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DENTAL HEALTH IN PRIMARY TEETH AFTER PREVENTION OF MOTHER-CHILD TRANSMISSION OF MUTANS STREPTOCOCCI

A Historical Cohort Study on Restorative Visits and Maternal Prevention Costs

by

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ABSTRACT

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Dental Health in Primary Teeth after Prevention of Mother-Child Transmission of Mutans Streptococci. A Historical Cohort Study on Restorative Visits and Maternal Prevention Costs.

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Annales Universitatis Turkuensis

The study aimed to examine the long-term effects of the inhibition of early mutans streptococci (MS) colonization on the health and on the amount of restorative treatment of primary teeth in assumed high-caries-risk children. Furthermore, the costs of maternal use of xylitol in relation to the timing of children's dental decay were evaluated.

The annual data on the dental health, dental treatments and costs of maternal caries prevention were gathered from the files in Ylivieska Public Health Care Centre. Altogether 507 study subjects included 148 participants in the Ylivieska mother-child study, which had compared maternal use of xylitol with maternal chlorhexidine or fluoride varnish treatments in assumed high-caries-risk subjects.

The children who had not been colonized by MS at 2 years of age maintained their primary teeth as caries-free 3.4 years longer ($p<0.001$), had significantly lower caries experience in their primary teeth until 10 years of age, and needed less restorative treatment ($p=0.005$) in their primary teeth until 10 years of age than MS-colonized children. With the lowest MS colonization figures, the children in the xylitol group had lower figures in caries experience and number of restorative treatment visits than the other two intervention groups. The costs of the maternal prevention programme with xylitol chewing gum were 116 euros; thus the costs for each additional caries-free year in the child were 37 euros. The prevention of MS transmission reduced caries occurrence figures in assumed high-risk children to the same level as the average figures for the whole age cohort.

The inhibition of early MS colonization seems to lead to long-term effects on caries experience and need for restorative treatment in primary teeth, and may offer a new strategy for control of caries in public dental care. The maternal use of xylitol chewing gum in children's caries prevention might be cost-effective when the xylitol chewing gum is purchased in large wholesale amounts by the public dental care.

Key words: mutans streptococci, colonization, dental decay, xylitol, long-term effects, costs

TIIVISTELMÄ

Marja-Liisa Laitala

Mutansstreptokokkitartunnan ehkäisemisen pitkäaikaisvaikutukset maitohampaiden terveyteen. Kohorttitutkimus korjaavan hoidon määrästä ja kariesehkäisyn kustannuksista.

Sosiaalihammaslääketiede, Hammaslääketieteen laitos, Turun yliopisto
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Tutkimuksen tarkoituksena oli selvittää varhaisen mutansstreptokokki (MS)-kolonisaation ehkäisyn pitkäaikaisvaikutuksia korkean kariesriskin omaavien lasten maitohampaistossa sekä tarkastella MS-tartunnan estämisen kustannuksia.

Tiedot lasten hampaiden terveydestä ja hammashoitotoimenpiteistä syntymästä 10-vuotiaaksi sekä äiteihin kohdistuneen kariesehkäisyn kustannuksista kerättiin Ylivieskan terveyskeskuksen asiakirjoista. Tutkimuksessa oli mukana yhteensä 507 lasta, heistä 148 oli osallistunut aikaisempaan Ylivieskan äiti-lapsitutkimukseen, jossa verrattiin äitien käyttämän ksylitolipurukumin ja äidille tehtyjen fluori- tai klooriheksidiinilakkausten vaikutusta pikkulasten hampaiden terveyteen.

Maitohammaskariesta esiintyi 10-vuotiaaksi asti merkitsevästi vähemmän lapsilla, jotka eivät olleet saaneet MS-tartuntaa alle 2-vuotiaana, heidän maitohampaansa säilyivät 3,4 vuotta kauemmin täysin ehjinä ($p<0.001$) ja he tarvitsivat vähemmän maitohampaiden korjaavaa hoitoa ($p=0.005$) kuin lapset, joiden hampaisto oli kolonisoitunut MS-bakteerilla jo 2-vuotiaana. Koska ksylitoliryhmän lasten MS-kolonisaatio oli vähäisintä, heidän maitohampaissaan oli vähemmän kariesta ja korjaavan hoidon tarvetta kuin kahden muun korkeariskisen ryhmän lapsilla. Äitien käyttämän ksylitolipurukumin kustannukset olivat yhteensä 116 euroa ja lapsen maitohampaiden säilyminen täysin ehjinä vuoden pidempään maksoi 37 euroa. Kun MS-tartunta oli saatu estettyä, korkean kariesriskin omaavien lasten hampaiden terveys oli samalla tasolla kuin keskimäärin koko ikäkohortilla.

Lapsen maitohampaat säilyvät terveinä pidempään ja korjaavan hoidon tarve vähenee, kun MS-kolonisaatio alle 2-vuotiaana saadaan estettyä. Lapsen MS-kolonisaatio vähenee merkitsevästi, kun äiti käyttää ksylitolipurukumia lapsen ollessa 0-2 vuoden ikäinen, siten pikkulapsen äidin säännöllinen ksylitolipurukumin käyttö saattaa olla julkisen terveydenhuollon kannalta tarkoituksenmukainen terveyttä edistävä menetelmä.

Avainsanat: mutans streptokokki, kolonisaatio, karies, ksylitoli, pitkäaikaisvaikutukset, kustannukset

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LIST OF ABBREVIATIONS

ANOVA	analysis of variance
ARR	absolute risk reduction
CFU	colony forming units
Chx	chlorhexidine
CI	confidence interval
dmfs	number of decayed, missing and filled tooth surfaces in primary teeth
DMFS	number of decayed, missing and filled tooth surfaces in permanent teeth
dmft	number of decayed, missing and filled primary teeth
DMFT	number of decayed, missing and filled permanent teeth
dt	number of decayed primary teeth
FDI	World Dental Federation
HR	hazard ratio
Md	median value
mo	month(s)
MS	mutans streptococci
NNT	number needed to treat
n.s.	not significant
PF	prevented fraction
p(p).	page(s)
ppm	parts per million
SBU	Swedish Council on Technology Assessment in Health Care
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
VAT	value-added tax
vs	versus
WHO	World Health Organization
WMA	World Medical Association
yr	year(s)
€	euro(s)

1. INTRODUCTION

Dental diseases, including dental caries, are among the most common and resources-demanding diseases in industrialized countries, albeit also highly preventable. Caries prevention in infants has mostly consisted of counselling parents about oral-health-promoting feeding behaviours, and teaching oral hygiene, with varying success. As early childhood caries greatly affects the quality of life of children the delay or inhibition of dental decay among infants is of significant importance.

At present, in Finland, as well as in other Scandinavian countries, budgets for health and social services have been put under pressure, and there is an increasing demand for reducing public spending. After enaction of the law on Guaranteed Access to Treatment in 2005 in Finland, the lack of resources in public dental care has increased, and the need for cost-effective prevention strategies has become even more obvious.

Söderling, Isokangas and co-workers carried out the Ylivieska mother-child study at the Ylivieska Public Health Care Centre in the beginning of the 1990s (Söderling *et al.* 2000, Isokangas *et al.* 2000). They investigated mutans streptococci (MS) transmission from mother to child and infants' caries occurrence after maternal use of xylitol chewing gum compared with biannual maternal fluoride or chlorhexidine varnish treatments. The children in the xylitol group were significantly less often MS-colonized and had less dental caries until 5 years of age than the children in the fluoride and chlorhexidine groups. On the basis of the results of this study, it is of interest to assess the long-term clinical effects of early MS colonization and the economic aspects of maternal use of xylitol chewing gum in the inhibition of MS transmission from mother to child.

2. REVIEW OF THE LITERATURE

2.1 Caries prevention

The prevalence of dental caries among children decreased from the 1970s to the 1990s in Finland, as in most developed western countries (reviewed by Petersson and Bratthall 1996). The mean DMFT levels among 12-year-olds in these countries achieved the World Health Organization's global standard of 3.0 for the year 2000 already in the 1990s (Marthaler *et al.* 1996, Marthaler 2004). At the beginning of the 1990s, the average dmft among 5-year-old Finnish children was reported to be 1.4, and 60% of the children of this age were caries-free (von der Fehr 1994). However, from the 1990s on, in several industrialized countries including Finland, the decline in average caries figures has levelled off, and the majority of caries lesions have concentrated in a small proportion of children (reviewed by Winter 1990 and Hicks and Flaitz 1993, Marthaler *et al.* 1996, Vehkalahti *et al.* 1997, Meriläinen 2004). Recently, a tendency towards increasing caries figures among Finnish adolescents was reported by Suni *et al.* (2008).

Generally, prevention of a disease can be divided into primary, secondary, and tertiary prevention. Primary prevention consists of measures that are applied before any signs of a disease have developed. Secondary prevention aims to promote recovery, to avoid terminal consequences, and to prevent recurrence of a disease, whereas tertiary prevention consists of rehabilitation and therapeutic treatments. In dentistry, primary prevention of dental caries aims to maintain intact dentitions while secondary prevention consists of measures applied after the first signs of caries are already present, e.g. fluoride varnish treatments or oral hygiene and diet counselling for subjects with white spot lesions on teeth enamel. Tertiary prevention of dental caries consists, e.g. of restorative treatment measures. In addition, the concept 'primary-primary prevention' of dental caries has been used to mean maternal use of caries-preventive measures to maintain the health of the infants' dentitions, e.g. by preventing the transmission of cariogenic bacteria from mother to child (Günay *et al.* 1998).

Preventive measures can be aimed at the whole population or can be targeted to groups or individuals. The most important population-based caries prevention strategies have been the regular use of fluoride toothpastes, the fluoridation of tap water, and oral health education. Other widely applied preventive strategies, which during the last decade have been aimed mostly at high-caries-risk individuals, are the use of fluorides as tablets, gels, mouth rinses and varnishes; the use of chlorhexidine in mouth rinses, gels and

varnishes; fissure sealants; and the use of sugar substitutes such as xylitol and sorbitol in chewing gums and lozenges. It has been suggested that in countries where caries has a highly skewed distribution there should be a shift from population-based prevention to a high-risk strategy (Messer 2000). By targeting prevention to those individuals most in need, the scarce resources could be allocated efficiently. However, Burt (1998, 2005) and Seppä (2001) argued that in Scandinavia, as well as in other countries with low caries incidence, population-based prevention is still needed, together with targeted preventive measures. Even though a high-risk prevention strategy can produce interventions directed to individuals most in need and may offer cost-effective use of resources, it also has disadvantages. First, the difficulties and costs of screening may be considerable. Second, the high-risk prevention strategy is behaviourally inappropriate; general life-style customs and social norms are required (Rose 2001). A social environment with a positive attitude towards twice-a-day tooth-brushing and an oral-health-related diet also encourages high-caries-risk people to follow caries prevention instructions. According to Wang (1998), in Nordic countries, dentists in Norway and Sweden in the 1990s applied mainly risk-based preventive strategies in the dental care of children and adolescents, while dentists in Denmark and Iceland preferred population-based strategies. In all these four countries, caries had the same kind of declining tendency during the last decades of the 20th century, although the resources used and the costs of prevention varied (Wang 1998).

