ORIGINAL ARTICLE

International Dental Journal 2013; 63: 210–224

doi: 10.1111/idj.12038

Topical xylitol administration by parents for the promotion of oral health in infants: a caries prevention experiment at a Finnish Public Health Centre

Kauko K. Mäkinen[1], Kirsti L. Järvinen[2], Carita H. Anttila[2], Leena M. Luntamo[2] and Tero Vahlberg[3]

[1]Institute of Dentistry, University of Turku, Turku, Finland; [2]Uusikaupunki Public Health Centre, Uusikaupunki, Finland; [3]Department of Biostatistics, Medical Faculty, University of Turku, Turku, Finland.

Objectives: This demonstration programme tested topical use of xylitol as a possible oral health promoting regimen in infants at a Finnish Public Health Centre in 2002–2011. **Methods:** Parents (usually mothers) began once- or twice-daily administration of a 45% solution of xylitol (2.96 M) onto all available deciduous teeth of their children at the age of approximately 6–8 months. The treatment (xylitol swabbing), which continued till the age of approximately 36 months (total duration 26–28 months), was carried out using cotton swabs or a children's toothbrush; the approximate daily xylitol usage was 13.5 mg per each deciduous tooth. **Results:** At the age of 7 years, caries data on the deciduous dentition of 80 children were compared with those obtained from similar, untreated children ($n = 90$). Xylitol swabbing resulted in a significant ($P < 0.001$) reduction in the incidence of enamel and dentine caries compared with the comparison subjects (relative risk 2.1 and 4.0, respectively; 95% confidence intervals 1.42–3.09 and 2.01–7.98, respectively). Similar findings were obtained when the children were 5 or 6 years old. The treatment reduced the need of tooth filling relative risk and 95% confidence intervals at 7 years: 11.86 and 6.36–22.10, respectively; $P < 0.001$). Compared with untreated subjects, the oral counts of mutans streptococci were reduced significantly ($P < 0.001$). **Conclusions:** Considerable improvement in dental health was accomplished in infants participating in a topical at-home xylitol administration experiment, which was offered to families in the area by the Public Health Centre as a supplement to standard oral health care. Caregiver assessment of the programme was mostly rated as high or satisfactory.

Key words: *Xylitol, infants' caries, caries prevention, public health centres*

INTRODUCTION

In most countries, dental caries affects nearly 100% of the populations[1]. Prevention of dental caries, especially in small children at the earliest possible age, can be viewed as an important health-promoting measure. Various public fluoride-based procedures, such as the consumption of fluoridated drinking water, and topical fluoride treatments, have generally yielded good results. Certain non-fluoride agents may still provide benefits as adjunctive therapies in children[2]. Special xylitol-based mother–child programmes have recently been implemented in Scandinavia. In these programmes mothers' use of xylitol chewing gum reduced both the intrafamilial transmission of mutans streptococci (MS) from mother to infant[3–6] and the incidence of dental caries in children[6–8]. Xylitol was more effective than periodic treatment of the mothers with fluoride- and chlorhexidine-varnish-based procedures[7]. In a subsequent Japanese study, infants whose mothers had not used xylitol gum, acquired MS about 8.8 months earlier than children whose mothers had received xylitol[9]. Special pacifiers designed to act as slow-release xylitol dispensers were found to have utility value in early caries prevention[10], and xylitol-containing tooth-wipes significantly reduced the incidence of caries in infants[11].

Early risk-based oral health programmes targeting families of MS-positive infants can reduce the risk of caries[12]. Studies reflect the importance of early caries prevention: indeed, several studies have reported that the earlier MS colonisation occurs, the greater the decay rate of children's teeth during the subsequent years[7,13–16]. Interventions to prevent transmission of

MS in pregnant women and new mothers have been effective[3,5,17]. It has been found that even just 2 months' regular exposure to sucrose was sufficient to induce dental caries in the deciduous dentition of children with elevated MS levels at baseline[18]. Elevated oral levels of MS are thus considered risk factors for caries, along with incipient caries and consumption of candies[19].

In congruence with the health care policy effective in Finland, the public health centres of each municipality are encouraged to promote oral health by adopting new caries prevention strategies in addition to implementing regular patient care. The public health centres play a key role in guiding the way people live. The chief dental officer of each public health centre is entitled, *ex officio*, to implement new and safe preventive measures at his/her dental care clinic by exploiting existing, established trial-based scientific information. Accordingly, caries-prevention programmes with xylitol have been performed with encouraging results at Finnish Public Health Centres under 'near-real-life conditions'[20–23]. During the past 30 years, the use of xylitol has become an integral part of public and home-based caries prevention in Finland[24–27]. Public Health Centres have played an important role in disseminating information to residents about the idea of xylitol-based limitation of caries. Examples of institutions in other countries that have recommended the use of xylitol to promote oral health have been mentioned elsewhere (see Table 7 in ref. 27). Despite the achievements made in the control of caries, this disease continues to defy eradication. An appeal has been made for regular, updated evaluation of community-based oral health promotion and oral disease prevention[28].

The present paper reports observations from a health-promoting experiment carried out at a Finnish Public Health Centre in a small town in southwest Finland during 2002–2011. In order to expand opportunities for health education, the objective of the experiment was to investigate the potential of a new topical xylitol administration procedure to promote oral health in small children. In this experiment, parents were asked to swab concentrated xylitol solution onto all available deciduous teeth of their infant children, starting at the age of approximately 6–8 months, and to continue this practice until the age of approximately 36 months. Final examinations for caries were carried out at the age of 5, 6 and 7 years. The presence of caries in treated subjects was compared with presence in similar children who had not been treated with xylitol. Although the use of xylitol as a caries-preventive agent was well known to the Finnish public health centre system (based on the over 40-year history of this research field), the topical administration (xylitol swabbing) approach was regarded as a new experimental method in efforts to prevent dental caries in infants. The local health authorities found that there was sufficient rationale, following long-term experience from the use of xylitol in Finland, to implement a practical demonstration programme at a public health centre. The health centre's objective was to discover whether the existing trial-based information on the non-cariogenicity of xylitol could be exploited in a practical programme, where families in the area with small children were asked to collaborate with the health centre in health promotion. This health-promotion campaign thus endeavoured to meet the challenge[29] of developing novel systems to deliver therapeutic amounts of xylitol, especially to young children. Our aim is to share these experiences with public dental health authorities of other countries.

MATERIALS AND METHODS

General description and the background of the experiment

The purpose of this experiment was to discover the feasibility and effects of topical xylitol application as a potential supplementary caries-preventive measure for infants whose families were served by the municipal public health centre of a small Finnish town. The objective was to employ regular health centre personnel in all family–dentist encounters, thus adhering to the normal Finnish health centre routines, which include recalls, dental treatments, counselling and other customary dental office procedures. However, the statistical treatment and the interpretation of the present data were retroactively carried out at University of Turku institutions (the Department of Biostatistics of the Medical School and the Dental School). The health centre is primarily funded by the municipality, partly subsidised by the national government, operates in accordance with national legislation on health centres and maternity clinics and is locally governed by the town's health board.

The initiation for this health-promotion experimentation came in early 2000 from the personnel of the Health Centre itself, the objective being exploitation of the information contained in existing literature on the non-cariogenicity of xylitol. As these centres operate under decrees issued by the government, and adhere to the supervision of each municipality's Health Board, this experiment was carried out in accordance with the following pre-agreements. (1) The examining teams were to consist of regular, salaried and experienced dentist–dental assistant pairs that enjoyed tenured offices within the municipality's Public Health Centre. (2) All dental examinations were to be carried out at regular dental offices of the Health

Centre using standard dental chairs, lights, instruments and internationally accepted World Health Organisation (WHO) criteria of dental caries, as controlled and monitored by national dental authorities. (3) The bacteriological examinations for the assessment of saliva and plaque levels of MS were to be carried out using test kits similar to those used routinely by several public health centres in Finland since the 1980s.

