Sealants and xylitol chewing gum are equal in caries prevention

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Alanen P, Holsti M-L, Pienihäkkinen K. Sealants and xylitol chewing gum are equal in caries prevention. Acta Odontol Scand 2000;58:279–284. Oslo. ISSN 0001-6357.

Sealants and xylitol have been demonstrated to prevent dental decay, but their effect has never been compared in the same study. Regular use of xylitol chewing gum during 2 or 3 school years was compared with application of occlusal sealants in a randomized study. The reliability of the clinical observations was controlled by examining the presence of dental decay in the same teeth from bitewing radiographs in a blind study. After 5 years, no statistically significant differences between the sealant and xylitol groups were found. The results were in line with the results from separate studies with sealants or xylitol. There were no great differences between the costs of the measures. The selection between the compared preventive measures has to be made on the basis of practical aspects such as caries occurrence, availability of personnel and other resources, opportunity costs, cooperation with schools, and other local conditions. □ *caries prevention; community trial; follow-up*

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The application of sealants has been demonstrated in several clinical and community trials to be a safe and effective method of preventing pit and fissure caries (for summaries see (1–4)). Similarly, all field trials with xylitol have demonstrated clear reductions in caries occurrence figures (5–9). According to the literature, these two measures give similar results, a 30–80% reduction in caries occurrence figures compared with control groups without any special preventive measures except education on healthy diet, good oral hygiene, and use of fluoride-containing tooth paste. The relatively large variation between the field studies on each measure can be assumed to be explainable, not only by the differences between materials, techniques, and examiners, but also by other local conditions, such as study groups, doses, frequencies and timing, presence of other preventive measures, differences in baseline caries experience, use of health services, socio-economic factors, and levels of fluorides in soil and tap water, etc.

Despite similar results, these two methods are quite different in clinical practice. The application of sealants, for instance, needs clinical chair-side time, visits to the dentist's office, professional skills in implementation, good equipment and materials, correct timing, the possibility to examine the children when necessary, and the ability to select correct risk subjects, teeth and surfaces in order to avoid unnecessary costs. It has also been suggested that sealants protect only occlusal surfaces. Therefore, later approximal caries could eliminate the benefits of sealants in the long run. Of course, covering the fissures (and pits on the buccal and lingual surfaces) with sealants should not only prevent occlusal (and pit) caries, but also, in principle, decrease the risk of approximal caries, but this suggested effect has never been empirically studied. The generally accepted opinion is that sealants are effective but expensive (10). Therefore, frequently renewed recommendations for a clinical decision-making rationale such as those given by the Workshop on Guidelines for Sealant Use (2) are very welcome.

The use of xylitol in caries prevention requires regularity but it does not require professionals, clinical visits and treatment, equipment, or repeated individual check-ups. Hujoel et al. have reported that the caries preventive effect with xylitol was very good in teeth which erupted during the second year of use of xylitol, and also very good even in teeth which erupted after cessation of regular use of xylitol (11). The reduction percentage was 88–93% in these subgroups. If it is true that the best preventive result can be obtained by starting regular use of the measure even before the eruption of the teeth, as suggested also by another study with xylitol (12), then sealants are out of the competition even before the starting line. This conclusion cannot, however, be too straightforwardly drawn on the basis of the above-mentioned studies. The possibility that the teeth, which erupt later than on average, can differ from the teeth erupting earlier, cannot be eliminated. However, if the months immediately after the eruption are crucial for the future health of the teeth, then it is quite difficult to organize the application of the sealants in the most effective way without adding to the number of check-ups, and thereby the costs. With regular use of xylitol, one can "be there" in time without any extra costs.

The use of sealants has become routine in all healthcare centers in Finland offering free dental care and prevention to all children up to the age of 19 years. Based on the clinician's opinion on the risk of decay, most occlusal surfaces of first and second permanent molars have been routinely sealed (up to 100% at some healthcare centers, especially for second molars). As a result, in Finland, it is

not possible at present to conduct a prevention trial where the control groups do not get any individual clinical caries prevention such as application of sealants or fluoride varnishes. This is, however, a universal ethical rule for clinical trials. The new measure has to be tested against currently running and accepted practice.

Sealants and xylitol have so far never been compared in the same study where the local conditions are similar for both groups. The aim of the present study was to compare the caries occurrence figures in children getting xylitol chewing gum on a regular basis at school but no sealants, with children whose teeth were sealed if the clinician assumed that those particular teeth were at risk of decay in the near future.