The methods for caries prevention have been studied intensively for decades, but disagreement on the effects and efficiency of different prevention measures and methods still exist, and the practices in caries prevention in dental health care vary. Especially, the effects of prevention strategies concerning primary dentitions have not been well demonstrated. The systematic review of the Swedish Council on Technology Assessment in Health Care (SBU 2002) suggested that the evidence of the effectiveness of fluorides in caries prevention was well established. The daily use of fluoridated toothpaste effectively prevented caries in the permanent teeth of children and adolescents, but the effect on primary teeth had not been shown. However, the authors did not find any evidence that fluoridated toothpaste would be ineffective in primary teeth. In addition, the preventive effect of biannual fluoride varnish treatments on permanent teeth had been demonstrated, but the evidence of the effect on primary teeth was insufficient (SBU 2002). Similar conclusions on the effects of fluoride varnish and fluoride toothpaste treatments were reported in the Cochrane systematic reviews (Marinho *et al.* 2002, 2003). The recent systematic review of Ismail and Hasson (2008) reported that the evidence for the use of fluoride supplements in the prevention of dental caries in primary teeth was weak and inconsistent. In the absence of studies concerning primary dentition, the Scottish

Intercollegiate Guidelines Network (SIGN 2005) explorated the evidence also for primary teeth and recommended twice-a-day tooth-brushing for pre-school children. In addition, repeated fluoride varnish treatments were recommended for pre-school children at increased risk of caries. The clinical recommendations for pre-school children given by The American Dental Association Council on Scientific Affairs (2006) were in the line with the opinion of the SIGN.

2.1.1 Xylitol

Xylitol is a five-carbon sugar alcohol and a naturally occurring polyol sweetener. It is found in fruits, seaweed, and in exudates of plants and trees, as well as being a normal intermediate in human carbohydrate metabolism. The first human studies concerning xylitol in caries prevention were carried out in the 1970s in Turku, Finland (Scheinin and Mäkinen 1976). An impressive reduction in caries incidence (prevented fraction, PF>85%) was found among the subjects who consumed the xylitol diet for two years, when compared with the subjects consuming a sucrose diet. In addition, it was shown that total substitution of sucrose with xylitol is not needed for caries reduction. After one-year habitual xylitol chewing gum consumption, significant reductions (PF>80%) in dental decay when compared with sucrose chewing gum were reported (Scheinin and Mäkinen 1976). Since then, the caries-preventive effect of xylitol has been demonstrated in various clinical studies, and the evidence that xylitol chewing gum and sweets reduce caries experience in adolescence and adults is well established. The preventive effect on caries occurrence has been demonstrated with a daily xylitol dosage of 0.8 g (Kandelman and Gagnon 1987, 1990) to 10 g (Isokangas 1987). As calculated from the original data of the studies, PF has varied from 21% (Machiulskiene *et al.* 2001) to 88% (Mäkinen *et al.* 1995), PF indicating the proportion of decay and/or fillings avoided due to xylitol usage. In addition to the preventive effect, it has been suggested that xylitol might also have a remineralizing effect. This suggestion has been based on the observations of rehardening of caries lesions, and results with a negative caries increment in the xylitol groups (Kandelman and Gagnon 1990, Mäkinen *et al.* 1995, 1998, Honkala *et al.* 2006).

The collaborative WHO field studies in Hungary (Scheinin and Bánóczy 1985) and French Polynesia (Kandelman *et al.* 1988) on school children demonstrated reductions in caries incidence after habitual use of xylitol gums and sweets. Both these studies were carried out in high caries prevalence circumstances. In the field study of Isokangas (1987) with 11- to 12-year-olds in a low caries area Ylivieska, Finland, two years' regular consumption of xylitol chewing gum with a daily xylitol dose of 7–10 g resulted

in a significant caries reduction (PF 30–57%), when compared with the no-gum group. After three years' consumption by the high-caries-risk children, the corresponding caries reduction was even higher (PF 59–84%). The results of the trial of Kandelman and Gagnon (1987, 1990) carried out in Canada, with 8- to 9-year-olds were in good agreement with the Ylivieska study; with 0.8–3.4 g daily xylitol consumption the prevented fractions after two years were 61–66% when compared with no-gum controls.

The effectiveness of xylitol, sorbitol, xylitol-sorbitol mixture, and sucrose chewing gum was compared with a no-gum group in a clinical trial in Belize, Central America (Mäkinen *et al.* 1995). The 40-month double-blind study with 10-year-olds living in a low socio-economic and high caries society consisted of nine groups: four xylitol groups with a daily xylitol consumption of 4.3–9.0 g, two xylitol-sorbitol groups with a total daily polyol consumption of 8.0–9.7 g, one sorbitol group with a daily 9.0 g sorbitol dosage, a sucrose gum group, and a no-gum group. The four xylitol chewing gums reduced the caries rates most effectively, the 100% xylitol-sweetened pellet gum used five times a day being the most effective. The pellet chewing gum with a daily 8.5 g xylitol dosage resulted in negative caries increment, while the prevented fraction was 88% with the stick gum used five times a day and a 9.0 g daily xylitol dosage. The xylitol-sorbitol mixtures were more effective than sorbitol alone, but less effective than xylitol alone. (Mäkinen *et al.* 1995)

It has been claimed that the caries-preventive effect of xylitol chewing gum might be related to the chewing process rather than being a specific effect of xylitol. However, xylitol sweets were also reported to be caries-preventive in a field trial in Estonia (Alanen *et al.* 2000). At baseline 10-year-old children used either xylitol gum or two different sweets (xylitol-maltitol or xylitol-polydextrose mixtures) on school days with a daily 5 g xylitol dosage. After three years, all xylitol groups showed a reduction in caries incidence compared with control groups, prevented fractions being 37–61%. The results of the study on physically disabled school children and adolescents in Kuwait (Honkala *et al.* 2006) were in good agreement with the Estonian study, even though the period of use of xylitol sweets was shorter and the daily xylitol dosage lower. In that study, xylitol sweets were used three times a day for an 18-month period, the daily xylitol dosage being as low as 1.8 g. In the Belize study, Mäkinen *et al.* (1995, 1998) reported a 1.20 relative risk of caries when sucrose gum was compared with the no-gum group; the chewing did not protect against caries when sucrose was present. On the other hand, Machiulskiene *et al.* (2001) suggested that the results of their trial with xylitol and sorbitol chewing gums in Lithuania indicated that the caries-preventive effect of chewing sugar-free gum is related to the chewing process itself rather than being an effect of gum sweeteners or

additives. When doing so, the authors emphasized the significance of enamel caries in their results. However, when only the caries lesions extending to dentin were included in the analyses, a caries-preventive effect of xylitol was found even with the low (3 g) daily dosages (PF 36%, compared with no-gum group, and PF 21%, compared with control gum group) (Machiulskiene *et al.* 2001, Hayes 2002). These results were in line with earlier xylitol studies.

Most of the xylitol studies have concerned permanent teeth, and there is still a lack of information about the effect of xylitol on primary teeth. Only three of the xylitol studies have described caries prevention in primary teeth. In a two-year clinical trial on 6-year olds carried out by Mäkinen *et al.* (1996a), the usage of xylitol chewing gum resulted in a significant decrease in caries occurrence in primary teeth. The study children were at high risk of caries with poor oral hygiene and they had not received systematic caries prevention. Kovari *et al.* (2003) and Oscarson *et al.* (2006) studied the effect of xylitol on primary teeth in low-caries communities. In comparison with daily tooth-brushing in Finnish municipal day-care centres, xylitol chewing gum intervention caused a clinically small but statistically significant difference in caries incidence in favour of the xylitol group (Kovari *et al.* 2003). In Sweden, Oscarson *et al.* (2006) reported a tendency towards less caries experience with two-year use of xylitol lozenges when compared with the non-intervention group, although the difference was not statistically significant. The daily xylitol dosage in this study was very low; at baseline 2-year-old Swedish children used xylitol lozenges at a daily dosage of 0.5–1 g, while in the study of Kovari with 3- to 6-year-old children, the corresponding dosage was 2.5 g. Furthermore, the caries-preventive effect of xylitol has been demonstrated by maternal use of xylitol (Isokangas *et al.* 2000, Thorild *et al.* 2006); the children themselves did not use xylitol, thus the reduction of children's caries experience cannot be explained by the salivary-stimulating effect caused by gum chewing or the sucking of sweets.

2.1.1.1 Timing of use and long-term effects

The effectiveness of caries-preventive measures seems to be associated with the timing of the preventive treatment in relation to the development of dentition (Isokangas *et al.* 1989, Hujoel *et al.* 1999, Kowash *et al.* 2000, Ekstrand and Christiansen 2005). Isokangas *et al.* (1989) reported further caries reduction two to three years after discontinuation of the use of xylitol chewing gum compared with the no-gum control group. In the teeth which erupted during the first year of the use of xylitol gum, the long-term preventive effect was greater than in the other teeth. Several explanations were suggested: long-lasting

effect of the changes in the oral microbiota, bacterial colonization on newly erupted teeth by organisms other than MS, and favourable physico-chemical circumstances during the teeth maturation. Five years after the cessation of xylitol use, the difference in caries experience between the xylitol and control groups in favour of xylitol had further increased (Isokangas *et al.* 1993). Ten years after the beginning of the trial the children who used xylitol chewing gum for two to three years had 4.0 restored tooth surfaces, whereas those in the no-gum control group had 9.3 (Virtanen *et al.* 1996).

In the trial with 6-year-old children carried out by Mäkinen *et al.* (1996a) in Belize, five years after the cessation of habitual gum chewing, the caries risk had decreased by 59% in the xylitol chewing gum group and 44% in the xylitol-sorbitol gum group compared with the no-gum controls (Hujoel *et al.* 1999). The effect of sorbitol gum was not significantly different from no-gum. The long-term effect of xylitol strongly depended on when the teeth had erupted. The results of Hujoel *et al.* (1999) supported the findings of Isokangas *et al.* (1989). In Finland, some of the study children continued the xylitol usage after the trial; the xylitol and control groups did not, however, differ significantly as regards the use of xylitol after the intervention (Isokangas *et al.* 1989, 1993). In Belize, post-experimental use of xylitol was not possible (Hujoel *et al.* 1999). It has been suggested that to maximize the long-term caries-preventive effect, the habitual use of xylitol chewing gum should be started at least one year before the eruption of permanent teeth (Hujoel *et al.* 1999).

2.1.1.2 Recommendations and statements

Clinical trials indicate that xylitol has a clear caries-preventive effect which is superior to the effects of other studied polyol sugar substitutes (reviewed by Tanzer 1995, Maguire and Rugg-Gunn 2003). According to the reviews of Hayes (2001), Burt (2006), and Deshpande and Jadad (2008), the scientific evidence is strong enough to support the regular use of xylitol-sweetened gum in caries prevention, and it can be promoted as a public-health preventive measure. However, opposite opinions do exist (Scheie and Fejerskov 1998, van Loveren 2004). According to the statement of The Swedish Council on Technology Assessment in Health Care (SBU 2002), the scientific evidence of the caries-preventive effect of xylitol as well as sorbitol as sugar substitutes in chewing gums and lozenges is still insufficient. The National Institutes of Health Consensus Development Conference statement (2001) in the United States and the Scottish Intercollegiate Guidelines Network (SIGN 2005), believe that there is substantial experimental evidence of the cariostatic effect (i.e. inhibition or arrest of caries) of xylitol. According to the recent policy statement of the World Dental Federation (FDI

2008), 'xylitol has a role to play in preventing dental caries because of its non-cariogenic nature and its salivary stimulating effect'. Additionally, in the European Food Safety Authority statement (2008), the scientific evidence of the effect of xylitol chewing gum on reducing caries risk in children was pronounced. In 2009, the Standing Committee/ General Food Law of the European Union unanimously accepted xylitol chewing gum as a dental-health-promoting product claiming 'chewing gum sweetened with 100% xylitol has been shown to reduce dental plaque. High content/level of dental plaque is a risk factor in the development of caries in children' (Act 1024/2009 of the European Union).

2.2 Mutans streptococci

2.2.1 Mutans streptococci and caries

Dental caries is regarded as a transmissible bacterial infectious disease which is modified, e.g. by a carbohydrate-rich diet, low saliva flow, and low oral pH conditions (reviewed by van Houte 1994, Marsh 2004, 2006, Selwitz *et al.* 2007). Dental plaque as a structurally organized biofilm has a diverse microbial composition, which in health remains relatively stable (microbial homeostasis). Fermentable carbohydrates such as sucrose are catabolized to acids which acidify plaque biofilms. Regular and frequent exposure to low pH conditions can break down the microbial homeostasis and lead to the enrichment of acidogenic and aciduric species such as mutans streptococci and lactobacilli. This process predisposes teeth surfaces to dental caries (reviewed by Selwitz *et al.* 2007). In addition, sucrose can also be metabolized to extracellular glucans that contribute to the plaque biofilm matrix (Banas and Vickerman 2003).