All clients received the same counselling regarding dietary and oral hygiene, regardless of their group assignment. Special counselling topics included instructions on bottle feeding (especially regarding sweetened juices), use of toothbrush and dentifrice, food tasting and consumption of sugar-based confectioneries. This oral health education adhered to the practices generally observed at Finnish public health centres. As part of these customary health-promoting services, circulars about the programme's general progress were mailed annually throughout the entire duration of this experiment to all participating families (regardless of group assignment). The primary objective of this was encouragement to focus on the dental health of children. Although the chief dental officer of the health centre merely executed her government-approved prerogative to experiment with this prevention programme, the town's health board (viz. ethical board) and the Centre's medical authorities also independently considered the ethical and safety aspects of the programme and approved and recommended its implementation. Before the recruitment of families began, the town's major newspaper teamed up with the health centre and the town's health board by running an editorial that provided preliminary information about the experiment. The present clinical and bacteriological data and in-office experience became retroactively accessible for statistical evaluations following the completion of the programme in May 2011. The Health Board and the medical management of the Health Centre were informed about the programme's progress and endpoint outcomes. This research was conducted in full accordance with the World Medical Association Declaration of Helsinki. Before the beginning of the prevention programme, the parent (most often the mother) accompanying the child on the first visit verbally consented to participate in the programme. This consent was repeatedly obtained from the accompanying parent at each of the subsequent 6-month recalls.

Programme venue and general programme implementation

This exploratory health-promotion experiment was implemented at the municipal Public Health Centre of the town of Uusikaupunki, located in southwest Finland. The average number of town residents during the recruitment period of September 2002 to October 2004 was 16,450. The town's population rather evenly represents the industrial, service and agricultural sectors. During the programme, the health centre's dental clinic normally employed eight dentists and ten auxiliary employees. This experiment employed two dentist–dental assistant pairs, one dental hygienist, and an office employee. The dental clinic is annually visited by approximately 7,200 patients, the total number of visits being approximately 16,000 per year. The annual number of births within the municipality ranged from 134 to 175. During the recruitment years, the families participating in the present programme were regular customers of the town's Public Dental Clinic where the dental records of the patients are kept. During the experiment, there were approximately six or seven private dental offices in town. Normally, $< 1\%$ of area infants were seen by private dentists. All families consumed tap water from the town's own waterworks. During the experiment, the mean ($\pm$ SD) fluorine content of the water measured at 22 consumer sites around town was 0.78 ± 0.07 ppm.

All mothers ($n = 285$) with births between September 2002 and October 2004 within the municipality were invited to visit the public dental clinic when their children were approximately 6–8 months old. A total of 275 children (96.5% of 285) from 270 families visited with their mothers (or in a few instances with fathers; from a few families, twin infants visited) for the first meeting at which each parent was informed about the details of the experiment. The parents were told that the experiment included 6-month recalls until the children were approximately 36 months old, and that semi-annual or annual caries registrations were thereafter planned until the age of approximately 7 years. Four families declined to participate in the xylitol experiment. After obtaining consent, the parent–child pairs were alternately assigned either to the treatment group or to the comparison group. Families were asked to begin topical xylitol application immediately and to continue the experiment until the child was approximately 3 years old. At baseline, a total of 271 children from 266 families started the experiment. At this stage, 133 infants were assigned to the xylitol swabbing group and 138 to the comparison group (from a few families twin infants participated). No special instructions were given concerning the type of dentifrice used within the families other than recommending the use of fluoride-containing products. The families of the treatment group were asked not to substitute infants' regular oral hygiene procedures with xylitol swabbing but to retain normal family practices and administer xylitol after tooth brushing. The intervention and the

comparison groups were considered comparable at baseline for all variables regarding the tooth status.

Following verification of the family's demographic information, baseline bacteriological and dental examinations were carried out at the same first visit. Next, the Orion Diagnostica (Espoo, Finland) test package was used for a microbiological evaluation of the infants' oral MS. These packages feature a screening strip for sample collection from saliva and a site strip for cultivating plaque MS from four tooth sites. A disposable 'mini-brush' (Quick-Stick® Dental Applicator; Dentonova AB, Huddinge, Sweden) was used to obtain plaque samples from the first erupted incisor or incisors of the 6- to 8-month-old children. Later, with new teeth erupting, plaque samples were normally obtained from four interproximal sites of the first deciduous molars (i.e. from one interproximal site of each of the four quadrants). The sample-containing end of the disposable mini-brush was rubbed against one of the four roughened surface areas present in the site strips. A maximum of four interproximal plaque samples were thus obtained when there were erupted teeth present in all four quadrants. Each site was sampled with a new mini-brush and the same tooth sites were sampled at subsequent visits. Next, the salivary MS test was performed without paraffin stimulation by rotating the screening strip in the child's mouth for approximately 10 seconds. Both strips were incubated as shown in the manufacturer's manual. The above bacteriological procedures were normally repeated at all 6-month recalls until the age of approximately 48 months (recording of caries continued up to the age of approximately 7 years). Following these tests, an evaluation of the dental status of the child was carried out. Until the age of 2–3 years, all operations were carried out with the child sitting in the parent's lap. At later ages, the children were examined in the presence of the parent. The children were not radiographed at any point. The overall timetable of the experiment is shown in *Figure* 1.

Following the above first-visit procedures, the accompanying parent was handed the necessary supplies: written instructions, a bottle of xylitol solution, a nozzle cap for the bottle, cotton swabs, a children's toothbrush for the administration of xylitol and a self-report paper diary. The use of all supplies and the diary was demonstrated. These procedures were normally repeated every 6 months until the child was approximately 3 years old, at which time the topical application of xylitol was terminated. At each visit all families, including those in the comparison group, were given a new child's toothbrush. The outcomes of the bacteriological tests were mailed to all families with information regarding the meaning of the bacterial scores obtained. Consequently, all participating families in both groups were informed semi-annually or annually if the child's bacterial scores indicated low or high growth of caries-associated MS. The diaries were used to make daily markings about the topical xylitol administrations, and were periodically returned to the clinic for evaluation and to obtain refill pages.

Use of xylitol

In this experiment, xylitol was used in the form of a 45% aqueous solution (2.96 M) that the parents were instructed to swab twice a day on the surfaces of all deciduous teeth present, using either a double-ended cotton swab (Q-tip) or a toothbrush designed for small children. Granulated xylitol, obtained from the Danisco (currently DuPont) factory in Kotka, Finland, complies with the pharmacological directives and monographs of both the USA and the European Union. Two 25-kg lots, manufactured in 2001 and 2002, were used for all solutions of this experiment The xylitol solutions (pH 6.28 at 25 °C; pH 6.48 at

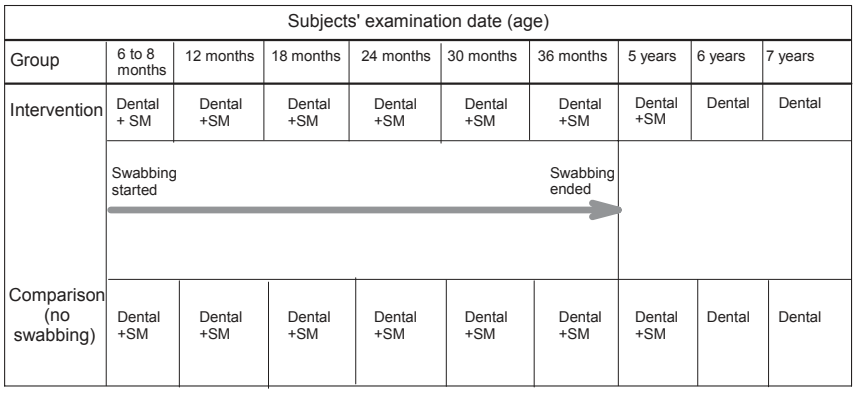

Figure 1. The overall schedule of the topical xylitol application (swabbing) programme. Parents started the topical xylitol treatment by means of cotton swabs or toothbrushes at the age of 6–8 months (when the first deciduous incisors started to erupt) and continued the treatment until the children were approximately 3 years old. Children in the comparison group did not receive topical xylitol treatment. The recording of the incidence of caries registrations (Dental) were carried out at the ages shown, while bacterial tests (MS) continued with most subjects until the age of approximately 48 months.

37 °C) were made in deionised sterile water (specific resistance 10^6 MΩ) at the University of Turku Dental School, and were stored in 100-ml plastic bottles at the health centre in a lockable refrigerator. At temperatures prevailing in the oral cavity, the viscosity of this solution was slightly lower than that of a corresponding sucrose solution.