Subjects and methods

In 1994, all school children in the 5th grade in 14 schools in Hämeenlinna and the surrounding four communities, together forming the Hämeenlinna healthcare center, were invited to participate in a 5-year trial comparing the caries preventive effect of sealants and xylitol chewing gum. With few exceptions, the children were born in 1983. The total population having access to the health services of the Hämeenlinna healthcare center consists of 65,000 inhabitants, 15,000 of them being under 19 years of age. The oral healthcare is well organized, and all children and adolescents can get free dental care up to 19 years of age, as do all children and adolescents in Finland. The systematic caries prevention program for children and adolescents in Hämeenlinna consists of regular examinations at individualized intervals (from 4 months up to 24 months) based on estimated caries risk, possible SM tests, diet counseling, education of children and their parents on the development of dentition and the importance of good oral hygiene, recommendations to use fluoridated tooth paste, and application of fluoride varnishes and sealants on an individual basis. During 1992–99, the average DMF index has been between 1.2 and 0.8 at the age of 12 years and between 2.5 and 2 at the age of 15 years, both figures indicating a slowly decreasing trend during the 1990s. The DMF figures are on the same average level as elsewhere in Finland, and lower than the WHO target figures for the year 2000.

The 14 participating school classes were randomly assigned as clusters into the sealant, the 2-year xylitol chewing gum, and the 3-year xylitol chewing gum groups. The dentists treating the children were asked to apply sealants on an individual basis when indicated for the children in the sealant groups, but never in the xylitol groups. The clinicians had the right to select the applied sealant (resin or glass ionomer), the teeth and the sealing time according to their own knowledge of the best choice on an individual level. For the xylitol groups, the teachers distributed the chewing gum to the children every school day but not on weekends or holidays including the 10-week summer holiday. The gum (Xylifresh, LEAF BV) was sweetened only by xylitol (65% w/w). If a child was absent from school, no gum was given for those days. The recommended chewing time was about 10 min, after which the gum was collected and put in a disposal basket. The daily amount of gum was 6 pieces, 2 in the morning, 2 after lunch, and 2 before the children went home. As a result, the daily dose of xylitol was 5 g for about 190 days per year.

The examining dentists would, of course, be able to identify the groups of the children. With this unavoidable weakness of sealant trials in mind, we tried to eliminate the possibility of examiner bias in several ways. (i) Before the study, all the participating dentists were informed that the literature on sealants and xylitol was inconsistent about the possible differences in caries prevention between these measures. There was therefore no reason to prefer either sealants or xylitol, so to try to be as objective as possible. (ii) The dentists were also informed that bitewing radiographs would be taken and analyzed in a blind study setting at the end of the study. The radiographs would reveal whether the examiners had registered dental decay in a biased way. (iii) Despite the fact that all the chewing gums were identical, they were coded with seven different symbols, and the same group got the gum marked with the same code throughout the study. The dentists were told that one of the seven gums was sweetened with sorbitol but nobody knows which one. This was supposed to be a test of their ability to make non-biased observations because the results in the sorbitol group were expected to be different from the results in the xylitol groups.

Clinical examinations were carried out annually. In 1994 and 1995 the examinations took place in September, and, after that, in 1996–9, in April or May. Because the products were used during the school year starting in the middle of August, and ending at the end of May, we had to make the baseline registrations on the same days as the use of xylitol started. After the start, we moved the examination date to April–May, in order to be able to examine the children as often as possible at even intervals. In September 1999, it would have been extremely difficult to find the children any more, because so many of them had moved away from their earlier schools after May 1999. As a result, the first examination interval in 1994–95 was 12 months, the second 8–9 months, and, after that, during the years 1996–99, 12 months. The numbers of children examined at each year are given in Table 1.