Mutans streptococci (MS), the most significant species of which are *Streptococcus mutans* and *S. sobrinus*, have widely been regarded as the principal bacteria responsible for dental caries in humans (de Stoppelaar *et al.* 1969, Loesche *et al.* 1975, Masuda *et al.* 1979, reviewed by Loesche 1986 and van Houte 1994). There is strong evidence that MS have a central role in the initiation of caries on the smooth surfaces and fissures of the teeth of adults and children, and a potent role in the aetiology of root surface caries (reviewed by Loesche 1986 and Tanzer *et al.* 2001). In young children, the risk of caries has been shown to be greater the earlier the MS colonization takes place in the mouth (Alaluusua and Renkonen 1983, Köhler *et al.* 1984, 1988). Several studies have indicated a strong relationship between the colonization level by MS and caries experience in the primary dentition (Aaltonen *et al.* 1985, Holbrook *et al.* 1989,

Weinberger and Wright 1989, Alaluusua *et al.* 1989, Tenovuo *et al.* 1990, Fujiwara *et al.* 1991, Thibodeau and O'Sullivan 1996, Autio 2002, Ge *et al.* 2008). Kopycka-Kedzierawski and Billings (2003) reported that low salivary MS levels at baseline have a significant effect on the longer survival times for the primary, mixed and permanent dentition. They concluded that caries-free children who had high salivary MS levels at baseline would be at greater risk of caries occurrence at any given time than caries-free children with lower baseline salivary levels of MS. Some current studies suggest that caries is not caused by MS "exclusively", and MS colonization is regarded more as an indicator of a cariogenic environment (reviewed by Marsh 2003, Beighton 2005). According to the review of Thenisch *et al.* (2006), the presence of MS either in the plaque or saliva of young caries-free children is associated with an increase in caries risk. Recently, Takahashi and Nyvad (2008) suggested that high MS proportions in oral microbiota may be biomarkers of rapid caries progression. The occurrence of demineralization of tooth enamel without any detection of MS has also been reported (Marsh *et al.* 1989), and a reduction in the levels of MS or plaque reduction does not necessarily result in caries reduction (Forgie *et al.* 2000, Dasanayake *et al.* 2002).

2.2.2 Virulence factors of mutans streptococci

The important virulence factor of MS is their ability to adhere to host surfaces (reviewed by Law *et al.* 2007). Adhesins from *S. mutans* and *S. sobrinus* interact with salivary proteins causing the sucrose-independent initial adherence to salivary pellicle (Lamont *et al.* 1991, reviewed by Jenkinson and Lamont 1997). The extracellular polysaccharides, glucans, are crucial for the sucrose-dependant bacterial adherence and colonization of MS. They increase the thickness of the biofilm on teeth surface, enhancing the acid production at deeper levels of the biofilm (van Houte *et al.* 1989).

The acidogenity and the acidurance of MS allow them to survive at low pH conditions and significantly promote their cariogenicity (Hamilton and Buckley 1991, Köhler *et al.* 1995). The ability of *S. mutans* (but not *S. sobrinus*) to produce intracellular polysaccharides permits continual acid production during the periods of low dietary carbohydrate concentration. This property contributes to tooth enamel demineralization even when the salivary secretion is low during sleep (van Houte *et al.*1989).

2.2.3 Xylitol and mutans streptococci

One of the most important mechanisms of the action of xylitol is most probably its non-fermentability. Oral micro-organisms are not able to transform xylitol into acids.

In addition, xylitol inhibits the growth and metabolism of MS. Knuuttila and Mäkinen (1975) were the first to show that xylitol inhibits the growth of MS *in vitro*. Since then, the mechanism of this inhibition has been studied by several research groups (reviewed by Maguire and Rugg-Gunn, 2003), and new reports on it have been published recently (Miyasawa-Hori *et al.* 2006). Naturally occurring, so-called 'xylitol-resistant' MS cells are not inhibited by xylitol (reviewed by Trahan 1995). Habitual xylitol consumers harbour higher counts of these 'xylitol-resistant' cells when compared with non-consumers (Trahan *et al.* 1992), but the clinical importance of this phenomenon is still to be shown. Some studies suggest that these cells could have reduced virulence properties (reviewed by Trahan 1995), but in the comparison of several virulence properties of MS *in vitro* no differences were detected between 'xylitol-resistant' and 'xylitol-sensitive' cells (Assev *et al.* 2002).

Xylitol, pulsed in a mixed culture of oral bacteria, prevented the enrichment of *S. mutans*, whereas sorbitol had the opposite effect (Bradshaw and Marsh 1994). Until recently (Modesto and Drake 2006), no extensive studies concerning the effect of xylitol on biofilm formation have been published.

The ability of xylitol to reduce the amount of MS in plaque and in saliva has been demonstrated under various experimental conditions in both short-term and long-term studies (Loesche *et al.* 1984, Mäkinen *et al.* 1989, Söderling *et al.* 1989, 1991, Miyasawa *et al.* 2003, Thaweboon *et al.* 2004, Haresaku *et al.* 2007). Already in the late 1980s, it was suggested that there is a dose and frequency effect in the MS reduction (Mäkinen *et al.* 1989, Isokangas *et al.* 1989). This relationship between xylitol chewing gum daily dosage, as well as daily frequency, and MS levels was thoroughly investigated by Milgrom and Ly *et al.* (Milgrom *et al.* 2006, Ly *et al.* 2006). A linear reduction in MS was found with xylitol amounts up to 6.88 g per day. Daily dosages of 6.88 g and 10.32 g reduced MS levels in plaque after five weeks, and after six months in plaque and saliva. Furthermore, after five weeks, a linear-response relationship between the increasing frequency of xylitol chewing gum use and the MS level reduction was reported. It was concluded that daily amounts exceeding 10 g are unlikely to increase the effectiveness of xylitol, while 3.4 g or less are not likely to show changes in MS levels, and a frequency of three times a day or more is necessary for effectiveness. Recent studies from Sweden have also shown that low doses and low consumption frequencies did not reduce MS (Stecksén-Blicks *et al.* 2004), while three daily intakes with a daily dose of 6.18 g did (Holgerson *et al.* 2007).

So far, both *in vivo* and *in vitro* studies suggest that MS seem to be the only oral target organisms of xylitol (Vadeboncoeur *et al.* 1983, Loesche *et al.* 1984, Bradshaw and Marsh 1994). Interestingly, in some long-term studies, MS counts determined from paraffin-stimulated saliva remained at baseline levels throughout the study in spite of the continuing xylitol consumption (Mäkinen *et al.* 1995, Söderling *et al.* 2000). Xylitol consumption appears to reduce the ability of MS to adhere to the teeth and render them easily shed into saliva from plaque, thus disrupting the correlation of MS commonly found in plaque and saliva (Söderling *et al.* 1991, Trahan *et al.* 1992). This could explain why habitual xylitol consumers show high MS counts in stimulated saliva (Mäkinen *et al.* 1996b, Söderling *et al.* 2000) but low counts in resting saliva (Milgrom *et al.* 2006).

2.3 Transmission of oral streptococci

2.3.1 Time of colonization and transmission of mutans streptococci

The first streptococci which colonize the oral cavity of the newborn infant during the first days of life are *S. mitis*, *S. oralis*, and *S. salivarius* (Smith *et al.* 1993, Pearce *et al.* 1995). The other two streptococci, *S. sanguinis* and *S. mutans* colonize the oral cavity later, at approximately 1 to 2 years of age, during the active erupting phase of the first primary teeth (Caufield *et al.* 1993, 2000). The consistency of the first oral pioneer microbiota influences the pattern of later microbial colonization. Caufield *et al.* (2000) reported colonization of *S. sanguinis* occurring at a median age of 9 months in infants. They found that early colonization of *S. sanguinis* in infants results in later colonization of MS, and this may have an influence on dental caries control. It is suggested that the harbouring of MS in the primary dentition leads to their colonization in the permanent dentition (Emanuelsson and Thornqvist 2000).

It is widely believed that tooth eruption is needed for MS to permanently colonize the mouth (Catalanotto *et al.* 1975, Berkowitz *et al.* 1975, Masuda *et al.* 1979, reviewed by Loesche 1986). According to Caufield *et al.* (1993), MS is harboured during a defined period of the child's stage of development. This so-called 'window of infectivity' occurs at the age of between 19 and 31 months, with a median of 26 months. MS may be transiently harboured in the oral cavity already in early infancy, and MS colonization may occur even in predentate infants (Carlsson *et al.* 1975, Berkowitz *et al.* 1975, Wan *et al.* 2001a). In the study of Wan *et al.* (2001b) among Australian children, it was found that over 50% of pre-term and 60% of full-term edentulous infants were colonized with MS

at the age of 6 months. The oral microbiota of children seems to develop continuously. In the longitudinal study of Klein *et al.* (2004), some genotypes of MS persisted and some were lost during their 20-month follow-up of newborn infants. Infants with acrylic obturators after cleft palate management have been colonized by MS shortly after birth before tooth eruption (Berkowitz *et al.* 1975, van Loveren *et al.* 1998). This finding is in line with the notion that MS require solid non-shedding surfaces as their preferred colonization site (Carlsson *et al.* 1969, Berkowitz *et al.* 1975). Therefore, Karn *et al.* (1998) have suggested that prevention of MS colonization may need to be initiated prior to the child's first birthday.

Transmission of MS is believed to occur primarily vertically from mother to child (Berkowitz and Jordan 1975, Berkowitz *et al.* 1975, Berkowitz *et al.* 1981, Masuda *et al.* 1985, Caufield *et al.* 1993, Li and Caufield 1995, Emanuelsson *et al.* 1998, Lapirattanakul *et al.* 2008). However, there are studies which suggest that also father-child transmission can occur (Kozai *et al.* 1999, Ersin *et al.* 2004). According to the studies of Emanuelsson *et al.* (1998) in Sweden, and Tedjosasongko and Kozai (2002) in Japan, children can acquire MS both inside and outside the family. Mattos-Graner *et al.* (2001) reported in their study on 12- to 30-month-old Brazilian infants that also horizontal transmission of MS occurs between the children in kindergarten.

2.3.2 Prevention of transmission of mutans streptococci

In clinical trials targeting the inhibition of MS transmission from mother to child, and hence the prevention of the child's dental decay, all the prophylactic measures are carried out in the mothers, with the children themselves not receiving any intervention. Altogether 96 publications including the search terms 'dental caries', 'mother or maternal', and '*streptococcus mutans* or mutans streptococci' published between 1966 and June 2008 were found in the Medline database. Of those, 11 were reviews. After the three publications in Chinese as well as the one in Dutch were excluded, altogether 12 original MS transmission studies concerning maternal caries prevention (primary-primary prevention) were found (Table 1, pp. 34-35). In addition, one study reported a decline in the MS levels of mothers after xylitol intervention, but no results of the MS or caries levels of the children were shown in that study (Nakai *et al.* 2005).

There is good evidence that the early colonization of MS in infants can be inhibited by reducing the MS levels of the mothers. The length and timing of maternal intervention, as well as the need for dental resources for the different preventive strategies have varied greatly. In addition, reduced MS transmission has been demonstrated in different

socio-cultural environments and baseline caries levels. The Finnish and Swedish xylitol transmission studies (Söderling *et al.* 2000, 2001, Isokangas *et al.* 2000, Thorild *et al.* 2003, 2004, 2006) were carried out in low-caries communities, whereas baseline caries levels were high in Turkey (Türksel Dülgergil *et al.* 2004, Ercan *et al.* 2007). The inhibition of MS transmission has been achieved by chlorhexidine treatments (Tenovuo *et al.* 1992, Brambilla *et al.* 1998, Gripp and Schlagenhauf 2002), by xylitol chewing gum (Söderling *et al.* 2000, Thorild *et al.* 2003), and also by combined caries prevention programmes (Köhler *et al.* 1983, Günay *et al.* 1998, Gomez *et al.* 2001, Türksel Dülgergil *et al.* 2004, Ercan *et al.* 2007).