Both application procedures were demonstrated to the parent upon the first visit. The parent chose the procedure that was considered most suitable. Before xylitol swabbing, excess saliva was removed from the tooth surfaces with a piece of paper towel. When cotton swabs were used in the administration of xylitol, the end of the swab was either dipped into the solution for a few seconds, or three to four drops of the solution were applied to the cotton tip, per each quadrant, using the nozzle-cap. In a normal situation when there were erupted teeth in all four quadrants, the parents were instructed to use one end of each cotton swab for each quadrant, rubbing the xylitol-containing cotton end of the stick against all tooth surfaces, including the gingival crevice areas. Consequently, a maximum of two double-ended Q-tips were used per each treatment when erupted teeth were present in all quadrants. When fewer teeth were present, correspondingly fewer cotton swabs and fewer xylitol drops were used. When the treatment was carried out with a toothbrush, three to four drops of the xylitol solution were applied to the bristles of the brush per each quadrant. The brush was merely used as an applicator of xylitol after regular tooth brushing with dentifrice that took place according to normal family routines. The families were instructed to keep the xylitol solution in a refrigerator and to obtain replacement bottles from the dental clinic. Normally, the 100-ml volume was sufficient for about 2–6 months of use, depending on the number of deciduous teeth present in the infant. The average length of the topical administration period was 26–28 months.

Using an analytical balance, it was estimated that the maximum computed amount of xylitol used in each application with Q-tips or toothbrushes (in the morning or in the evening, and when all four quadrants were treated) was approximately 360 mg per child, or approximately 720 mg daily. These quantities of xylitol applied to infants older than approximately 2 years; younger subjects with fewer deciduous teeth were treated with correspondingly smaller quantities. However, laboratory tests of Q-tips and toothbrushes by means of high-pressure liquid chromatography (HPLC) showed that approximately 75% of their xylitol content became available in a typical administration. Therefore, it was estimated that the computational amount of xylitol applied at each treatment onto each deciduous tooth was approximately 13.5 mg.

Clinical registrations

The primary pre-programme specified response variable was the onset of a caries lesion on a previously sound or unerupted surface. Two experienced examiners scored the teeth according to the definitions of WHO codes, with the exception of WHO code 0 (sound surface) and WHO code 1 (white spot lesions and enamel and dentine surfaces impenetrable to a sharp explorer), which were regarded as sound surfaces and were scored 0. Enamel caries was diagnosed as clinically detectable loss of substance, normally represented by early pit and fissure caries with softness at the base of the pit near the dentino-enamel junction (enamel caries with detectable loss of substance), and was scored 1. Caries lesions associated with a fracture of the surrounding enamel were diagnosed as dentine caries and were scored 2. Caries lesions with probable pulpal involvement and shelling out of virtually the entire structure of the tooth were classified as deep cavities, and were scored 3. Sealants were scored as sound. The primary outcome variable was the development of an unequivocal cavity on a previously structurally intact surface. These definitions adhered in principle to the guidelines enacted by Finnish health authorities for the country's public health centres and were effective during the implementation of this experiment. The two caries raters had graduated from the same Finnish dental school and had worked in close mutual collaboration at the same clinic for about 25 years, predominantly with children; the caries concepts of the raters were considered identical. The subject–examiner assignment was fixed for the duration of the experiment. The health centre's routine allowed analysis of the caries assessors' inter-examiner error near the termination of the experiment on 20 randomly chosen 7-year old subjects. Intra-examiner analyses could not be carried out.

Storage of data; role of examining parties

The dental records were entered into and stored in a normal database in a manner similar to that employed at public health centres in Scandinavia. The attending dentists and dental assistants were, in their capacity as regular public health-care providers, aware of the group assignment. As the children had to be examined within the framework of normal Public Health Centre routines, the dentist–assistant pair also had, at all visits, access to the previous computerised dental records of the subjects. The participating personnel carried out all procedures adhering to the highest possible professional standards and always for the benefit of the child. The author who estimated the bacterial scores was not aware of group assignment and did not participate in clinical diagnoses or in the statistical treatment of

bacteriological or clinical data. The personnel involved in clinical examinations did not participate in the statistical treatment of any data. The statistical personnel did not participate in clinical or bacteriological procedures and worked solely on the dental and bacteriology records obtained from the Health Centre following the termination of the experiment in May 2011.

Statistical analysis of caries and bacteriological data

Although the endpoint recording of caries was normally carried out at the age of 7 years, caries data obtained at earlier ages were also computed. Results from subjects whose last bacterial counts were obtained after 24–36 months of participation were included in the calculations. Consequently, in the final bacteriological examinations, several children were approximately 48 months old. Poisson regression analyses were used to compare the risk of carious teeth (enamel, dentine or deep caries), enamel caries surfaces, dentine caries surfaces and tooth fillings between the xylitol-treated group and the comparison group. In the Poisson regression models, the number of carious teeth was divided by the number of all teeth present, while the number of enamel caries surfaces, dentine caries surfaces and tooth fillings were divided by the number of all surfaces present. Models included the main effects of group and gender. The significance of interaction between gender and group was also tested. Results are expressed using relative risks (RR) with 95% confidence intervals (95% CI). Group differences on plaque and whole-mouth saliva MS at different ages were tested with Poisson regression. *P*-values <0.05 were considered statistically significant. Statistical analyses were done using the SAS System for Windows, release 9.3 (SAS Institute Inc., Cary, NC, USA).

Questionnaire evaluation

Upon the termination of the topical application of xylitol when the children were approximately 3 years old, each visiting parent (most often the mother) returned the final diary sheets and completed a written questionnaire evaluation concerning their experiences during the experiment. The parents of the comparison group were interviewed similarly. The tasks and questions presented to the attending parent are shown in *Table* 2.

RESULTS

Acceptance of the xylitol swabbing experiment within families

Table 1 summarises the strategies employed to promote compliance within families. Interviews and questionnaire responses showed the following:

- A total of 231 parents (usually the mothers) participated in the written questionnaire evaluation when the children were approximately 3 years old (*Table* 2). A total of 115 of these families (49.8%) had been assigned to the xylitol group and 116 to the comparison group (50.2%). These numbers are slightly lower than those used in the caries and MS analyses because some parents were not available for the questionnaire evaluation.
- Most families regarded the topical xylitol application procedure as either very easy or fairly easy. The questionnaire showed that the compliance of the children improved slightly towards the end of the 26- to 28-month xylitol administration period, possibly owing to increased use of a toothbrush as the vehicle for xylitol application. The overall in-office experience reported by the visiting parents was mostly appreciative.
- Most parents used both Q-tips and toothbrush, although it became evident that the use of a brush was favoured. Overall satisfaction with the health-centre-imposed experiment was rated as good or satisfactory among both groups.
- Approximately 75% of the families appreciated the relatively frequent (6-month) recalls, and regarded the recalls as useful.

Table 1 Strategies to promote compliance within participating families

Category	Xylitol swabbing group	Comparison group
Programme staff activities	Training of parents (usually mothers) with xylitol programme involvement	Regular 6-month recalls (normally)
	Regular 6-month recalls (normally)	Regular dietary counselling and oral hygiene instructions
	Regular dietary counselling and oral hygiene instructions	MS reports to parents at 6-month intervals
	MS reports to parents at 6-month intervals	Once-a-year Christmas greetings emphasising dental health issues
	Once-a-year Christmas greetings emphasising dental health issues	Questionnaire evaluation
	Questionnaire evaluation	
Families' involvement	One or two daily xylitol swabbings	Regular family-administered infants' tooth brushing
	Regular family-administered infants' tooth brushing	Questionnaire responses
	Regular filling of the self-report paper diary (xylitol swabbing)	
	Questionnaire responses	
Materials handed to families at proper intervals	Children's toothbrushes, xylitol solution, nozzle caps, self-report paper diary, refill pages	Children's toothbrushes

Table 2 Results of the questionnaire evaluation carried out at the termination of the topical xylitol administration, when the children were approximately 3 years old

Objects of evaluation				
1. The use of the xylitol solution was experienced as	Very difficult	Fairly difficult	Fairly easy	Very easy
	1	14	44	43
2. The child accepted the use of the solution at	Generally well	Generally poorly		
6–12 months	82	18		
12–24 months	86	14		
24–36 months	90	10		
3. The use of the xylitol solution mostly took place took place	Q-tips	Toothbrush	Both	
	3	40	57	
4. Average number of daily treatments (recommendation: 2)	Once a day	Twice a day		
	45	55		
5. Usefulness of the semi-annual visits	Very useful	Fairly useful	Less useful	
Intervention group	77	14	9	
Comparison group	75	14	11	
6. Importance of mailing MS score information to homes	Very important	Fairly important	Less important	
Intervention group	91	9	9	
Comparison group	88	12	11	
7. Mean number of weekly uses of commercial xylitol products by child (mostly concerning 2- and 3-year-olds)	Intervention group			
Intervention group	5			
Comparison group	5			
8. Mean number of weekly uses of xylitol products by family members (mother, father, siblings)	Intervention group			
Intervention group	6			
Comparison group	5			

The survey (items 1–8) was based on 120 responses by parents (usually mothers), whose children received the treatment over 26–28 months. Items 5–8 were presented to the parents in the comparison group (121 responses). Apart from items 7 and 8, the results shown are percentages of all answers given in each group.

