for the homologous teeth on the right and left sides of the mouth were found to be similar and were combined in the figures. In fissures and pits of all molar teeth, first restorations were done in the year of tooth eruption, causing a vertical 'post-eruptive step' on the curve (Figs. 1 and 2). Thereafter, a steadily increasing filling increment was observed until the curves for the first molars plateaued after 4 to 7 post-eruptive years at about 40–50% in the X group and at about 60–70% in the C group (Fig. 1). Plateaus for the second molars were at 30–40% in the X group and at 60–70% in the C group (Fig. 2).

The height of the post-eruptive step for the occlusal surfaces of the first permanent molars was about 10–15% in the X group and about 20–30% in the C group (roughly 4–6 years before the trials) (Fig. 1). Girls in the C group had a higher step (23%, maxilla, and 33%, mandible) than boys (18% and 19%, respectively) (Fig. 1). The difference in height of the step between the X group and the C group was statistically significant for girls (for example, lower first molar, 95% CI for the difference between the proportions was 4% to 30%). The height of the step for the occlusal surfaces of the second molars was between 5% and 15% for both the X group and the C group. The girls in the C group had a higher step than those in the X group (Fig. 2).

For the proximal and other smooth surfaces in all teeth, including molars, the time lag before the first restorations was longer and the increase in filling

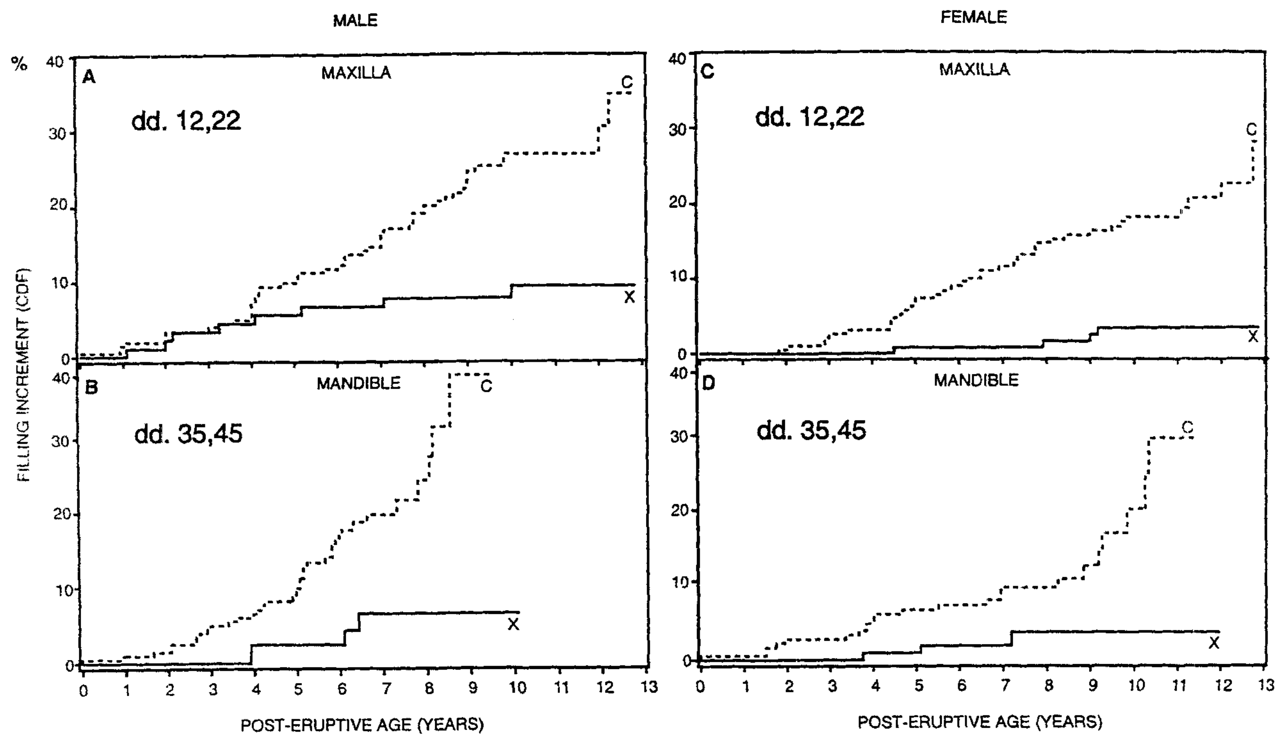

Fig. 3. Annual filling placement rate calculated post-eruptively for proximal and other smooth surfaces in the X group and the C group. (Maxilla = mesial surface of lateral incisor; mandible = distal surface of second premolar.)