Köhler *et al.* (1983, 1984, 1988) reported delayed MS colonization, later caries occurrence, and less dental decay in young children whose mothers' MS salivary levels had been reduced by caries-preventive strategies. These strategies included diet and oral hygiene instructions, professional tooth cleaning, topical fluoride and chlorhexidine application, and excavating large caries lesions. The preventive strategies started when the babies were 3 to 8 months old, and discontinued once the babies were colonized by MS. The study ran until the children were 3 years old, but still at the age of 7 years, favourable long-term effects on children's MS colonization and caries occurrence were found (Köhler *et al.* 1994). The proportion of MS carriers was lower among the children of the treated mothers than in the control group. In addition, the number of children without caries experience, as well as the mean caries experience was significantly lower among the study children when compared with the controls. Also in the studies of Söderling *et al.* (2001) and Thorild *et al.* (2006), a similar long-term effect could be observed, although the follow-up period did not extend as far as in the study of Köhler *et al.* (1994).

In the study carried out by Tenovuo *et al.* (1992), mothers who were highly colonized by MS were treated with chlorhexidine (1%) - sodium fluoride (0.2%) gel twice a year for three years during the teeth eruption of their children. MS colonization of the children's primary dentition at the age of 3 and 4 years was delayed and even prevented when compared with both 'high MS' and 'low MS' control groups. The association of MS colonization with caries occurrence was significant, but differences in caries occurrence between the study groups were not found, most probably due to the low caries level among Finnish infants. A similar effect on MS colonization was reported in the study of Brambilla *et al.* (1998) by using sodium fluoride combined with chlorhexidine. The pregnant mothers began to rinse daily with 0.05% sodium fluoride and 0.12% chlorhexidine at the end of the sixth month of pregnancy and continued until delivery. The bacterial levels of the children were measured every six months until the age of 24

months. Rinsing with sodium fluoride together with chlorhexidine significantly reduced salivary MS levels in pregnant mothers and delayed the colonization of MS in their children for about four months. No analysis of the caries occurrence of children was reported.

In a transmission study with high MS-level mothers carried out by Gripp and Schlagenhauf in Germany (2002), the mothers of young infants received 40% chlorhexidine varnish applications after professional tooth cleaning at three-month intervals. At the beginning of the trial, all the children were edentulous, the age of the children varying from 20 to 137 days. As the study continued until the child was 2 years old, the total duration of the intervention varied. A significantly lower number of MS-colonized 2-year-old children were found in the chlorhexidine treatment group when compared with the untreated controls.

In Germany, an individual preventive programme with oral hygiene and diet counselling, professional tooth cleaning, topical fluoride and chlorhexidine rinsing, starting at pregnancy, with biannual recalls after delivery, resulted in significant differences in MS colonization and caries occurrence in 4-year-olds compared with non-treated controls. In addition, the oral health of the mothers was also improved (Günay *et al.* 1998). The results are in line with the studies carried out in rural Turkey (Türksel Dülgergil *et al.* 2004, Ercan *et al.* 2007). The authors suggested that the reduction in MS levels of mothers by preventive and operative caries treatments combined with fluoride and chlorhexidine rinsing effectively reduced both MS colonization and caries incidence of their infants until the age of 4 years. In Chile, a special preventive programme aimed at avoiding or minimizing the transmission of MS from mother to child showed a significant reduction of dental caries in 5-year-olds in Chile (Gomez and Weber 2001, Gomez *et al.* 2001). The programme started during pregnancy and continued every six months, including oral hygiene and diet counselling, as well as preventive and restorative treatment in mothers. However, the dropout rate was remarkably high, less than 30% of the mothers originally enrolled being available for the last analyses.

Topical applications of antibacterial agents may reduce the transmission of oral MS from mother to child, but this does not necessarily result in less caries. Dasanayake *et al.* (1993) carried out a randomized clinical trial where six applications of sodium fluoride or placebo solution were applied to the mothers' dentition at the time of tooth eruption of her infant. Both the study subjects and the controls received the necessary restorative treatment, while in the study of Köhler *et al.* (1983, 1984), restorative treatments were performed only on the study group. Among the 3-year-old children

in the trial of Dasanayake *et al.* (1993), the incidence of MS colonization and the time of acquisition of MS or caries experience did not differ significantly between the study and control group. The authors concluded that short-term application of fluoride to the maternal dentition of predentate infants significantly lowers MS in mothers' saliva, but does not influence the incidence and the time of acquisition of MS or the caries experience in children. The lack of effect on children's MS and caries levels has also been reported after 10% chlorhexidine varnish applications (Dasanayake *et al.* 2002). Chlorhexidine varnish was applied to the mothers for the first time when the babies were 6 months, and the application was repeated weekly, altogether four times. Subsequent applications were carried out at six-month intervals. This intervention did not significantly alter the MS colonization in children or the caries increment in either the mother or the child. However, maternal salivary MS levels in the treatment group remained significantly lower compared to the control group up to 12 months after the initial application.

2.3.2.1 Transmission studies with xylitol in Sweden and Japan

Thorild *et al.* (2003, 2004, 2006) carried out a transmission study in Sweden with 173 participating mothers with high levels of MS (CFU≥150 000/ml). Their screening with the MS strip test was carried out when the babies were 3 months old. Mothers in the first (xylitol) group used chewing gum containing xylitol as the only sweetener, those in the second group used chewing gums containing chlorhexidine, xylitol and sorbitol, whereas the chewing gums in the third study group contained sodium fluoride, xylitol, and sorbitol. The daily xylitol dosages were 2.0 g, 1.6 g and 0.9 g, respectively. All study groups started to use chewing gum for five minutes three times per day when their infants were 6 months old and continued until the age of 18 months. In the 3-year-old children of mothers who used high-content xylitol gums compared with those who used lower amounts of xylitol, lower but non-significant levels of salivary MS and dental decay were observed. However, at 4 years of age, the occurrence of dental decay was significantly lower among the children in the high-xylitol-content group than in the other groups. A tendency towards a dose-response relationship was reported, and it was concluded that infants' early MS colonization can be inhibited even with low daily xylitol dosages.

In Japan, pregnant mothers with high MS levels used xylitol chewing gum from the sixth month of pregnancy until their child was 9 months old. After the first three months of the intervention, 47.7% of the study group mothers and 13.8% in the non-chewing gum control group showed low levels of MS. Both groups had received professional

tooth cleaning and oral hygiene counselling, the daily dosage of xylitol being ca. 5 g (Nakai *et al.* 2005). Recently, the children in the xylitol chewing gum group were reported to be significantly less colonized by MS (at the age of 9-24 months) and they had acquired MS later than those in the control group (Nakai *et al*. 2010).

2.3.3.2 Ylivieska mother-child study

Söderling, Isokangas and co-workers carried out a clinical study at the Ylivieska Public Health Care Centre in the beginning of the 1990s (Figure 1, p. 28). The study aimed to explore the effects of maternal xylitol use on mother-child transmission of MS, and on the children's risk of future caries development. At the beginning of the study, 338 pregnant women were screened for salivary MS by strip test (Orion Diagnostica®). Altogether 195 women with high levels of MS (CFU≥100 000/ml) were invited to participate in the study. Of those, 120 were randomly assigned to the xylitol gum group, 32 to the chlorhexidine group, and 36 to the fluoride group. In addition, seven mothers who had been daily xylitol chewing gum users were assigned to the xylitol group. The mothers in the xylitol group were recommended to chew xylitol gum two to three times a day with a 6-7 g daily dosage of xylitol. The gum chewing started when the infants were 3 months old and continued for altogether 21 months. The chewing gum contained xylitol as the only sweetener (65% w/w). In the chlorhexidine and fluoride groups, the mothers received 40% chlorhexidine (EC 40®) or fluoride (Duraphat®) varnish applications at 6, 12 and 18 months after delivery. Only the mothers were treated, the children's teeth were not treated with varnish and no chewing gum was given to them.

The microbiological results were reported when the children were 2 and 6 years old (Söderling *et al.* 2000, 2001) and the clinical results of the annual examinations when the children were 5 years old (Isokangas *et al.* 2000). At the age of 2 years, a statistically significant reduction in the mother-child transmission of MS in the xylitol chewing gum group was reported. The children's risk of MS colonization was five-fold in the fluoride group and three-fold in the chlorhexidine group when compared with the xylitol group. The first caries experience occurred later in non-MS-colonized children than in the MS-colonized in all study groups. The children in the xylitol group showed significantly less total caries than those in the chlorhexidine and fluoride groups; prevented fraction of caries in the xylitol group was 74% compared with the chlorhexidine group, and 71% compared with the fluoride group (Isokangas *et al.* 2000; Tables a and b in the Appendix with the permission of the copyright owner and the authors).

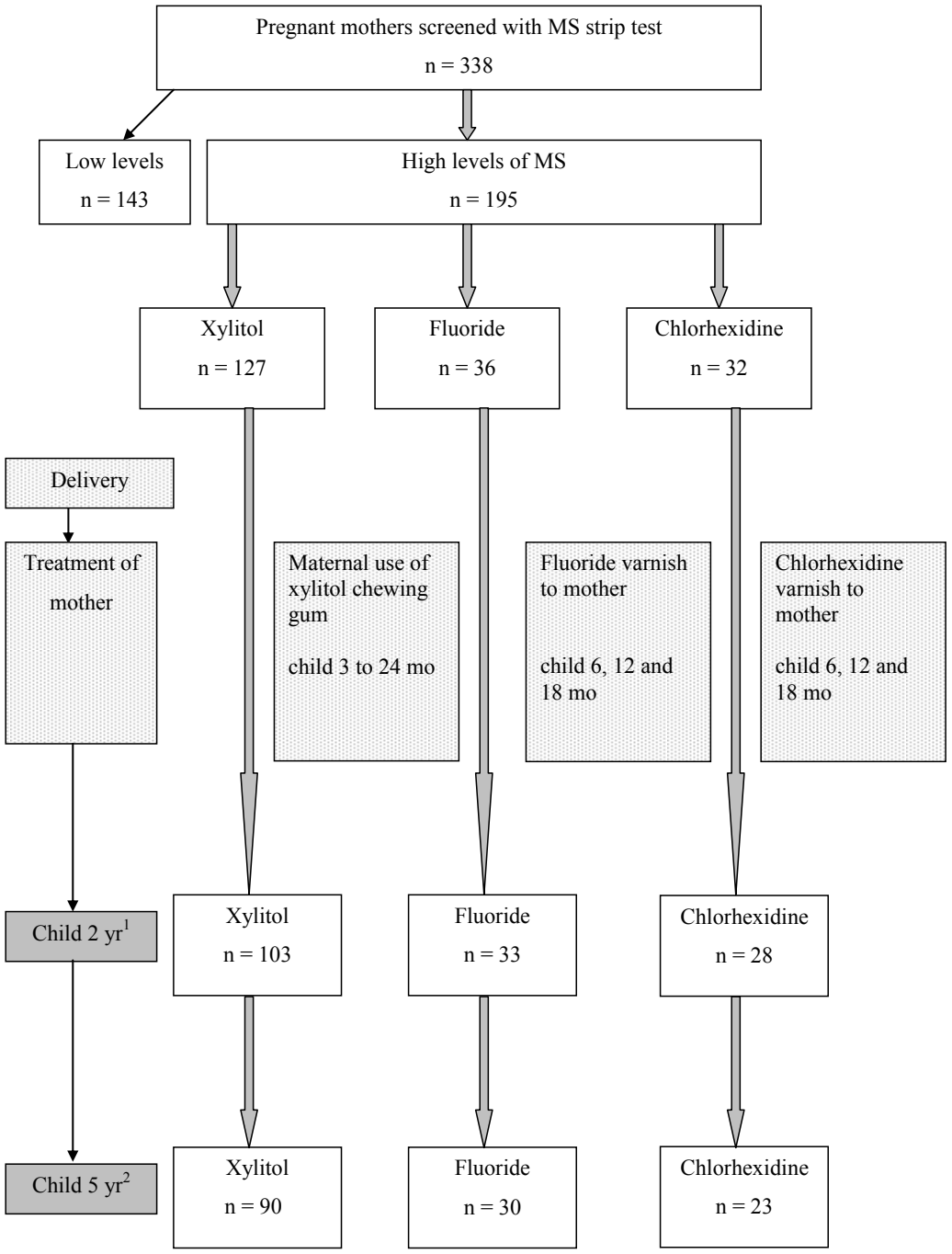
In spite of the high MS counts in stimulated saliva the mothers showed throughout the study, the mother-child transmission of MS in the xylitol group was significantly reduced. The total MS counts of the mothers were most probably reduced by the habitual xylitol consumption, and the unstimulated saliva involved in salivary contacts between the mother and the child actually contained reduced MS counts. Another possibility is that because the MS of the xylitol consumers were easily shed into saliva, this had also reduced the ability of the MS to colonize the teeth of the child. In fact, it has been shown that xylitol consumption is associated with a reduction in adhesive glucans of plaque (Mäkinen *et al.* 1985). The high MS colonization figures of the children in the fluoride varnish group were in good accordance with earlier published studies (Berkowitz *et al.* 1981, Köhler *et al.* 1983). According to the authors, the unexpectedly high percentage of MS colonization within the chlorhexidine group children could be due to the relatively long intervals between the varnish treatments, and a higher frequency of chlorhexidine varnish treatments might have improved the results. Due to the small size of the chlorhexidine group, the authors did not recommend drastic conclusions to be drawn. The confounding effects of infants' feeding practices, dietary habits in the family or type of day-care on MS colonization were reported to have been minimal. (Söderling *et al.* 2000)