- The intervention group and the comparison group did not differ from each other regarding the families' attitude toward the services offered by the health centre. The groups did not differ regarding the frequency of the use of commercial xylitol products during the experiment.
- A separate survey carried out during the first 1–2 years of the experiment focused on the length of breast-feeding. The duration of breast-feeding normally ranged between 4 months and 12 months and the groups did not differ in this regard.
- The self-report paper diaries' return rate (in the treatment group) was 74% during the first year, and 64% and 54% during the second and third year, respectively.
- None of the parents in the xylitol swabbing group reported side-effects in the children.

Attrition

A total of 11 children out of the initial 133 subjects who began xylitol treatment discontinued the experiment during the first year. A further four children dropped out before the age of 2 years. The remaining attrition took place after the age of 2 years. At the age of 7 years, a total of 80 children (60% of 133) in the treatment group were regarded as active participants. Most dropouts resulted from the parents' fatigue with observing the twice-daily xylitol swabbing procedure, the unsuitability of the relatively frequent recalls or the family moving away from the area. Out of the 138 children who started the programme in the comparison group, a total of 90 (65%) were available for the 7-year endpoint examinations. In this group, most dropouts resulted from a change of residence or from failure to respond to recalls. The numbers of children, who visited at ages 5 years and 6 years, are shown below. The dropout rate at the age of 4 years was approximately 20% in both groups. The dropout subjects who remained in the area, continued to receive standard dental care as regular health centre clients.

Onset of caries in deciduous teeth

Out of the 133 subjects who started the experiment in the intervention group and the 138 subjects in the comparison group, approximately 80–120 and 99–122 children, respectively, were available at different 6-month recalls during the programme. At ages 5, 6 and 7 years, when the final caries registrations were carried out, the number of children subjected to statistical analysis were 106, 84 and 80 in the xylitol group and 108, 99 and 90 in the comparison group. The inter-examiner reliability kappa statistics of the two examiners for diagnosing a structurally intact surface *versus* a cavitated surface was 0.98.

The first observations of enamel caries were normally made at the age of 18 months while the number of caries onsets normally reached their maximum when the subjects were 4–5 years old. In the final child population, which included both the xylitol-treated subjects and the comparison subjects, a total of 156,254 tooth surfaces were examined during the entire follow-up of up to 7 years. There were, in total, 568 enamel and 319 dentine onsets of caries, respectively, during this period. The total number of fillings was 368. However, the treated and the comparison groups differed significantly from each other regarding the number of onsets of caries and the need to fill cavities. These results are summarised below in the next section.

The total numbers of carious teeth plotted as a function of the age of the children are shown in *Figure* 2 in the form of a box plot. The treated and the comparison groups started to differ significantly at the age of approximately 2 years, while the greatest differences were observed at the ages of 5, 6 and 7 years. The differences between the groups were also remarkable when enamel caries and dentine caries were analysed separately (*Figures* 3 and 4). In both instances, the box plots showed clear differences between the groups at the age of approximately 2–3 years, the differences generally increasing by the age of 7 years. Results of a similar nature were obtained when the number of fillings was plotted *versus* time (*Figure* 5); the need for tooth filling was significantly greater in the comparison group than in the xylitol swabbing group. Xylitol swabbing especially protected the occlusal surfaces of molars. The most vulnerable molar surfaces in this child population were (in decreasing order) occlusal, mesial and distal surfaces of the mandible (data not shown). The most vulnerable incisor sites were maxillary distal and mesial surfaces (data not shown).

The statistical differences between the groups, shown in terms of relative risk and 95% confidence intervals values, are presented in *Figure* 6 separately for the total number of teeth attacked by caries, the number of enamel caries surfaces, the number of dentine caries surfaces and the number of tooth fillings acquired during the experiment. *Table* 3 summarises the statistical data and includes the significance levels between groups. These data indicate that the xylitol swabbing of the deciduous teeth had significantly reduced the risk of caries attack in the present child cohort.

Gender differences became evident when the children were approximately 5 years and older. In this child population, boys in general benefited from the xylitol experimentation more effectively than girls (gender by group interaction effect on number of carious teeth, $P = 0.0035$, $P = 0.0005$ and $P = 0.0237$ at ages 5, 6 and 7 years, respectively). In summary, the rate of caries in deciduous teeth of the present comparison group subjects at ages 5–7 years appeared to reflect the normal incidence of caries of children at these ages in this location. The rate of caries was significantly lower in the xylitol swabbing group.

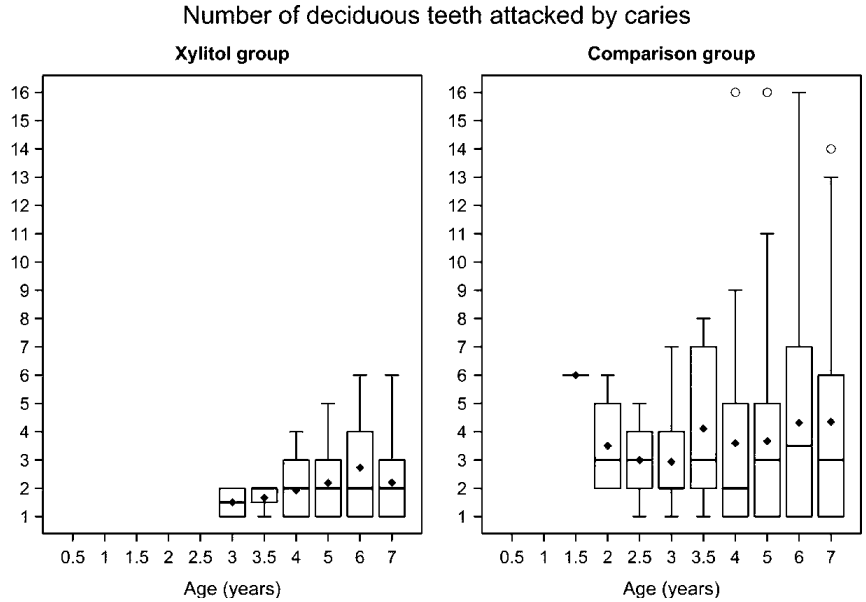

Figure 2. The number of carious deciduous teeth in the xylitol-treated group and in the comparison group as a function of the age of the subjects. The box plot shows the 25th and the 75th percentiles, the medians, the whiskers (25th–1.5 *quartile range and 75th + 1.5 *quartile range) and the outlying points. The relative risk (95% confidence intervals) values are shown in *Figure* 6 for ages 5, 6 and 7 years, and are summarised in *Table* 3 for all events at ages from 3 to 7 years. The asterisk means that the quartile range must be multiplied by 1.5.