increment slower in the X group (Fig. 3). In all premolars and proximal surfaces of second molars, a marked benefit in favor of the X group was detected (Fig. 3). The proximal surfaces of the second molars remained practically filling-free in the X group but not in the controls. A marked difference was seen between groups in the proximal surfaces of the upper incisors, such as the mesial surface of the upper mesial incisor for girls (log-rank chi-square = 11.1, $p < 0.001$) (Fig. 3). The statistical significances of the differences among the girls are presented in Table 1 as an example.

Table 1. Surfaces with statistically significant differences in favor of the X group in the filling curves for girls. DF = 1

Tooth surface	Log-rank test		Wilcoxon test	
	Chi-square	*P* value	Chi-square	*P* value
D. 17^1	5.53	0.019	5.03	0.025
D. 17^4	3.85	0.050	2.88	0.090
D. 16^1	4.70	0.030	3.81	0.051
D. 16^2	10.25	0.001	9.57	0.002
D. 16^5	8.06	0.005	9.27	0.002
D. 15^1	10.28	0.001	6.53	0.011
D. 15^2	4.11	0.043	1.90	0.169
D. 15^4	6.86	0.009	5.10	0.024
D. 14^1	10.25	0.001	7.35	0.007
D. 14^4	8.73	0.003	6.06	0.014
D. 12^2	5.74	0.017	5.29	0.022
D. 11^2	11.10	0.001	10.58	0.001
D. 11^4	4.65	0.031	3.94	0.047
D. 45^4	4.35	0.037	3.85	0.050
D. 46^1	10.36	0.001	9.64	0.002
D. 46^3	4.28	0.039	4.88	0.027
D. 47^1	11.05	0.001	11.12	0.001

The canines and lower incisors remained almost filling-free during the 10 post-eruptive years in the X group but not in the C group.

The number of restorations on different tooth surfaces per 100 subjects was 305 in the X group and 460 in the C group before the onset of the original gum trials in 1982. In the X group 4.0 first restorations were made on different tooth surfaces per subject during the trial and thereafter, whereas 9.3 such restorations were made in the C group during the decade in question (Table 2). On the basis of the calculations of the cost of restorations, the X group saved 595 FIM/subject during the follow-up. The cost of the xylitol gum regimen used in the trial was 600 FIM/subject.

Discussion

There are some principal methodologic problems in the original Ylivieska study (5, 6). First, there is the

Table 2. The number of first restorations on different tooth surfaces per 100 subjects in the X group and the C group during and after the original gum trials in 1982–91

	Xylitol (total = 401)					Control (total = 931)				
Tooth	Occl.	Mes.	Bucc.	Dist.	Ling.	Occl.	Mes.	Bucc.	Dist.	Ling.
7	141	1	31	3	17	223	29	55	20	29
6	35	27	14	18	16	52	50	17	36	22
5	22	5		19		83	34		61	
4	13	1		6		52	12		38	
2		8		3	5		37		14	6
1		4		12			28		33	
Total	211	46	45	61	38	410	190	72	202	57

difference in favor of the X group in base-line oral health between the X and C groups in girls, which is clearly seen with the present survival analysis method (Fig. 1) and was also reported in the original study in terms of DMFS (5). Second, neither subjects nor practitioners were blind to which group the subject was in (5). Third, the incidence data in these caries trials were as usual based on the chronologic age of subjects. Because of the notable variation between individuals in the timing of tooth eruption, however, the cariogenic challenge of different teeth varied considerably, even by a couple of years, which was not measured in Ylivieska. To partly eliminate these drawbacks, a new analysis system was developed (12, 13) and applied here.

The subjects were 11 or 12 years old at the time of the start of the 2- to 3-year trials. The principal trial was conducted for 2 years and extended for a 3rd year for the so-called risk population (5). When the time of eruption of individual teeth was taken into consideration, the timing of the xylitol chewing gum trial of 2 or 3 years varied widely for different teeth. This new system can be used accurately to measure the time of cariogenic challenge.