There were some methodological problems in the Ylivieska mother-child study. First, the examiners were not calibrated as regards caries registrations. Secondly, no power analysis had been carried out when estimating the needed study samples. Third, in most cases, the examiners knew or could remember the group of the mother (xylitol, chlorhexidine or fluoride). Therefore, they might have registered the clinical status of the children's teeth in a biased manner. The authors of the study discussed these problems in the original studies as follows:

The calibration of the examiners was not possible due to practical obstacles. However, most of the examiners, who were experienced clinicians, had earlier been calibrated, and their inter- and intra-examiner variations had been analysed in association with the earlier clinical caries prevention trial with xylitol (Isokangas 1987, Isokangas *et al.* 1988). The variations had been found to be on an acceptable level. As regards the power analysis, this was the first mother-child transmission study ever carried out with xylitol. Therefore, it was not possible to calculate or estimate in advance the size of the needed groups because there were no hints as regards the clinical effect. The lack of blinding between the study groups was an obvious problem. However, due to the fact that there were no earlier studies, none of the examiners had any possibility to guess the clinical result beforehand. What is more convincing is that all the examiners,

clinicians, mothers and children were absolutely blinded as regards the presence of MS in the children's dentitions at the age of 2 years. The colonization analyses had been carried out at the University of Turku, 600 kilometres away from Ylivieska, totally blinded, and without telling the results of these analyses to anyone in the Ylivieska Health Care Centre during the clinical phase of the study. It is not possible for a clinician to see the colonization status of the dentition with the naked eye alone. The results revealed that within all groups, the children with MS at the age of 2 years had systematically more often dental decay than the children in the same study group without MS. The authors concluded that it had been impossible for the examiners to get systematic results of this kind without true differences between the study groups. (Isokangas *et al.* 2000)

Despite the methodological weaknesses, the results of the Ylivieska mother-child study can be considered reliable because the blinding was complete throughout the study as regards MS colonization, the key variable in the study. This practice-based study design reflected real-life circumstances in public dental care in Finland, even if carried out among assumed high-caries-risk subjects. In the evaluation of the Ylivieska mother-child study, the level of the evidence has been evaluated to be good (Anderson and Hujoel 2001, Den Besten and Hujoel 2001). Additionally, the results of the randomized controlled studies of Thorild *et al.* (2003, 2004, 2006) in Sweden were in line with the Ylivieska mother-child study.



[1] Microbiological examination
[2] Report of annual caries occurrence in children

Figure 1. The schedule of the Ylivieska mother-child transmission study

2.4 Costs in relation to benefits in caries prevention

Two main problems exist in evaluation of the inputs or costs in relation to benefits in health care; measurement of costs and benefits and uncertainty of costs and benefits arising in the future. The costs can be direct or indirect costs, and intangible costs such as anxiety, pain, and unsightliness. Drummond (1980) suggested that when evaluating the costs in health care, all significant costs and outcomes must be identified regardless of whom they are focused on. The costs of health treatments do not all fall on the health service, in addition they fall on patients, their families, and other public sector agencies. Nor are the benefits from health treatments confined to the person receiving treatment. The public institution providing services should also pay attention to the costs of customers. Time spent travelling to the dentist, waiting and being treated, may involve a loss of productive output of patients. Another cost of dental care to patients is the fear, anxiety and possible pain, which is an important factor in comparing the costs of preventive and restorative treatment (Yule *et al.* 1986). When evaluating the costs in health care, the opportunity costs must also be taken into consideration. The opportunity cost is the value of the best alternative use of resources consumed by the intervention or programme (Weinstein 1981, Forbes and Donaldson 1987). If a resource is used for one purpose, it can not be used for another. Opportunity costs may be too high; even if a preventive measure is known to be effective it may be so expensive or time-consuming that it is not ethically right to use it. Weighing up the costs and benefits is especially important at the margin. The additional benefits and the additional resources allocated must critically be taken into account.

The benefits can be measured either in monetary or non-monetary units depending upon the selected economic analysis. In the case of preventive dentistry, non-monetary benefits can be measured, e.g. by dmft or DMFT indices (Gisselsson *et al.* 1994, Davies *et al.* 2003, Mariño *et al.* 2007), or by oral-health-related quality of life (Oscarson *et al.* 2007).

In health care programmes, costs and benefits typically do not occur at the same time. Particularly preventive care involves sacrifice of resources at the present time in order to achieve benefits even far in the future. The health conditions at the present time are generally considered more valuable than those in the future, while sickness or disadvantages in the future are not considered as harmful as at the present. Moreover, costs which are paid in the future seem to be lower than those paid at the present time. Discounting is used to compare benefits and costs occurring in different years, and the difference between the future value and the present value is determined by the rate of

discount. The discounting is different from adjusting for inflation; discounting derives from the idea that the value of one monetary unit (e.g. a euro) paid today is higher than one paid one year from now (Drummond 1980, Weinstein 1981, Tuominen 1994). The euro received now could be invested to yield more than one euro in a year's time. With the high discount ratio, the costs in the past have more impact on the total costs. In this situation, it is obvious that health benefits should also be discounted (Yule *et al.* 1986, Weinstein *et al.* 1996).

The proportion of economic evaluations in dentistry is small if health-care studies are considered as a whole. Most of the studies of cost-effectiveness of caries-preventive programmes have been based on clinical studies which were carried out before the 1990's when caries levels were relatively high compared with the levels over the past few years. When caries occurrence was high and affected the majority of the population, even modest prevention procedures led to substantial reductions in dental decay, and cost-effectiveness was not very important. Burt (1998) suggested that one response to altered caries distribution is the emergence of the targeting of prevention in a cost-effective manner. Moreover, Schwarz (1998) argued that almost any prevention would have been effective in caries reduction during the high caries prevalence period and he called for long-term economic evaluations of preventive strategies. Niessen and Douglass (1984) showed that the main caries-preventive measures vary markedly in the length of time to attain maximum effectiveness; about a year in the case of the school-based fissure sealant programme, up to five years for the school-based fluoride mouth rinsing programme, and nearer to ten years in the case of piped water fluoridation.

In their review based on systematic search, Källestål *et al.* (2003) concluded that there was no evidence in published economic evaluations of caries-preventive measures for the benefit of caries prevention. This review included 17 articles selected from 156 original research and reviews from 1966 to May 2003. The articles were judged in relation to their odontological as well as their health economic value. Of the studies evaluated, five concerned different kinds of preventive programmes, four fissure sealants, and seven fluoride interventions with fluoride tablets, varnish treatments, mouth rinsing, or water fluoridation. Additionally, one study concerned the use of chlorhexidine (Gisselsson *et al.* 1994), this study being the only one on the primary teeth. Gisselsson *et al.* (1994) analyzed the effect of chlorhexidine gel flossing on approximal caries incidence among 4-year-olds in Sweden. The children in the two study groups were treated four times a year with 1% chlorhexidine gel or placebo gel, while the control group got neither flossing nor gel treatment. The economic evaluation

was based on the total treatment time including gel flossing and necessary restorative treatments. The time required for the gel flossing treatment performed by a dental nurse, and for the restorative treatments performed by a dentist-assistant team were registered, and the average costs of the dental nurse and the dentist-assistant team for public dental care per hour were estimated. After three years, the mean incidence of approximal enamel and dentin caries lesions and the numbers of approximal fillings were significantly lower in the chlorhexidine gel flossing group than in the placebo-gel group and non-gel control group. More time was spent by the dentist-assistant team on the restorative treatment of the control group and, correspondingly, higher costs were observed in the control group.

By using the same search criteria as Källestål *et al.* (2003), 35 articles published from May 2003 to June 2008 were found in the Medline search. Only four of the original studies included cost evaluations of caries prevention on primary teeth; one concerning a fluoridated toothpaste programme (Davies *et al.* 2003), one milk-fluoridation (Mariño *et al.* 2007), and two early prevention programmes (Kobayashi *et al.* 2005, Kowash *et al.* 2006). In addition, the use of fluoride varnish was assessed using a model by Quinoñez *et al.* (2006).

A randomized controlled study by Davies *et al.* (2003) evaluated the cost-effectiveness of a fluoride toothpaste programme. Children in the study group received toothpaste free of charge from 1 to 5 years of age, leading to significantly lower dmft indices at the age of 5 years compared with the control group. In addition, the number of caries-free children was higher among the study children. The calculation of costs included the labour costs of establishing and running the postal programme, overheads and product costs. The average cost per dmft reduction, per child kept free of caries and per child kept free of extraction experience were calculated. However, because the treatment costs of caries were not taken into account the results of the cost-effective analysis overestimated the total costs of the toothpaste programme group in comparison with the control group.

In a community trial in Chile carried out by Mariño *et al.* (2007), fluoridated milk products were supplied to children between 6 months and 6 years of age for four years, while the children in the control group received corresponding non-fluoride products. In addition to the programme costs of milk fluoridation, caries treatment costs, travel costs, and costs of the working time loss of the accompanying adult were also included in the cost-effectiveness analysis. The clinical results measured by incremental dmft showed a significant decline in caries experience among the study

children. Cost savings were also achieved; the reported total costs were 70% higher in the non-fluoridation control group. The authors suggested that milk fluoridation is cost-effective and leads to a decline in caries experience and a reduction in costs.