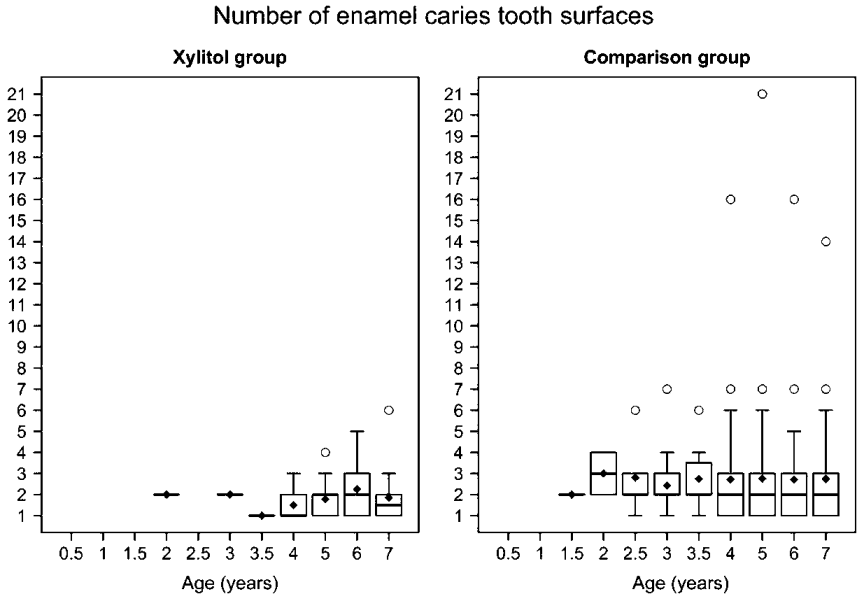

Figure 3. The number of deciduous tooth surfaces attacked by enamel caries in the xylitol-treated and in the comparison groups as a function of the age of the subjects. The box plot shows the 25th and the 75th percentiles, the medians, the whiskers (25th–1.5 *quartile range and 75th + 1.5 *quartile range), and the outlying points. The relative risk (95% confidence interval) values are shown in *Figure* 6 for ages 5, 6 and 7 years, and are summarised in *Table* 3 for all events at ages 3–7 years.

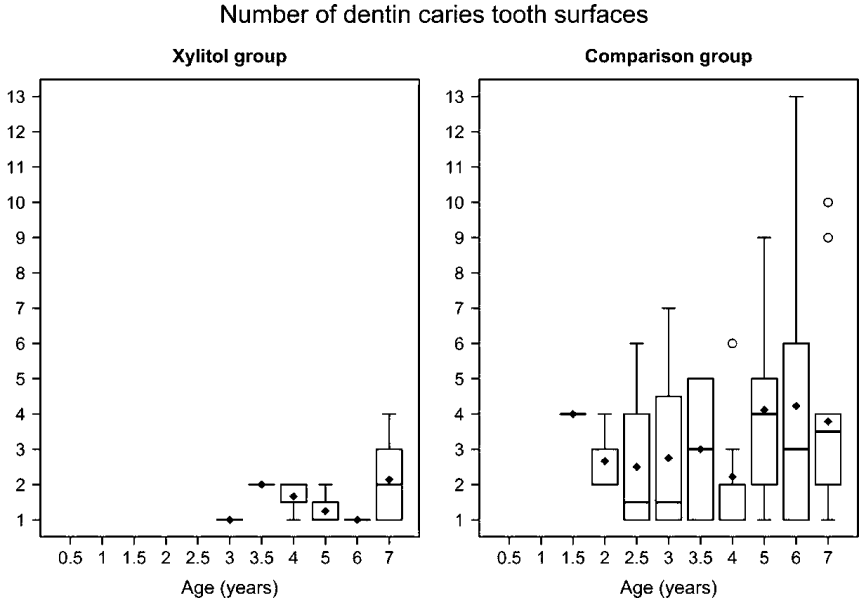

Figure 4. The number of deciduous tooth surfaces attacked by dentine caries in the xylitol-treated and in the comparison groups. The box plot shows the 25th and the 75th percentiles, the medians, the whiskers (25th–1.5 *quartile range and 75th + 1.5 *quartile range), and the outlying points. The relative risk (95% confidence interval) values are shown in *Figure* 6 for ages 5, 6 and 7 years, and are summarised in *Table* 3 for all events at ages 3–7 years.

Oral counts of MS

Results of plaque and whole-mouth saliva MS studies carried out during the first 48 months are summarised in *Figure* 7. Both MS counts started to differ significantly after the age of approximately 24 months. Lower salivary and plaque bacterial counts occurred consistently in the group that had received topical xylitol treatment at home until the age of approximately 48 months.

DISCUSSION

Finnish Health Centre policy guarantees the chief dental officer of each centre the authority to introduce new, established prevention and treatment procedures to clients. In Finland, the use of xylitol in the prevention of dental caries enjoys the status of an official procedure recommended by government health-care authorities, the Finnish Dental Association and several

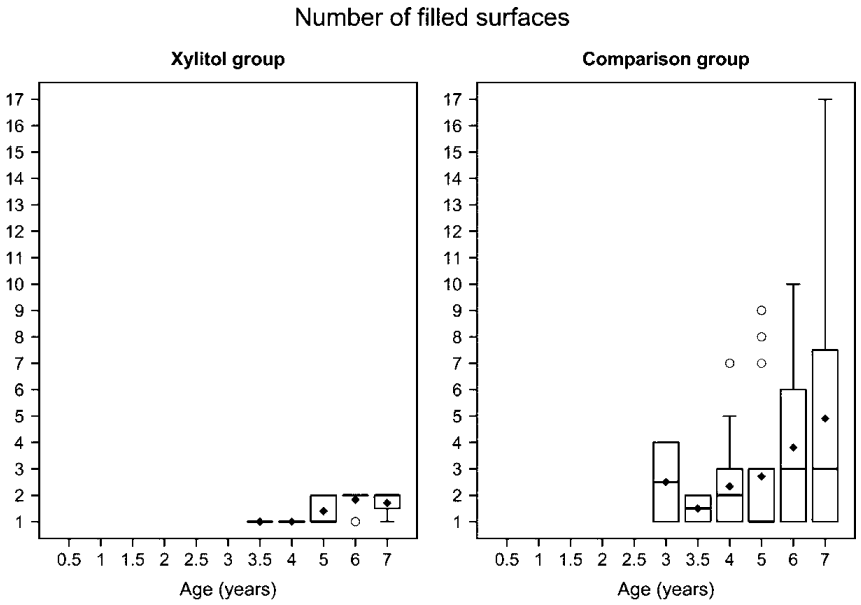

Figure 5. The number of deciduous tooth surfaces filled because of caries in the study groups as a function of the age of the subjects. The box plot shows the 25th and the 75th percentiles, he medians, the whiskers (25th–1.5 *quartile range and 75th + 1.5 *quartile range), and the outlying points The relative risk (95% confidence interval) values are shown in *Figure* 6, and are summarised in *Table* 3 for all events at ages 3–7 years.

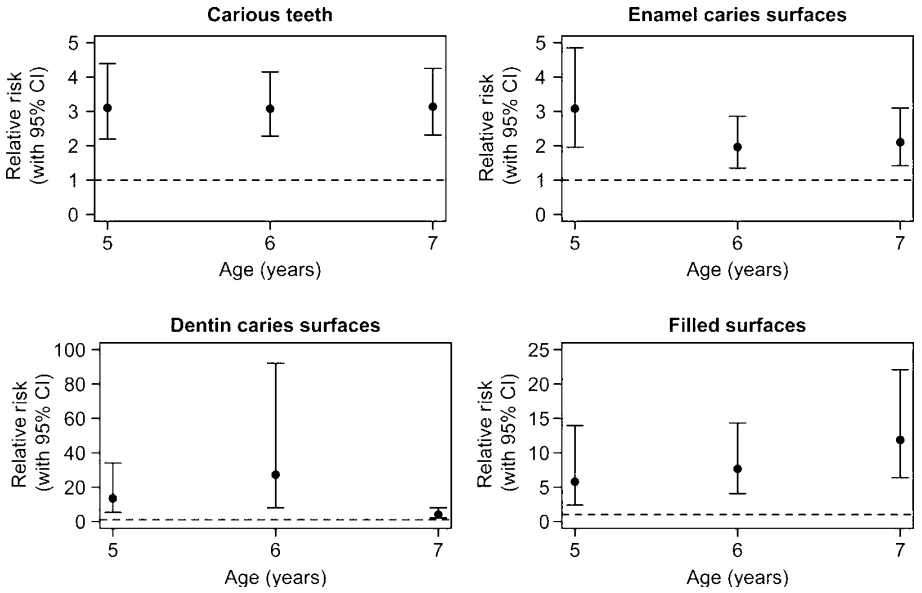

Figure 6. Summary of the relative risk (RR) with their 95% confidence interval for events presented in *Figures* 2–5 at ages 5, 6 and 7 years. A RR > 1 indicates a higher number of caries or filled tooth surfaces in the comparison group compared to the xylitol-treated group.

other public welfare-oriented associations active in medical or dental fields. The ordinance issued by the authorities requests that dental care personnel recommend the use of xylitol as a supplementary caries-prevention procedure. The recommendations have not gone beyond advising the use of products available at regular supermarkets and a xylitol solution similar to the one used in this experiment is not commercially available anywhere. However, based on the experience of this study, commercialisation of such a product should be relatively simple. The xylitol solution used was made in water without any additives, such as preservatives, as concentrated xylitol solutions normally resist bacterial growth. In possible future applications it may be necessary to add a preservative, or possibly mineral salts that contribute to remineralisation or other oral health-promoting agents. In the present experiment, the sweet taste of the xylitol solution most likely facilitated its administration to infants.