The same 11 dentists who treated the children on a regular basis examined them. The dentists were all calibrated before the study in 3 special sessions at which all the dentists working in the local offices and one of the authors (M-L.H.) who participated in all the calibration sessions examined the same 30 children in each office (altogether 90 children) without knowing the observations of the other dentists. After the examinations, the results were compared and discussed, and common criteria for the caries registrations were selected. For the registrations, the WHO recommendations (13) were applied. Dental decay reaching dentine and assessed as needing filling was

Table 1. Number of participating children in the study schools at each annual examination

School group	1994	1995	1996	1997	1998	1999
1 Xylitol 2 years	63	64	64	62	59	60
2	32	32	31	31	31	30
3	22	23	20	18	19	18
4	29	29	28	25	27	26
5 Xylitol 3 years	38	39	37	36	35	34
6	59	59	56	55	55	54
7	62	62	60	60	60	59
8 Sealant	34	34	33	30	28	28
9	33	33	33	32	33	33
10	45	45	45	45	43	42
11	29	31	26	26	31	30
12	25	25	25	24	24	24
13	28	28	28	27	27	27
14 (not included)	28	28	27	27	27	27
Total	527	532	513	498	499	492

coded as D_2. The examinations took place in a normal dental chair with good illumination, the teeth dried with an air booster, and using a sharp dental explorer for fissures and pits, fiber optics (FOTI) and a mouth mirror to reveal the decayed lesions and their size. However, due to the local school system, one sealant class changed schools after 2 study years, and as a result also the treating and examining dentist changed. It was observed afterwards in the analyses that the first dentist had systematically registered many more decayed surfaces than had the second dentist later in this group of children. This was the only class where the examiner at the final examination in 1999 was not the same dentist as at baseline in 1994. For this reason, we left this sealant class with 27 children out of the final analyses. After this exclusion, the 5 dentists in the sealant group had examined the same child in 97% of the cases at baseline and final examinations. The corresponding figure was 96% in the xylitol groups with 5 dentists. The few exceptions resulted from occasional leaves due to sickness, holiday, etc. Only subjects who had participated in both the first and last examinations were included in the comparisons.

The DMFS-index was calculated annually at D_2 level. The children were retrospectively classified as being at low or high caries risk by using their earlier caries experience as a risk indicator. All the children, whose DMFS-index was 0 in 1994 were classified as being at low caries risk. All the other children with any earlier caries experience in permanent teeth were classified as being at a high caries risk.

Bitewing radiographs were taken from all children during the last study year in 1999. The clinicians were able to take a total of 489 pairs of bitewing radiographs from the clinically examined 492 children. These radiographs were sent to the Institute of Dentistry in Turku, where one of the authors, an experienced specialist in cariology (KP), examined all the radiographs in random order without knowing the group of the child. These results were then compared with the clinical registrations.

For economic considerations, all the participating dentists treating the children in the sealant groups were asked, during a period of 2 months, to measure the time needed to apply sealants for the children belonging to the study during 1994. The time needed for 123 sealants for 53 children was measured. The average cost of one visit to the dentist's office during the study years 1994–99 was taken from the center's files. The commercial price of the xylitol chewing gums was used for the comparisons. No cost was estimated for the delivery of the products by the teachers.

The Ethics board of the Hämeenlinna healthcare center accepted the study in 1994. An informed consent form was sent to all children and their parents at their home addresses. All the teachers and people working in the healthcare administration were informed before the study started. The analyses were carried out with the Statistica® program, applying the analyses of variance (ANOVA).

Results

The main result was that no statistically significant differences between sealant (1.62 DMFS) and xylitol groups (1.83 and 2.14) were observed (ANOVA, $P = 0.21$) in caries increment figures (Tables 2, 3). The result was similar in low and high caries risk subgroups. The average caries increment figures for the low-risk subjects was 0.9 DMFS in the sealant group and 1.2 in the xylitol group, and for the high-risk subjects 2.7 and 3.2, respectively (Table 4).

The variation among the school classes within the sealant and xylitol groups was large and suggested no systematic trends between the applied measures (Table 3). In total, 47% of all second molars in the sealant group compared to 0.8% in the xylitol group were sealed at the last examination. The corresponding figures for first molars (sealed before the study) were 33% in the sealant group and 42% in the xylitol group.

The number of decayed or filled surfaces observed in the radiographs was slightly higher than in the clinical

Table 2. Mean DMFS indices and 5-year caries increments and S.D.s in groups with 2-and 3-year use of xylitol chewing gum, and in the sealant group. Only subjects who participated in baseline and final examinations are included. Comparison of groups in relation to the 5-year caries increment, ANOVA, $P = 0.21$

Group	Children N	Mean DMFS and S.D. 1994	1995	1996	1997	1998	1999	5-year increment 1994–99
Xylitol								
2-year use	132	1.1 2.0	1.4 2.3	1.6 2.7	1.8 2.7	2.2 3.0	2.9 3.9	1.8 2.8
3-year use	147	1.0 1.9	1.3 2.1	1.6 2.4	2.2 2.9	2.7 3.4	3.1 3.7	2.1 2.8
Sealants	179	1.2 2.4	1.5 2.5	1.7 2.8	2.0 3.0	2.4 3.4	2.9 3.8	1.6 2.5
	458							