Since the measured mean eruption age of the second molars for these subjects was 12.6 years for boys and 12.1 years for girls, their eruption occurred during the trials in most subjects. The filling increments for the occlusal surfaces were clearly lower in the X group (Fig. 2). Among the boys the filling increment curves for the maxilla diverged after 2 post-eruptive years (Fig. 2A). This observation seems to support the notion of the 'period effect', which implies that there was a lag between the start of the xylitol program and the start of the preventive effect (8).

The use of xylitol chewing gum was associated with a significant favorable effect on the number of restorations on all smooth surfaces, including the proximal surfaces of all molars (Table 2). This association was most prominent for teeth that erupted during the trial—that is, during the second phase of mixed dentition. This supports the view of the 'post-eruptive age' effect (8) on smooth surfaces. These results also showed that when the risk for caries on smooth surfaces was high, xylitol effectiveness was high, and when the risk for caries was low, xylitol effectiveness was also low. Different filling patterns for fissures of first and second molars also support this concept.

Even the proximal surfaces of permanent teeth that erupted 4–5 years before the gum trial were favorably affected by the use of xylitol chewing gum. This is not surprising, as the lag phase of restorations on these tooth surfaces (in the C group) was about 3–4 years (13); thus the trial started early in the beginning of placement of restorations on these tooth surfaces in control subjects. This suggests that the use of xylitol postponed the placement of restorations on all surfaces at risk during the trial.

One surprising feature was the delay of restoration placements by 3–4 years on distal surfaces of the second premolars in the X group (Fig. 3B, D). These teeth had erupted during the trial, and thus the effect was demonstrable after termination of the trials. This may be called a 'lag effect' of the trial (8), but it may also result from the fact that the start of filling increment on the contact mesial surface of first molars was also delayed in the X group (not shown in the figures). Both the distal surface of second incisors and the mesial surface of first premolars have been reported to experience 50–70% less caries than their contralateral surfaces, although there are no evident reasons why caries susceptibility would vary on different proximal surfaces of the same tooth (17). The phenomenon was attributed to the fact that canines are the most caries-resistant teeth (9, 12), and the interdental spaces around them also seem to form a caries-resistant environment.

The X effect followed the pattern of fluoride effect when analyzed separately for different tooth surfaces (18, 19). This highlights the importance of enhancing remineralization on surfaces easily accessible to saliva, at least during the stages of tooth eruption. Thus the clinical effect of xylitol may be similar to that of fluoride, as demonstrated in vitro (2).

The findings of the present analysis support the proposed hypothesis that the maturation of teeth under favorable physicochemical conditions has a long-term beneficial effect (20). Use of xylitol chewing gum during high-risk post-eruptive periods enables the smooth surfaces to mature under favorable conditions, resulting in remineralization of enamel lesions (3) and sometimes even rehardening of dentinal lesions (21). Evidently, the role of saliva in this maturation is crucial because less or no xylitol benefit was demonstrable in fissures that are not as easily accessible to saliva-induced maturation. After 3–4 years, however, the post-eruptive xylitol benefit became evident even in the fissures and pits of second molars. This analysis indicates that xylitol seemed to prevent and/or delay the need for restorations on all surfaces that were at risk for restoration during the trial, no matter how old they were, the effect, however, being greater on erupting surfaces.

Our study model showed that the preventive effect of xylitol gum use was observable especially on tooth surfaces where the onset of filling increment took place during the trials. Our study model also clearly demonstrated that girls in the X group had much healthier teeth at the start of the trials, causing a false X effect (Fig. 1). The use of xylitol chewing gum, however, resulted in significantly fewer restored tooth surfaces in these subjects, followed up a decade after the start of the trials (Figs. 2 and 3, Table 2). Thus the methodologic problems of the original trial do not invalidate the conclusions, which are here supported by an independent analysis of the standard patient records of the health center. The cost of the xylitol regimen during the 2–3 years was roughly the same as the cost of the restorations avoided during the following decade. From the cost-effect point of view, the cost of xylitol is covered by savings in restorations only after 10 years of follow-up.

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