Table 3 The relative risk (RR) with 95% confidence interval (CI), and the *P*-values for group difference (comparison *vs*. xylitol-treated group) at different ages of the subjects

Age (years)	Event	RR	95% CI	*P*
3	Number of carious teeth	6.97	2.84–17.09	<0.0001
	Number of enamel caries surfaces	7.37	2.62–20.78	0.0002
4	Number of carious teeth	4.83	3.13–7.44	<0.0001
	Number of enamel caries surfaces	4.58	2.68–7.84	<0.0001
5	Number of carious teeth	3.10	2.19–4.39	<0.0001
	Number of enamel caries surfaces	3.08	1.96–4.85	<0.0001
	Number of dentine caries surfaces	13.47	5.33–34.03	<0.0001
	Number of filled tooth surfaces	5.79	2.40–13.96	<0.0001
6	Number of carious teeth	3.08	2.28–4.15	<0.0001
	Number of enamel caries surfaces	1.96	1.35–2.86	0.0004
	Number of dentine caries surfaces	27.22	8.05–92.11	<0.0001
	Number of filled tooth surfaces	7.65	4.08–14.34	<0.0001
7	Number of carious teeth	3.14	2.31–4.25	<0.0001
	Number of enamel caries surfaces	2.10	1.42–3.10	0.0002
	Number of dentine caries surfaces	4.01	2.02–7.98	<0.0001
	Number of filled tooth surfaces	11.86	6.37–22.10	<0.0001

The figures shown compare the xylitol-treated children with the comparison group subjects regarding the number of deciduous teeth attacked by caries (enamel, dentine or deep caries), the number of enamel caries surfaces, the number of dentine caries surfaces and the number of tooth fillings, respectively. The corresponding box plots are shown in *Figures* 2–5. Dentine caries values are shown for ages 5, 6, and 7 years only, owing to the small number of dentine caries events in younger children. For the same reason, the values for filled deciduous tooth surfaces are shown only when the children were 5, 6, or 7 years old. A RR > 1 indicates a higher number of caries or filled surfaces in the comparison group compared to the xylitol-treated group.

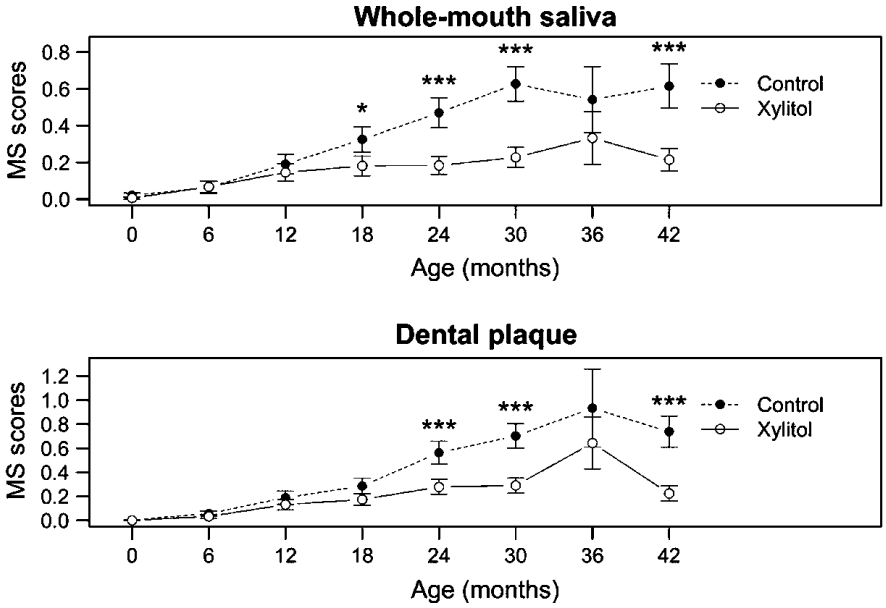

Figure 7. Development of oral mutans streptococci (MS) scores as a function of the age of children whose parents applied 45% xylitol solution once or twice a day on children's available tooth surfaces. The values shown are means ± SEM of bacterial scores determined according to the instructions of the manufacturer of the test kits. The number of subjects in both groups ranged from 60 to 100 depending on point in time. The differences between treatment and comparison groups were significant as shown: $*P < 0.05$, $***P < 0.001$.

In accordance with the original objective and the pre-agreements involved, this effort was *a priori* designed as a health-centre-imposed demonstration experiment that could not meet the criteria set for controlled clinical trials – a large number of such caries trials and laboratory studies with xylitol have been carried out during the past 40 years or more (reviews in refs. 27, 30). The present demonstration programme thus benefited from the established non-cariogenicity of xylitol. It was developed as the health centre's own innovation to test, under real-life circumstances, the feasibility of a new xylitol application procedure with the potential to be recommended for home use to expand families' opportunities to improve infant oral health. The results obtained suggest that considerable additional caries prevention can be achieved by topical administration of a concentrated xylitol solution onto the surfaces of the

deciduous teeth of young children. The clinical success of this type of prevention effort implemented in homes presumes parents' far-sightedness and commitment. The relatively high dropout rate indicates that some parents were not ready to adhere to all of the requirements of the long-term experiment. Upon the termination of the experiment, the study subjects reached their early pre-school years or became first-graders of area public schools. School programmes have shown that significant further health promotion can be achieved by means of long-term use of xylitol-containing chewing gums and hard caramels[22,27,31–33]. The results obtained suggest that topical xylitol administration could be incorporated into a caries-prevention strategy in a manner similar to the way in which xylitol was included in a 'multiple-measures' programme[34].

This experiment was characterised by shortcomings that should be taken into consideration in similar future efforts. Although the group assignment was primarily conducted systematically, it is possible that some of the families that declined the offer to begin the topical xylitol application, but were willing to participate in the comparison group, were clients who generally responded poorly to public health-care services. It is possible that parents who consented to participation in the treatment group, were generally more health conscious. However, all participating families experienced the experiment as an encouragement to pay attention to oral health; the families in both groups shared approximately the same experience regarding the type of services offered by the health centre. It transpired that the relatively frequent 6-month recalls maintained heightened interest in dental health within most families. The groups also did not differ appreciably in terms of xylitol use within families.

A further shortcoming of the present report may be the lack of information on the caregivers' precise socioeconomic background. It has been shown previously[35] that the early MS colonisation in preschool children is strongly associated with the socioeconomic status of the family, and that children's oral health is strongly related to the lifestyle of their caregivers[36]. However, the caregivers' occupation was known to the health centre and the groups did not differ in this regard. A more detailed investigation into each family's circumstances was viewed as intrusive in this experiment. Another shortcoming may be the lack of accurate information about tooth brushing and snack habits within the families; the intervention group parents may have engaged in more regular tooth brushing habits than the parents of the comparison group. The mere application of xylitol may have maintained regular tooth brushing, although exactly the same tooth brushing instructions were given to the parents in both groups. The possibility of application of only water with Q-tips or toothbrushes in the comparison group was rejected before the programme's start, because of the inappropriate nature of such a requirement in the present environment. However, as stated above, the objective of the experiment was to deliberately explore possible additional dental benefits among the users of the topical xylitol programme in normal family situations, and to compare the outcomes with non-users. The xylitol-using cohort benefited from the experiment under the conditions of the study. Milgrom & Chi[37] have presented specific prevention-centred caries management strategies for clinical interventions targeted at infants, which should be considered in future experiments.