The economic aspects of the early childhood caries prevention programmes have been evaluated in countries with different caries levels and dental health care policies. In the United Kingdom, a dental health education programme with home visits to mothers of young infants gave better benefit-cost and cost-effectiveness ratios than a slow-releasing fluoride device, community water fluoridation, or a school-based fissure sealing programme (Kowash *et al.* 2006). In the United States, Kobayashi *et al.* (2005) estimated the effectiveness and costs of a special baby and child dental care programme by comparing the dental health of children in the county with the programme and in a demographically similar county without it. The programme included preventive and restorative dental treatments for the children and education for the parents and dental professionals. It was demonstrated that an early prevention programme improved the dental health of primary teeth with relatively low incremental costs; the authors suggested that cost savings would accrue over time. The results of a Finnish study on pre-school children are in line with this opinion. Jokela and Pienihäkkinen (2003) suggested that early risk-based prevention can be effective in reducing both costs and dental caries. Seven years after the cessation of the targeted prevention programme including fluoride varnish treatments and oral hygiene counselling, long-term clinical and economic benefits were reported (Pienihäkkinen *et al.* 2005). Similar conclusions were also suggested by Quinoñez *et al.* (2006) who evaluated the cost-effectiveness of an early fluoride varnish application model in the United States. The clinical outcomes of fluoride varnish, as well as the assumed costs, were analyzed using the results of earlier published studies. In the model, fluoride varnish applications carried out during well-child clinic visits of infants at the age of 9, 18, 24, and 36 months effectively reduced early childhood caries, but the programme was not cost-saving in the first 42 months of life. The authors argued that longitudinal cohort studies are needed for conclusions of potential total cost reductions.

Extra resources allocated to the caries prevention of high-caries-risk subjects do not necessarily lead to additional health benefits. The study with Finnish young teenagers by Hausen *et al.* (2000) reported only a negligible difference in caries increment during three years between intensive and basic prevention models among the high-caries-risk Finnish 13-year-old children. The authors suggested that by offering all children broad-scale basic prevention, almost the same preventive effect could have been obtained with less effort and lower costs. Similar results among high-caries-

risk children have been published by Källestål and Fjeddahl (2007) in Sweden. In a population with a low caries level, such as Finland or Sweden, an additional reduction of caries seems to need fresh approaches with extended prevention procedures and large inputs, as demonstrated in the later study of Hausen *et al.* (2007). In their study with caries-active 11- to 12-year-olds, caries increment was significantly reduced with a regimen that contained multiple individually designed caries-preventive measures, and strong population-based campaigns. The costs were not calculated, but the authors reported that the programme required huge resources.

The prevention of dental caries has been studied intensively for decades and new studies are currently underway. However, the economic aspects of the different preventive measures, especially concerning primary teeth, have not been widely evaluated. The significance of the inhibition of MS transmission in relation to the need for the restorative caries treatment of primary teeth has not been studied so far. The studies of Söderling and Isokangas *et al.* (Söderling *et al.* 2000, 2001, Isokangas *et al.* 2000) in Ylivieska, Finland, and Thorild *et al.* (2003, 2004, 2006) in Sweden showed that MS transmission from mother to child can be significantly reduced with maternal use of xylitol chewing gum, but its effectiveness in caries occurrence after 5 years of age, as well as in the need of restorative treatment is not yet known. The Ylivieska mother-child study offered a good possibility to observe the long-term effects of early MS transmission inhibition and maternal use of xylitol chewing gum on the timing and occurrence of caries, and on the need of restorative treatment in the primary teeth of the children. Furthermore, the costs of the maternal caries-preventive programme in relation to long-term dental health benefits might be estimated. The subjects in the original Ylivieska mother-child study were known to be children whose mothers had had high levels of MS and thus, the subjects were at high risk of caries. Eleven years after the study onset, the majority of the participants were still living in the area of the Ylivieska Public Health Care Centre, and reliable and exhaustive data on their dental status and treatments were available. All the children in the area, like practically all children in Finland, used public health-care services, and all dental visits, treatments and materials had been carefully documented.

Table 1. MS transmission studies; study designs and results

Study	Intervention	Control group	n		Age of child during intervention	f	MS mother		MS child		Caries child	
			test	c			effect	p	effect	p	effect	p
Köhler *et al.* 1993,1984, 1988, 1994	special prevention programme	no intervention	37	40	3-8 → 36 mo	3 yr	↓	<0.02	↓	<0.01	↓	<0.02
			26	33		7 yr	↓	<0.05	↓	<0.01	↓	<0.05
Tenovuo *et al.* 1992	1% chx+ 0.2% fluoride gel	no intervention	56	50/45	12 → 48 mo	4 yr	not st		↓	n.s.	-	n.s.
Dasanayake *et al.* 1993	6 x iodine-NaF solution in two weeks	placebo solution	23	25	during first tooth emergency	3 yr	↓	0.04	↑	n.s.	↑	n.s.
Brambilla *et al.* 1998	daily 0.05%NaF+ 0.12% chx rinse	systemic fluoride 1mg daily	31	29	6th mo of pregnancy → delivery	2 yr	↓	<0.001	↓	<0.05	not st	
Günay *et al.* 1998	individual prevention programme	no intervention	47	45	pregnancy → 48 mo	4 yr	↓	<0.001	↓	<0.001	↓	<0.001
Söderling *et al.* 2000, Isokangas *et al.* 2000	xylitol chewing gum	fluoride/chx varnish	103	33/28	3 → 24 mo	2 yr	-	n.s.	↓	<0.05	-	n.s.
			90	30/23		5 yr	not st		not st		↓	<0.001

Gomez *et al.* 2001, Gomez and Weber 2001	prevention program	no intervention	67	69	pregnancy → 48 mo	5-6 yr	not st		not st		↓	<0.05
Dasanayake *et al.* 2002	10% chx varnish	placebo application	38	37	6 → 36 mo	4 yr	↓	<0.05	↓	n.s.	↓	n.s.
Gripp and Sclagenhauf 2002	40% chx varnish	no intervention	16	13	20-137 days → 24 mo	2 yr	↓	<0.05	↓	<0.05	not st	
Türksel Dülgergil *et al.* 2004	preventive and operative caries treatment, fluoride and chx rinses	simple dental care and advice program	15	12	2-18 mo → 24 mo	2 yr	↓	<0.001	↓	<0.001	↓	<0.001
Thorild *et al.* 2003, 2004, 2006	xylitol chewing gum	chx+ xyl+sorbitol /NaF+xyl+ sorbitol chewing gum	52	44/ 48	6 → 18 mo	4 yr	not st		↓ (18 mo)	<0.05	↓	<0.05[1]
Ercan *et al.* 2007	preventive and operative caries treatment, fluoride and chx rinses	no intervention	11	10	2-11 mo → 36 mo	4 yr	not st		↓	<0.01	↓	<0.001

n = number of participants
c = control
f = follow-up age of child
p = p-value

n.s. = not significant
chx = chlorhexidine
xyl = xylitol
not st = not studied

[1]xylitol vs NaF+xyl+sorbitol
↓ = reduction
↑ = increase

3. AIMS OF THE STUDY

The aims of the study were

- to examine the long-term effect of the prevention of mother-child transmission of mutans streptococci (MS) on the health of and on the amount of restorative treatment in the children's primary dentition in children whose mothers were known to have had high MS levels

- to measure, until the age of 10 years, the health of and the amount of restorative treatment in the primary teeth of the children who participated in the original Ylivieska mother-child study; and to compare them to the reference children of the same age cohort not included in the original Ylivieska mother-child study

- to calculate - from the public dental care point of view - the costs of the maternal use of xylitol chewing gum in relation to the timing of dental decay and the amount of restorative treatment in children's primary teeth

4. SUBJECTS AND METHODS

4.1 Ylivieska Public Health Care Centre, Finland

The study was carried out at the beginning of the 2000s at the Ylivieska Public Health Care Centre covering the public health care for the communities of Ylivieska, Alavieska, and Sievi. The area is typical of rural central Finland with little migration and relatively large families. During the study, the total number of inhabitants was about 21,000, of which 13,000 were in Ylivieska, 5000 in Sievi, and 3000 in Alavieska. The birth rate was on average 200 babies per year in Ylivieska, 80 in Sievi, and 40 in Alavieska. The fluoride concentration of the piped water was low (< 0.1 ppm).

In Finland, all public dental health care is free of charge up to 18 years of age. During the study, a total of 12 dentists worked at the Ylivieska Public Health Care Centre, seven of them based in Ylivieska, three in Sievi, and two in Alavieska. In addition, there were one orthodontist, three dental hygienists, two of them in Ylivieska and one in Sievi, and 16 dental assistants. The personnel were permanent and experienced, most of the dentists and assistants, as well as all three oral hygienists, had worked for 15–20 years at this health care centre. In the area of the Ylivieska Public Health Care Centre, all children used the public dental services and orthodontic treatment was also available for all inhabitants. There was only one private dental clinic (one dentist) in Ylivieska during the study.

All the children attended the oral health care programme including regular examinations, health education, advice on diet and oral hygiene, sealants and use of fluorides and, when necessary, restorative treatment. This is in line with programmes commonly applied to children in the Finnish public health care system. In Ylivieska, an experienced dental assistant screened children younger than 2 years of age, the dental hygienists from 2 to 4 years, and after 4 years of age the children were examined by the dentists. In Sievi, the dental hygienist screened all the children up to the age of 5 years. In Alavieska, all the examinations were made by the dentists. However, the children who took part in the Ylivieska mother-child study in the early 1990s were annually examined by the dentists until 6 years of age. If needed, restorative treatment was generally given by the same dentist who had carried out the examination.

4.2 Subjects

The total number of subjects in the four groups (xylitol, fluoride, chlorhexidine, and reference) was 507: 257 boys and 250 girls. Observations on boys and girls were pooled throughout the study, as no significant differences between the genders were found. According to the annual records of the Ylivieska Public Health Care Centre, the children born in 1991 or 1992 did not differ from the other cohorts born at the beginning of the 1990s in relation to their dental health measured by DMFT indices (Appendix, Table c).

4.2.1 Experimental groups: xylitol, fluoride and chlorhexidine

The inclusion criteria for the experimental groups in the prospective study were that the mothers of the children had been participants in the Ylivieska mother-child study, which had been carried out between 1990 and 1997 (Söderling *et al.* 2000, 2001, Isokangas *et al.* 2000), and that information on the children's dental visits and treatments, as well as dental status from birth until 10 years of age, were documented in the registers of the Ylivieska Public Health Care Centre. The mothers had been screened for a high level of mutans streptococci with the MS strip test and were considered to be high-caries-risk subjects (CFU≥100 000/ml). The mothers in the xylitol group had used xylitol chewing gum when their babies were 3 to 24 months old, while the mothers in the two control groups had received fluoride or chlorhexidine varnish treatments when their babies were 6, 12, and 18 months old. Of those children whose mothers were included in the original mother-child study, information on a total of 148 subjects was available in the files of the Ylivieska Public Health Care Centre; 93 in the xylitol, 30 in the fluoride, and 25 in the chlorhexidine group; altogether 67 boys and 81 girls.