Table 3. Mean DMFS indices and 5-year caries increments, and S.D.s in all study groups 1994–99. Xylitol 2 = groups that used xylitol chewing gum for 2 school years. Xylitol 3 = groups that used xylitol chewing gum for 3 school years. Only subjects who participated in baseline and final examinations included. In 1995–98, the number of children in some groups and years was smaller than the N indicates

School	Children N	Measure	Mean DMFS and S.D. 1994	1995	1996	1997	1998	1999	5-year increment 1994–99
1	59	Xylitol 2	1.0 2.0	1.2 2.2	1.3 2.4	1.5 2.6	1.7 2.9	2.0 3.0	1.0 1.6
2	30	"	1.1 1.7	1.3 1.9	1.7 2.5	1.6 2.3	1.9 2.5	2.8 3.3	1.7 2.1
3	17	"	0.8 1.3	1.2 1.6	1.7 2.9	2.3 2.9	3.2 3.3	4.4 4.4	3.6 3.6
4	26	"	1.6 2.5	2.0 3.1	2.0 3.3	2.3 3.1	2.8 3.6	4.3 5.4	2.7 3.8
5	26	Xylitol 3	0.4 1.0	0.8 1.7	0.8 1.5	1.1 2.3	1.5 2.6	2.1 3.1	1.7 2.5
6	54	"	1.0 2.0	1.2 2.0	1.5 2.3	2.2 2.7	2.9 3.6	3.1 3.7	2.2 2.6
7	59	"	1.3 2.1	1.7 2.3	2.2 2.8	2.8 3.2	3.4 3.6	3.7 4.0	2.4 3.1
8	28	Sealants	1.0 2.6	1.1 2.6	1.2 2.7	1.5 3.0	2.1 3.9	2.7 4.3	1.6 2.3
9	32	"	1.8 2.3	2.7 3.0	2.7 3.0	3.1 3.2	3.8 3.9	4.1 4.5	2.3 3.2
10	42	"	0.6 1.3	0.8 1.4	0.8 1.8	1.2 2.1	1.2 2.2	1.7 2.8	1.1 2.0
11	26	"	1.6 3.0	2.2 3.4	2.7 4.1	3.6 4.4	4.0 4.3	4.7 4.5	3.1 3.3
12	24	"	1.3 2.8	1.0 1.7	1.2 1.7	1.4 1.9	1.5 1.8	1.9 1.8	0.5 1.7
13	27	"	1.1 2.5	1.3 2.3	1.7 2.6	1.9 2.7	2.0 2.9	2.3 3.2	1.1 1.4
	458								

observations, 0.53–0.60 DFS, the pattern being similar for all groups. Therefore, no bias between the study groups was observed. Occurrence of decay or fillings was higher on the occlusal surfaces than on the approximal surfaces in all groups. The frequency of decayed or filled occlusal surfaces tended to be somewhat higher (0.31 DFS clinically, 0.28 DFS in radiographs) in the combined xylitol group than in the sealant group (ANOVA, $P = 0.06$). On the approximal surfaces, the xylitol group showed less (0.18 DFS clinically, 0.24 DFS in radiographs) decay and fewer fillings than the sealant group (Table 5) but this difference was not statistically significant.

The average cost of one visit to a dentist's office in Hämeenlinna had been 260–280 FIM (equal to 43–47 Euros or USD) during the study years. The average time taken to apply one sealant was 6.2 min, but the time needed depended very much on the organization of the work. If only one sealant was applied, the time needed was 17.5 min on average. If several sealants were applied during a visit, when also other dental treatment was carried out, the average time needed for one sealant was 4 min. Thus, the cost of one sealant application varied between 50 and 250 FIM (8–40 Euros or USD). The price of the xylitol chewing gums was 0.9 FIM per day giving a

Table 4. Mean DMFS indices and S.D.s at baseline and the 5-year (1994–99) caries increment in low-risk children (DMFS = 0) and those with any DMF surfaces at baseline. Differences between corresponding xylitol and sealant groups statistically not significant