As the information in *Table* 2 suggests, some parents regarded the topical xylitol procedure as somewhat difficult. The use of a toothbrush was favoured over Q-tips. A child's toothbrush should perhaps be recommended as a primary vehicle for possible commercialised xylitol solutions as parents normally oversee their children's tooth brushing anyway. The compliance of about 20% of the families in implementing xylitol swabbing was regarded as poor despite the simultaneously available free dental care services. Within these families, even twice-a day brushing of their children's teeth, or controlling older children's own brushing efforts, did not systematically materialise in a long-term programme. Bailey *et al.*[38] concluded that self-report paper diaries have questionable feasibility as a compliance data collection tool and that prompt compliance analysis is advisable. In the present experiment, the contents of the returned diaries were promptly acknowledged with requests for continued compliance. As this effort was a demonstration programme that exploited families' voluntary participation and observance of normal health-centre routines, no special compliance (trial) personnel could be employed. This issue should receive robust attention in similar future programmes.

The dropout rate in this follow-up was somewhat difficult to assess because some subjects did not show up for all 6- or 12-month examinations. The most important recordings of presence of caries were obviously carried out at ages of 5, 6 and 7 years, when the number of children examined in both groups ranged between approximately 80 and 106. If the age of 7 years is regarded as the endpoint of the entire experiment, the final participation percentage in the intervention group was about 60. However, important observations were also obtained at earlier ages when the dropout rate was smaller. The groups also differed significantly at the age of 4 years when approximately 85% of the children in the xylitol group were regarded as actively participating. Considering the length of the up to 7-year family-centred effort (of

which approximately 26–28 months required daily xylitol treatments), the extent of participation may be regarded as satisfactory.

The theoretical quantity of xylitol administered onto the tooth surfaces could be readily evaluated based on the amount of the concentrated xylitol solution used. However, the actual amount of xylitol that came in contact with the tooth surfaces and the bacterial integuments in each case cannot be accurately determined as the infants' salivation may have diluted the xylitol solution. Therefore, the maximum figure shown (up to 13.5 mg xylitol per tooth and per day) applies to situations where all deciduous teeth were present and the administration was impeccably performed. It is estimated that the actual quantities of xylitol that chemically affected each deciduous tooth and its bacterial coverings, were in some instances smaller than 13.5 mg.

The decline in xylitol-associated caries activity in the treatment group compared with the untreated subjects may be regarded as normal. Various xylitol programmes have generally resulted in large reductions in caries compared with the consumption of a regular sugar-based diet (for a review see ref. 27). In this sense, the experiment did not yield new results concerning the effects of xylitol *per se*. However, the present follow-up effort was the first of its kind where infants systematically received relatively small quantities of xylitol directly on tooth surfaces. As this delivery of xylitol did not presume mastication (i.e. so-called salivary effects) because mere physical contact with the tooth enamel and the oral biofilm was involved, the results may be regarded as supporting the role of generic xylitol as a pharmacologically acting agent in the prevention of caries in the deciduous dentition. The MS observations were also in accord with previous 40-year experience: the use of xylitol is associated with lower bacterial scores compared with the comparison group. Recent Japanese MS tests in preschoolers[39] support these results and underscore a pandemic involvement of MS in dental caries. The present results also strongly underline the importance of the participation of entire families in disseminating proper oral health habits in children. Further, the diminished need for tooth filling (*Figure 5*) in the treated subjects supports the claim that this type of programme could bring economic benefits. The use of xylitol chewing gum was found to be as effective as fissure sealants[22]. Topical administration of xylitol may be considered relatively cost-effective as manufacturing of the 100 ml xylitol lots can cost only a few Euros. The potential of dental-protecting chewing gums in oral health interventions has also been recognised[40] and xylitol-containing 'Gummy-bear' snacks have been shown to effectively prevent caries in small children[41].

The experience gathered during the course of this study suggests that concentrated xylitol solutions (or syrups) could also be used in custom-made mouthpieces. Experience has shown that even a few minutes' exposure of fissures, pits and gingival margin areas to xylitol can result in beneficial oral biological effects (in terms of reduced plaque acidity and increased remineralisation potential), provided that such applications are repeated frequently or become habitual. The present Orion Diagnostica MS test was found suitable for this type of long-term follow-up implemented at a dental office.

In summary, most families participating in the xylitol swabbing experiment related positively to the overall health promotion effort organised by the public health centre. An unfortunately high number of families failed to comply with the required daily procedures that were considered relatively easy to manage, even when the use of the xylitol solution could be combined with regular tooth brushing. It is possible that child-care centres could share part of the oral health education with parents. Several Finnish child-care centres have implemented their own oral health promotion by handing out xylitol-containing saliva stimulants as part of lunch meals. The long-term commitment required from the families and the laborious efforts of the clinic personnel may explain why the present type of data can be regarded as rare (one of the first efforts to study the composition of infants' whole-mouth saliva was carried out almost 30 years ago)[42]. Overall, this experiment showed that the oral health of the xylitol-treated children improved during the follow-up years and that programmes similar to the present one could possibly be modified to encompass parents who lack motivation to oversee their children's dental health. Dental caries and enamel demineralisation are multifactor disease processes and their inhibition requires proactive interventions before more extensive treatment becomes necessary[43].

Oral diseases in general are not a niche area of health and as soon as this is recognised, lasting progress can be made[44]. It is possible that the present type of joint health centre/home programmes as a supplement to existing comprehensive prevention could help contribute to this goal. This demonstration was not designed to elucidate possible differences between polyols as caries-limiting agents (a valid scientific study object[45,46]), as the current Finnish Health Centre practice calls for the use of xylitol-containing dental adjuvants. The present results support the recent conclusions on the caries- or MS-reducing effects of xylitol in young children and adults[47–53]. It should be noted that the xylitol concentrations used in this programme were much lower than the 5- to 7.5-g daily doses found to be well-tolerated by 6- to 36-month-old infants[54].

Conflicts of interest

None declared.

Acknowledgements

The authors are indebted to J. E. Viitanen, U-M. Vuorinen, and M. K. Halonen for skilful technical assistance. The Public Health Centre and Health Board of the town of Uusikaupunki provided the physical environment and the facilities required for this experiment, which is acknowledged with gratitude.