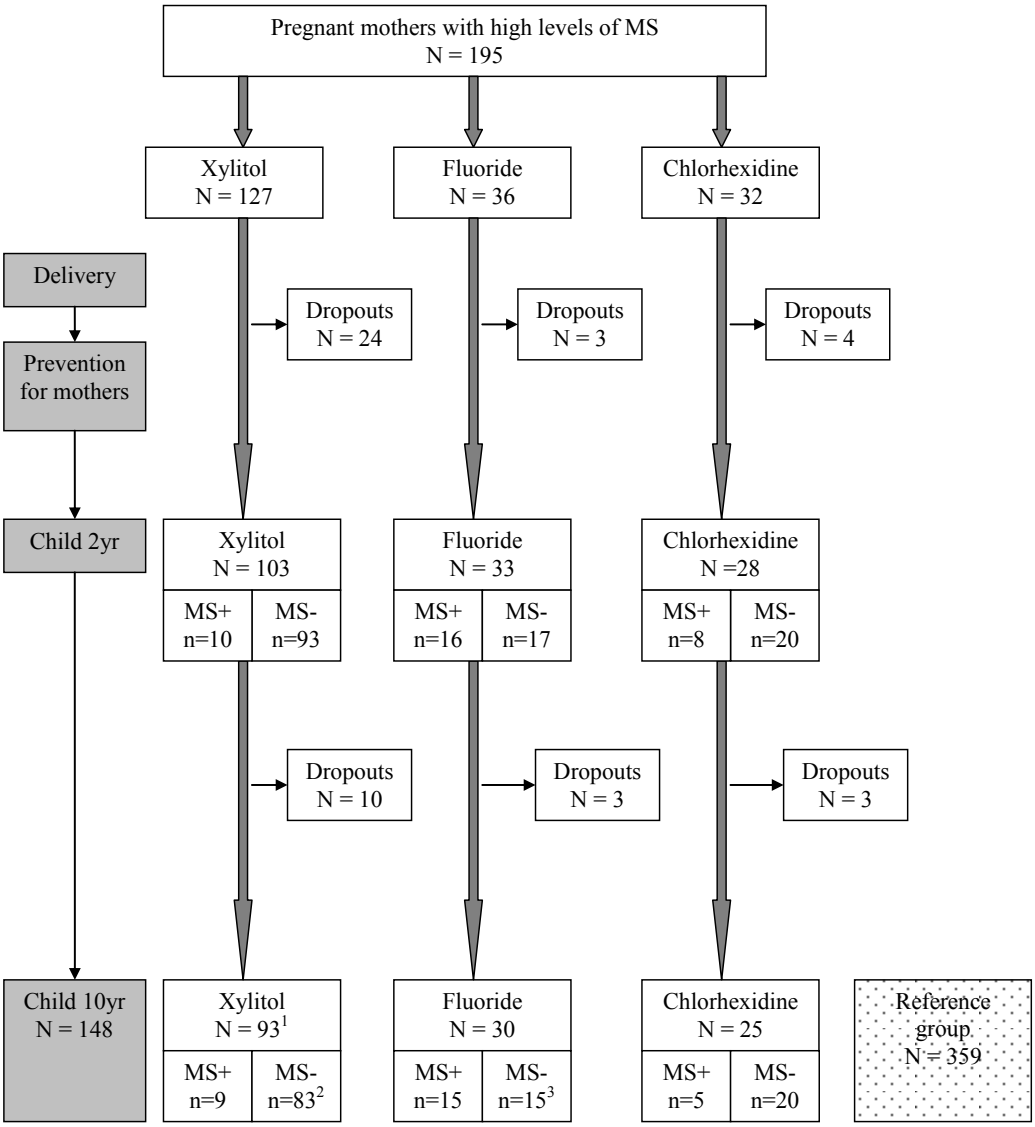
The dropout rate eleven years after the beginning of the Ylivieska mother-child study was 24%. The reason for dropping out of 16 out of 164 children after 2 years of age (the dropout rate being 10%) was moving away from the district of the Ylivieska Public Health Care Centre. As regards the colonization by MS at 2 years of age, the loss of subjects during the follow-up from 2 to 10 years was similar in the xylitol and fluoride groups, while in the chlorhexidine group, all the dropouts were MS-colonized children. Two children had incomplete dental visit registrations; one boy in the xylitol group from 1 to 5 years of age, and one girl in the chlorhexidine group from 1 to 3 years of age. In addition, the MS colonization at 2 years of age of one boy in the xylitol group was not defined. These three children were included in the study (Figure 2, p. 40).

4.2.2 Reference group

A reference group was formed retrospectively on the basis of the Finnish Population Register. Altogether 623 children born in 1991 or 1992 were found to live in the communities of Ylivieska, Alavieska and Sievi at the beginning of January 2003 (10th January 2003). The reference group included all the children in the age cohorts 1991 and 1992 who were not participants in the original Ylivieska mother-child study, i.e. all the 10-year-old children whose annual information on dental health and dental visits from birth until 10 years of age was available in the files of the Ylivieska Public Health Care Centre. The dropouts and the siblings of the children in the xylitol, fluoride, or chlorhexidine groups were not included in this reference group. The final group size was 359 children. About one third of the mothers of the children in the reference group had been screened with the MS strip test and had shown low levels of MS (CFU=0 or CFU<100 000/ml), the rest of the mothers had not been screened (Figure 3, p. 41). As 195 children whose mothers had shown high MS levels had been screened out from the age cohort, it can be assumed that in the reference group, the proportion of children of low-MS-level mothers was higher than on average in the population. The MS colonization of the children at the age of 2 years in the reference group had not been measured. The data of the dental health and dental visits of the reference group children were collected during the same collection procedure as the data of the children in the experimental groups.

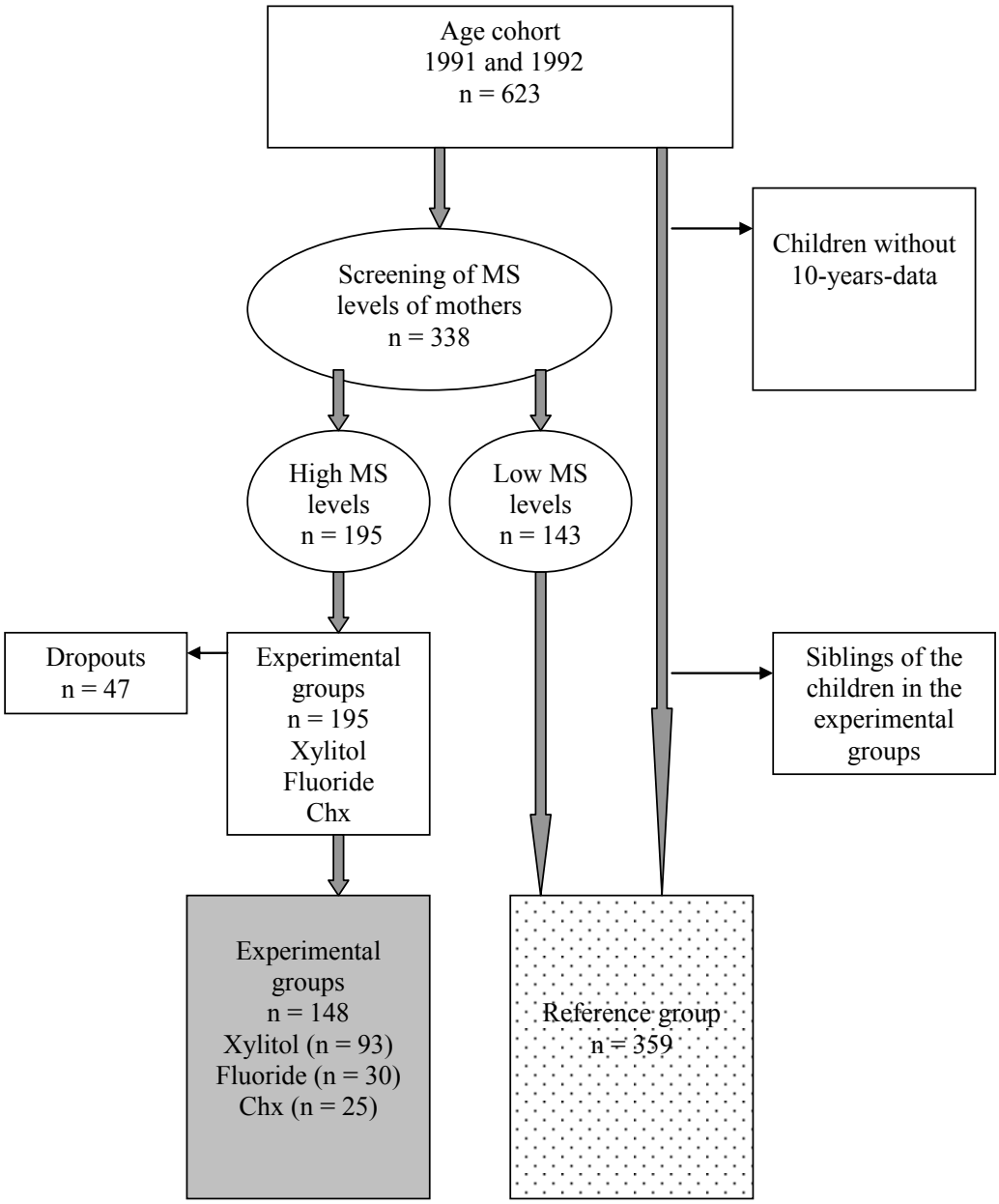
4.2.3 Blinding

In the original Ylivieska mother-child study, the blinding of the examiners as regards study groups had not been possible. However, the blinding as regards the MS colonization at the age of 2 years was maximal throughout the original as well as the present study. The mothers, their children, all the personnel treating the children, and the author of the present study during the data collection were blinded as regards MS colonization. The microbiological analyses during the Ylivieska mother-child study had been carried out in the laboratory of Turku University 600 kilometres away from Ylivieska and the results had never been made known in Ylivieska. Only after the data collection for the present study, was the information about the MS colonization for each child given to the author.



[1]one child with no data of MS colonization at 2 yr
[2]one child with no data on dental status and treatments from 1 to 5 yr
[3]one child with no data on dental status and treatments from 1 to 3 yr
N = number of children
n = number of MS-colonized (MS+) or non-MS-colonized (MS-) at the age of 2 yr

Figure 2. The flow chart of the groups



Chx = chlorhexidine

Figure 3. Flow chart of the experimental groups (xylitol, fluoride and chlorhexidine) and the reference group

4.3 Methods

4.3.1 Dental health and visits to dental care

Information on the children's dental status, treatments and visits from birth until 10 years of age was collected in alphabetical order from the registers of the Ylivieska Public Health Care Centre by one experienced dentist (author) with the permission of the Chief Dental Officer. The data were collected from the files and checked case by case to control the clinical relevance of the registrations and the logic of the collection procedure. The dental health of children's primary teeth was measured by dt and dmft indices. For every child, the age at the first dentinal decay in primary teeth (dmft>0) was defined as the caries-free survival time. For the survival analyses, the missing dmft values were interpolated when the preceding and the following dmft values were known. The dental health of children's permanent teeth at the age of 10 years was measured using the DMFT index. Additionally, numbers of erupted and sealed permanent teeth at the age of 10 years were observed. For the indices, only lesions extending to dentin, fillings and extractions because of dentinal caries were included. The clinical caries examinations had taken place in a fully equipped dental chair with good illumination. X-rays had been taken on an individual basis when appropriate, but not due to the study programme.

The Chief Dental Officer and other clinicians were interviewed concerning the time reserved for dental visits of different kinds. The reserved times were based on long experience and had remained stable for years. The documents and files of the appointments and reserved times in Ylivieska Public Health Care Centre were available to them as well as to the author. The dental visits were categorized in relation to the provider and to the type of treatment given. The numbers of all visits to the dentist, dentist with assistant, dental assistant, or dental hygienist were calculated separately. The type of dental treatment was classified into examinations or screenings, caries-preventive treatments, restorative caries treatments of primary or permanent teeth, orthodontic treatments, and 'other visits', which included, e.g. trauma-related visits. During the visit for the restorative caries treatment of primary teeth, other treatments, e.g. orthodontics or caries treatment of permanent teeth, could also have been given. The preventive visits had included measures to prevent and control caries, such as dietary and oral hygiene counselling, and fluoride varnish treatments. During the examinations and screening visits after 2 years of age, preventive measures such as fluoride gels and varnishes could also have been applied to children. No chlorhexidine products had been applied to children and no sealants had been applied to the primary teeth. The permanent

teeth had been sealed individually according to the estimated need. In order to create conditions where the dental care would be as typical as possible for the Ylivieska Health Care Centre, the personnel of the Centre had not been informed about the possibility that the dental health and the dental care of the children would be studied retrospectively by using the files of the Centre.