Group	N	1994 Mean	1994 S.D.	1999 Mean	1999 S.D.	5-year increment Mean	5-year increment S.D.	
Xylitol	168	0.0	0.0	1.2	2.2	1.2	2.2	DMFS = 0 at baseline
	111	2.6	2.3	5.8	4.1	3.2	3.1	DMFS > 0 at baseline
Sealants	106	0.0	0.0	0.9	1.6	0.9	1.6	DMFS = 0 at baseline
	73	3.0	2.9	5.7	4.2	2.7	3.2	DMFS > 0 at baseline

Table 5. Occlusal and approximal status (DFS) of premolars and first and second molars at the final examination according to clinical observations and blinded radiological findings (comparison of groups in relation to DFS, ANOVA)

	Clinical findings				Radiological findings				Diff. between rtg and clinical findings		
	Approximal		Occlusal		Approximal		Occlusal				
Group	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Approximal	Occlusal	N
Xylitol	0.45	1.10	1.49	1.98	0.99	1.86	1.99	2.09	0.54	0.50	293
Sealant	0.63	1.34	1.18	1.58	1.23	2.33	1.71	1.78	0.60	0.53	196
Difference	−0.18		+0.31		−0.24		+0.28				
Stat. sign.	$p = 0.10$		0.06		0.19		0.13				489

cost of 170 FIM (28 Euros or USD) per child for one school year.

Discussion

All the results were in good agreement with earlier studies. The preventive measures seemed to be almost equally effective. Owing to the fact that the average caries increment figures varied between the 13 schools, indicating no systematic trends between the tested preventive measures (Table 3), there is no justification to conclude that one of the measures is more effective than the other in caries prevention.

Studies have repeatedly shown that if caries figures are low, the relative share of occlusal caries is high. Therefore, it is important to be successful in preventing occlusal caries. Thus, sealants may, from the biological point of view, seem to offer a better alternative than xylitol in societies with good dental health in children. On the other hand, prevention of approximal caries may be more beneficial because high quality is easier to achieve for occlusal than approximal fillings. Approximal fillings may also increase the risk of gingival problems. There is, however, no reason to interpret the situation as a competition between two mutually exclusive alternatives. If the figures for approximal caries are high, there is no point trying to save only the occlusal surfaces with sealants. Therefore, an effective way to prevent approximal caries may favor also the use of occlusal sealants.

The result that the 2-year use of xylitol did not differ from the 3-year use was in line with the Estonian xylitol study. The Estonian study was carried out simultaneously with the present study, with the same school-based delivery system, the same daily dose of xylitol, partially the same commercial products, and among adolescents of the same age (9).

The loss of subjects during the 5 study years was very low. About 93% of the subjects at baseline were still available for clinical examinations 5 years later. The stability of the population provides a good opportunity for a preventive program calling for regular use of the applied measure. The radiographic analyses carried out blindly were in good agreement with the clinical observations. The number of decayed surfaces increased in the same relation in all groups. It can be concluded that no systematic error was introduced as a result of the fact that it was not even theoretically possible to carry out the clinical examinations in a blinded study setting. All published studies with sealants, but without radiographic information, are methodologically problematic if sealants are compared with other measures because a placebo sealant is an impossibility.

On the basis of the results from the Ylivieska study (12), suggesting good preventive results for those teeth which erupted during the period of use of xylitol, we tried to organize the study with this aspect in mind. The results from the Belize study published during the field phase of our trial (11) may, however, mean that it would have been better to start the use of xylitol even 1 or 2 years earlier. In addition to the problem of timing, the result that there were no differences between the 2-year and 3-year groups suggests that we do not yet know what is the shortest use period giving the same preventive result. Therefore, our results with xylitol may be below the optimum, from both the biological and the economical points of view. The same is naturally true for sealants. New materials may today be better than those applied during 1994–96. These kinds of problems cannot be solved in long-lasting trials testing rapidly developing measures and materials.

In addition to the real differences in caries occurrence among the schools, the differing opinions of dentists may play a role here. We did not, however, try to eliminate any examiner variation, which possibly remained after the calibration session and selection of the diagnostic criteria to be applied during the study for the following reason. In any case, even an "objective" examiner, an outsider has to accept the variation caused by the practicing clinicians, i.e. the fillings made by the local dentists as a part of the DMFS index. This fact affects all clinical studies in countries like Finland offering regular dental care for children; about 90% of the DMFS index consists of the F-component.