REFERENCES

1. Petersen PE, Bourgeois D, Ogawa H *et al.* The global burden of oral diseases and risks to oral health. *Bull World Health Organ* 2005 83: 661–669.
2. Pickett FA. Nonfluoride caries-preventive agents: new guidelines. *J Contemp Dent Pract* 2011 1: 469–474.
3. Söderling E, Isokangas P, Pienihäkkinen K *et al.* Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants. *J Dent Res* 2000 79: 882–887.
4. Söderling E, Isokangas P, Pienihäkkinen K *et al.* Influence of maternal xylitol consumption on mother–child transmission of mutans streptococci: 6-year follow-up. *Caries Res* 2001 35: 173–177.
5. Thorild I, Lindau B, Twetman S. Effect of maternal use of chewing gums containing xylitol, chlorhexidine or fluoride on mutans streptococci colonization in the mothers' infant children. *Oral Health Prev Dent* 2003 1: 53–57.
6. Thorild I, Lindau B, Twetman S. Salivary mutans streptococci and dental caries in three-year-old children after maternal exposure to chewing gums containing combinations of xylitol, sorbitol, chlorhexidine, and fluoride. *Acta Odontol Scand* 2004 62: 245–250.
7. Isokangas P, Söderling E, Pienihäkkinen K *et al.* Occurrence of dental caries in children after maternal consumption of xylitol chewing gum, a follow-up from 0 to 5 years of age. *J Dent Res* 2000 79: 1885–1889.
8. Thorild I, Lindau B, Twetman S. Caries in 4-year-old children after maternal chewing gums containing xylitol, sorbitol, chlorhexidine, and fluoride. *Eur Arch Paed Dent* 2006 7: 241–245.
9. Nakai Y, Shinga-Ishihara C, Kaji M *et al.* Xylitol gum and maternal transmission of mutans streptococci. *J Dent Res* 2010 89: 56–60.
10. Aaltonen AS, Suhonen JT, Tenovuo J *et al.* Efficacy of a slow-release device containing fluoride, xylitol and sorbitol in preventing infant caries. *Acta Odontol Scand* 2000 58: 285–292.
11. Zhan L, Cheng J, Chang P *et al.* Effects of xylitol wipes on cariogenic bacteria in young children. *J Dent Res* 2012 91(Suppl. 7): 85S–90S.
12. Meurman P, Pienihäkkinen K, Eriksson A *et al.* Oral health programme for preschool children: a prospective controlled study. *Int J Paediatr Dent* 2009 19: 263–273.
13. Köhler B, Andréen I, Jonsson B. The earlier the colonization by mutans streptococci, the higher the caries prevalence at 4 years of age. *Oral Microbiol Immunol* 1988 3: 14–17.
14. Fujiwara T, Sasada E, Nima N *et al.* Caries prevalence and salivary mutans streptococci in 0–2-year-old children in Japan. *Community Dent Oral Epidemiol* 1991 19: 151–154.
15. Straetemans MM, Van Loveren C, De Soett JJ *et al.* Colonization with mutans streptococci and lactobacilli and the caries experience of children after age of five. *J Dent Res* 1998 77: 1851–1855.
16. Laitala M, Alanen P, Isokangas P *et al.* A cohort study on the association of early mutans streptococci colonisation and dental decay. *Caries Res* 2012 46: 228–233.
17. Köhler B, Andréen I. Influence of caries-preventive measures in mothers on cariogenic bacteria and caries experience in their children. *Archs Oral Biol* 1994 39: 907–911.
18. Anttonen V, Halunen I, Päkkilä J *et al.* A practice-based study on the effect of a short sucrose/xylitol exposure on survival of primary teeth caries-free. *Int J Paediatr Dent* 2012 18: 124–130.
19. Pienihäkkinen K, Jokela J, Alanen P. Assessment of caries risk in preschool children. *Caries Res* 2004 38: 156–162.
20. Isokangas P, Alanen P, Tiekso J *et al.* Xylitol chewing gum in caries prevention: a field study in children at caries-active ages. *J Am Dent Assoc* 1988 117: 315–320.
21. Isokangas P, Mäkinen KK, Tiekso J *et al.* 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: 495–498.
22. Alanen P, Holsti M-L, Pienihäkkinen K. Sealants and xylitol chewing gum are equal in caries prevention. *Acta Odontol Scand* 2000 58: 279–284.
23. Kovari H, Pienihäkkinen K, Alanen P. The use of xylitol chewing gum in kindergartens. A follow-up study in Savonlinna, Finland. *Acta Odontol Scand* 2003 61: 367–370.
24. Nordblad A, Suominen-Taipale L, Murtomaa H *et al.* Smart Habit Xylitol Campaign, a new approach in oral health promotion. *Community Dent Health* 1995 12: 230–234.
25. Honkala E, Rimpelä A, Karvonen S *et al.* Chewing of xylitol gum – a well-adopted practice among Finnish adolescents. *Caries Res* 1996 30: 34–39.
26. Honkala S, Honkala E, Tynjälä J *et al.* Use of xylitol chewing gum among Finnish schoolchildren. *Acta Odontol Scand* 1999 57: 306–309.
27. Mäkinen KK. Sugar alcohol sweeteners as alternatives to sugar with special consideration of xylitol. *Med Principles Pract* 2011 20: 303–320.
28. Petersen PE, Kwan S. Evaluation of community-based oral health promotion and oral disease prevention – WHO recommendations for improved evidence in public health practice. *Community Dent Health* 2004 21(Suppl.): 319–329.
29. Featherstone JDB. Delivery challenges for fluoride, chlorhexidine and xylitol. *BMC Oral Health* 2006 6(Suppl. 1): S8.
30. Mäkinen KK. Sugar alcohols, caries incidence, and remineralization of caries lesions. A literature review. *Int J Dent* 2010: 23p, 981072 doi: 10.1155/2010/981072.
31. Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention: results of a field study in Estonian children. *Community Dent Oral Epidemiol* 2000 28: 218–224.
32. Honkala E, Honkala S, Shyama M *et al.* Field trial on caries prevention with xylitol candies among disabled school students. *Caries Res* 2006 40: 508–513.
33. Shyama M, Honkala E, Honkala S *et al.* Effect of xylitol candies on plaque and gingivitis indices in physically disabled school pupils. *J Clin Dent* 2006 17: 17–21.
34. Hausen H, Seppä L, Poutanen R *et al.* Noninvasive control of dental caries in children with active initial lesions. A randomized clinical trial. *Caries Res* 2007 41: 384–391.
35. Meurman P, Pienihäkkinen K, Eriksson A *et al.* Mutans streptococci colonization associates with the occupation of caretaker, a practice-based study. *Int J Paediatr Dent* 2010 20: 144–150.
36. Meurman P, Pienihäkkinen K. Factors associated with caries increment: a longitudinal study from 18 months to 5 years of age. *Caries Res* 2010 44: 519–524.

37. Milgrom P, Chi DL. Prevention-centered caries management strategies during critical periods in early childhood. *J Calif Dent Assoc* 2011 39: 735–741.
38. Bailey DL, Campain AC, Tsao CE *et al.* Compliance in a school-based caries trial of a sugar-free chewing gum. *Contemp Clin Trials* 2011 32: 492–497.
39. Seki M, Karakama F, Kawato T *et al.* Effect of xylitol gum on the levels of oral mutans streptococci of preschoolers: a block-randomized trial. *Int Dent J* 2011 61: 274–280.
40. Ly KA, Milgrom P, Rothen M. The potential of dental-protective chewing gum in oral health interventions. *J Am Dent Assoc* 2008 139: 553–563.
41. Ly KA, Riedy CA, Milgrom P *et al.* Xylitol gummy bear snacks: a school-based randomized clinical trial. *BMC Oral Health* 2008 8: 20.
42. Ben-Aryeh H, Lapid S, Szargel R *et al.* Composition of whole unstimulated saliva of human infants. *Archs Oral Biol* 1984 29: 357–362.
43. Goldstep F. Proactive intervention dentistry: a model for oral care through life. *Compend Cont Edu Dent* 2012 33: 398–402.
44. Benzian H, Hobdell M. Guest Editorial: seizing political opportunities for oral health. *J Am Dent Assoc* 2011 142: 242–243.
45. Fontana M, Gonzáles-Cabezas C. Are we ready for definitive clinical guidelines on xylitol/polyol use? *Adv Dent Res* 2012 24: 123–128.
46. Mickenautsch S, Yengopal V. Effect of xylitol versus sorbitol: a qualitative systematic review of clinical trials. *Int Dent J* 2012 62: 175–188.
47. Milgrom P, Söderling EM, Nelson S *et al.* Clinical evidence for polyol efficacy. *Adv Dent Res* 2012 24: 112–116.
48. Shinga-Ishihara C, Nakai Y, Milgrom P *et al.* Xylitol carry-over effects on salivary mutans streptococci after 13 months of chewing xylitol gum. *Caries Res* 2012 46: 519–522.
49. Alamoudi NH, Hanno AG, Masoud MI *et al.* Effects of xylitol on salivary mutans streptococcus, plaque levels, and caries activity in a group of Saudi mother-child pairs. An 18-month clinical trial. *Saudi Med J* 2012 33: 186–192.
50. ElSalhy M, Sayed Zahid I, Honkala E. Effects of xylitol mouthrinse on *Streptococcus mutans*. *J Dent* 2012 40: 1151–1154.
51. Milgrom P, Zero DT, Tanzer JM. An examination of the advances in science and technology of preventing tooth decay in young children since the Surgeon General's Report on Oral Health. *Acad Pediatr* 2009 9: 404–409.
52. Campus G, Cagetti MG, Sale S *et al.* Six months of high-dose xylitol in high-risk caries subjects – a 2-year randomized clinical trial. *Clin Oral Invest* 2013, in press.
53. Milgrom P, Ly KA, Tut OK *et al.* Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy. *Arch Pediatr Adolesc Med* 2009 163: 601–607.
54. Vernacchio L, Vezina RM, Mitchell AA. Tolerability of oral xylitol solution in young children: implications for otitis media prophylaxis. *Int J Pediatr Otorhinolaryngol* 2007 71: 89–94.

Correspondence to:
Kauko K. Mäkinen,
Professor Emeritus,
Institute of Dentistry,
University of Turku,
Lemminkäisenkatu 2,
20520 Turku, Finland.
Email: kauko.makinen@uusikaupunki.fi