Because every child is keen to get free chewing gum, targeting of xylitol only to high-risk subjects is not possible in a school-based delivery system. Therefore, unnecessary cost cannot be avoided. On the other hand, a school-based delivery system can control the regular use of recommended amounts and frequencies in a reliable way, as demonstrated recently by Alanen et al. (9). If the use of

xylitol were based on the subject's own selection, subjects with high caries risk would not necessarily cooperate with the health personnel or teachers.

Even though the costs caused by sealant applications and xylitol were calculated, there is no justification for strict economic conclusions, because the cost of the sealant applications depended very strongly on the organization of the clinical treatment. If all 4 molars in all children were to be sealed, then chewing gum would be the cheaper alternative. If the dentist could select only the correct risk subjects and teeth for sealing, then the application of sealants could be the relevant choice. However, it is a well-documented fact that, in adolescence, identification of risk subjects is not possible with an acceptable sensitivity and specificity (14). Another aspect not favoring the sealants is that sometimes they are lost and the application has to be repeated. In addition, the children do not always show up at the clinics, and the reserved clinical treatment time is lost. With chewing gum, these kinds of problems are not present. With regard to the opportunity costs, altogether 1 month's working time of 1 dentist/assistant pair could have been saved in the present study if the prevention had been totally based on the use of chewing gum.

As a result of the fact that we had no control group without any preventive measure, our study cannot report the absolute effects of the applied preventive measures. Despite this, our results show no reason to deny the effect of sealants or xylitol in caries prevention or to challenge the results from practically all earlier trials. The results on both occlusal and approximal surfaces also suggest that the applied measures have affected the caries figures in the present study (Table 5).

In conclusion, our results suggest that selection between the measures tested in the present study should be based on practical aspects, such as the cost of treatment, occurrence of caries, co-operation between schools and healthcare, availability of healthcare personnel and equipment, opportunity costs, etc. Most societies have a well-running school system, but are short of healthcare personnel. Therefore, one can quite easily start a preventive program with xylitol, while the professionals can use their clinical hours for treating subjects with more acute need.

Received for publication 26 June 2000
Accepted 15 September 2000

Acknowledgements.—We cordially thank all the teachers for the careful delivery of the xylitol products during the study years, all the dentists, the hygienists and the dental assistants involved, and all the participating children and their parents in the Hämeenlinna healthcare center. Special thanks go to the LEAF company, Turku, Finland for donating the xylitol products for the study.

References

1. Dental sealants in the prevention of tooth decay. NIH Consensus Development Conference Summary. Br Dent J 1984;156:295–8.
2. J Pub Health Dent 5/1995, Special Issue: Proceedings of the Workshop on Guidelines for Sealant Use.
3. Kumar JV, Siegal MD. A contemporary perspective on dental sealants. CDAJ 1998;36:378–85.
4. Ripa LW. Sealants revisited: an update of the effectiveness of pit-and-fissure sealants. Caries Res 1993;27:77–82.
5. Scheinin A, Bánóczy J. Collaborative WHO xylitol filed studies in Hungary. An overview. Acta Odontol Scand 1985;43:321–5.
6. Kandelman D, Bar A, Hefti A. Collaborative WHO xylitol field study in French Polynesia. I. Baseline prevalence and 32-month caries increment. Caries Res 1988;22:55–62.
7. Isokangas P, Alanen P, Tiekso J, Mäkinen KK. Xylitol chewing gum in caries prevention: a field study in children. J Am Dent Assoc. 1988;117:315–20.
8. Mäkinen KK, Bennet CA, Hujoel PP, Isokangas PJ, Isotupa KP, Pape HR, Jr. Xylitol chewing gum and caries rates: a 40-month cohort study. J Dent Res 1995;74:1904–13.
9. Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention. Estonian study in children. Community Dent Oral Epidemiol 2000;28:218–24.
10. Burt B. Prevention policies in the light of the changed distribution of dental caries. Acta Odontol Scand 1998;56:179–86.
11. Hujoel PP, Mäkinen KK, Bennet CA, Isotupa KP, Isokangas PJ, Allen P, et al. The optimum time to initiate habitual xylitol gum chewing for obtaining long-term caries prevention. J Dent Res 1999;78:797–803.
12. Isokangas P, Mäkinen KK, Tiekso J, Alanen P. Long-term effect of xylitol chewing gum in the prevention of dental caries. A follow-up 5 years after termination of a prevention program. Caries Res 1993;27:495–8.
13. A guide to oral health. Epidemiological investigations. Geneva WHO 1979.
14. Hausen H. Caries prediction—state of the art. Community Dent Oral Epidemiol 1997;25:87–96.