4.3.2 Oral-health-related behaviour of children

During the examination at 10 years of age, the children in the experimental groups were interviewed concerning their oral health-related behaviour. In the questionnaire, the manners of tooth-brushing and usage of fluoridated dentifrices, xylitol, sucrose sweets, and soft drinks were assessed. In addition, the level of oral hygiene and amount of visible plaque of the children were recorded by the dentist who performed the examination. The questionnaire was based on the earlier questionnaire used in the Ylivieska mother-child study (Söderling *et al.* 2000, 2001, Isokangas *et al.* 2000). Before the interview, the questionnaire was evaluated by experienced dentists. (Questionnaire 1 in Appendix)

4.3.3 Costs of maternal prevention programmes

The costs were calculated from the perspective of the public health institution. The data for the costs analyses were gathered from the annual records of the Ylivieska Public Health Care Centre and from the registers of the producers of the xylitol chewing gum Xylifresh® (Leaf, Turku, Finland) and the chlorhexidine varnish EC40® (Biodent, Nijmegen, The Netherlands). All the costs of prevention in the mothers occurred at the beginning of the mother-child study. To eliminate possible changes in the costs rate during the ten-year study period, the figures for the year 2002 were used.

4.3.3.1 Material costs

The programme-related material costs varied among the three experimental groups and they were calculated separately. All the costs for the xylitol chewing gum, the fluoride varnish and the chlorhexidine varnish were calculated from their actual monetary values and quantity discounts of the year 2002. Due to the Finnish legislation, the material costs for the public health care institutions did not include value-added taxes (VAT), which were 17% for the xylitol chewing gum and 8% for the fluoride and chlorhexidine varnishes.

a. Xylitol chewing gum

The xylitol chewing gum had been made for the Ylivieska mother-child study by Leaf (Turku, Finland) free of charge. The corresponding commercial 100% xylitol sweetened chewing gum in 2002 was Xylifresh® (Leaf). According to the registers of Leaf in 2002, the wholesale price of Xylifresh® (for the wholesale dealer MetroTukku, Helsinki, Finland) was 243 euros (including 17% VAT)/10 kg box containing ca. 7692 pieces of chewing gum. When VAT was excluded, the price of one piece was 0.02622 euros. Mothers used, on average, 6 g of xylitol daily, which corresponds to seven pieces of Xylifresh® containing 0.845 g of xylitol each. The total consumption of xylitol over 21 months (7 x 630 days) corresponded to 4410 pieces of Xylifresh®. The material costs of xylitol chewing gum for 21 months' consumption were 115.63 euros per mother.

b. Fluoride varnish

The fluoride varnish used in the study was Duraphat® (Rhône-Poulenc Rorer GmbH, Köln, Germany). The market price of Duraphat® for the Ylivieska Public Health Care Centre in 2002 was 108.34 euros per package of 5 x 30 ml tubes. The approximate amount of Duraphat® in a single application has been estimated to be 0.5 ml (Vehmanen 1993). The costs of the brushes for Duraphat® application were not included in the extra material costs. The material cost of one fluoride varnish treatment was calculated as

108.34 euros/150 ml = 0.72 euros/1 ml

0.72 euros/2 = 0.36 euros = the price of one application of Duraphat®

The material costs for each mother in the fluoride group were 1.08 euros.

c. Chlorhexidine varnish

The 40% chlorhexidine varnish EC40® (Certichem, Nijmegen, The Netherlands) was donated free of charge for the Ylivieska mother-child study. At the time of the mother-child study, there was no corresponding chlorhexidine varnish available for purchase in Finland. For the economic evaluation, the price of the EC40® varnish was obtained from the registers of Biodent, the producer of EC40® in 2002. The market price of the 1.7 ml cartridge in 2002 was reported to have been 9.07 euros (8% VAT excluded), and with a 45% quantity discount for public health care institutions, 4.08 euros. The average amount for one application was estimated to be 0.25 ml (Biodent). The prices of syringes and needles needed for applications were not included in the extra material costs. The material cost for one chlorhexidine varnishing was calculated as

1.7 ml/0.25 ml = 6.8 applications from one cartridge

4.08 euros/6.8 = 0.60 euros = the price of one application of EC40®

The material costs for each mother in the chlorhexidine group were 1.80 euros.

4.3.3.2 Costs of programme-related visits

The total costs of the dental visit included wage costs, material costs, services, depreciations of the equipment and machines, and allocated costs such as rents, electricity, and administrative expenses. According to the annual reports, in the year 2002, the total costs of the dental health care in the Ylivieska Public Health Care Centre were 1,997,870 euros. The wage costs accounted for 74% of the total. The wage costs included salaries, social costs (consisting of social insurance, pension payment, and unemployment insurance), and holiday remuneration. The social costs accounted for 29.15%, and the holiday remuneration for 5.5% of the salaries. The salaries of the dentists included treatment remunerations. Material costs accounted for 7.5% of total costs. To assess the total costs for the dental visits 'other costs' (26%) including materials, allocated costs, etc. were added to the wage costs (Appendix, Table d).

The annual salaries of all the eight dentists who had worked full-time during the year 2002 were calculated together and divided by eight to get the mean annual salary for a dentist. The average annual wage costs of the dentists were 63,375.34 euros. According to the National Municipal Agreement of Public Servants (2001), the working time of a dentist was 37 hours weekly. After deducting the holidays and absence due to medical leave or professional education, the actual working time for the dental staff was 44.4 weeks annually, corresponding to 1,642.8 hours per year for the dentists. The salaries of dental hygienists and dental assistants were calculated correspondingly. The mean annual wage costs of the dental hygienists were 29,841.47 euros, and of the dental assistants 26,378.65 euros. The weekly working time for the hygienists and dental assistants was 38.25 hours, which corresponds to 1,698.3 hours annually (Table 2).

All the pregnant mothers who participated in the Ylivieska mother-child study had been examined and screened with the MS strip test at the beginning of the study. The preventive programme of the mothers had included three alternative types of preventive measures. The mothers in the fluoride and chlorhexidine groups had had three varnishing visits, 6, 12, and 18 months after the delivery. For the fluoride varnish treatment, the reserved time was twenty minutes, and for the chlorhexidine varnish treatment, thirty minutes. The application of high concentration chlorhexidine varnish required a longer appointment time because it was technically more demanding than the application of fluoride varnish. The chlorhexidine varnish was applied with a needle to a dry tooth surface, and according to the directions of the producer, after the treatment it was carefully removed from the teeth using hand instruments. The fluoride varnish was applied with a brush and did not need removal. All varnish treatments for the study groups had been carried out by a

dentist with a dental assistant. The costs for one fluoride varnish treatment were 24.37 euros, and for one chlorhexidine varnish treatment 36.56 euros. The mothers in the xylitol group had not needed extra visits for their prevention; the xylitol chewing gum had been picked up in large amounts at the reception desk without a prearranged appointment.

Table 2. Wage costs of dental personnel in Ylivieska Public Health Care Centre in 2002, and total costs for dental visits per one hour, when wage costs represent 74% of total costs

Personnel	Mean annual wage costs (€)	Wage costs per hour (€)	Total costs per hour (€)
Dentist	63,375.34	38.58	52.14
Dental hygienist	29,841.47	17.57	23.74
Dental assistant	26,378.65	15.53	20.99
Dentist with assistant		54.11	73.12

4.3.3.3 Costs of additional caries-free year and saved restorative visit

The differences in costs of the maternal prevention programmes were calculated as:
costs of prevention programme (test group) – costs of prevention programme (control group).

The differences in caries-free time were calculated as:
median value (Md) for the age of the first dentinal caries experience in primary teeth (test group) –
Md for the age of the first dentinal caries experience in primary teeth (control group),

and the costs of an additional caries-free year of life was calculated as:

a) the difference in costs / difference in caries-free time, and
b) the costs of xylitol / difference in caries-free time between xylitol and fluoride groups.

The differences in number of restorative visits were calculated as:
mean value for the cumulative restorative visits due to caries in primary teeth until 10 years of age (control group) – mean value for the cumulative restorative visits due to caries in primary teeth until 10 years of age (test group),

and the costs of one saved restorative visit was calculated as:

a) the difference in costs / difference in number of restorative visits, and
b) the costs of xylitol / difference in number of restorative visits between xylitol and fluoride groups,

where test group = xylitol group, and control group = fluoride or chlorhexidine group.

4.4 List of main variables

- Dental health
  - timing of the first dental decay in primary teeth (in years)
  - proportion of children with caries experience in primary teeth at the age of 6, 8, and 10 years
  - dmft at the age of 6, 8, and 10 years
  - DMFT at the age of 10 years

- Restorative treatment
  - number of restorative visits due to dental decay in primary teeth until the age of 4, 6, 8, and 10 years

- Effect of early MS colonization and effectiveness of maternal use of xylitol
  - NNT at the age of 6, 8, and 10 years
    - xylitol in comparison with fluoride and chlorhexidine
  - Additional caries-free time between the xylitol and the experimental control groups (fluoride and chlorhexidine)
    - difference in timing of the first dental decay in primary teeth (in years)
  - Saved restorative visits between the xylitol and the experimental control groups (fluoride and chlorhexidine)
    - difference in the number of restorative visits until 10 years of age

- Costs of maternal prevention of early MS colonization
  - material costs of the maternal preventive measures (xylitol, fluoride and chlorhexidine) (in euros)
  - costs of dental visits due to maternal prevention (in euros)

- Costs in relation to effectiveness of maternal prevention of early MS colonization
  - costs of additional caries-free year of life (in euros)
  - costs of one saved restorative visit (in euros)

- Oral-health-related behaviour of children
  - tooth-brushing habits
  - usage of xylitol, sucrose sweets and soft drinks
  - visible plaque amount

4.5 Data handling and statistical analyses

The main outcome measures were the caries-free survival time and the number of restorative visits for primary teeth. Additional measures of dental health were the dmft index and the proportion of children with dmft >0. First, the data of the children in the experimental groups (xylitol, fluoride and chlorhexidine) were analyzed in relation to MS colonization at 2 years of age. Secondly, the differences between the experimental groups in relation to MS colonization and main outcome measures were analyzed. Third, the differences between the groups (xylitol, fluoride, chlorhexidine and reference) in relation to the main outcome measures were analyzed.

Survival analysis was used to analyse the caries-free survival time in relation to the MS colonization at baseline at 2 years of age and the group. The Cox model was used to estimate the effect of MS and group (and their interaction term) on the survival time. Hazard ratios (HR) and 95% confidence intervals (CI) between the MS-colonized and the non-MS-colonized children, between the experimental control groups (fluoride or chlorhexidine) and the xylitol group, and between the reference group and the xylitol group were calculated. Additionally, the hazard ratio between the reference group and the experimental control groups was calculated; for this analysis, the fluoride and chlorhexidine groups were pooled.

Absolute risk reductions (ARR) with 95% CI in relation to the proportion of children with dmft >0 between the xylitol group and the experimental control groups (fluoride or chlorhexidine) at 6, 8, and 10 years of age were calculated, and if the ARR was significant, number needed to treat (NNT) values and 95% CI were calculated.

Differences in relation to dmft indices at 6, 8, and 10 years of age between the children who were MS colonized and those who were not MS colonized at 2 years of age were tested with the Mann-Whitney U-test. Differences between the experimental groups in relation to dmft values at 6, 8, and 10 years of age were tested with the nonparametric Kruskal-Wallis test, and if the difference was significant, pair-wise comparisons were carried out using the Mann-Whitney U-test.

Univariate analysis of variance, general linear model (ANOVA) was used to estimate the effect of MS colonization at baseline, the experimental groups, and their interaction term on the number of restorative visits at the age of 4 and 10 years. In addition, the differences in the numbers of restorative visits between the reference group and the xylitol group, and between the reference group and the experimental control groups were tested; for this analysis the fluoride and chlorhexidine groups were pooled. As the

original values of the variables were skewed to the right, the natural logarithmic values were used in the statistical analyses.

The Chi-Square (χ^2) test was used to analyze the association between the oral-health-related behaviour variables at 10 years of age and the experimental groups.

The data were analysed using SPSS® 16.0 for Windows (Chicago, IL, USA) software, and p-values less than 0.05 were considered statistically significant.

4.6 Ethical considerations

All the analyses were based on the records alone. The children themselves were not examined for the present study. Therefore, the Ethical Board of the Faculty of Medicine, University of Turku, stated that permission for the current study can be based on the earlier permission of the ethical board given for the Ylivieska mother-child study.

5. RESULTS

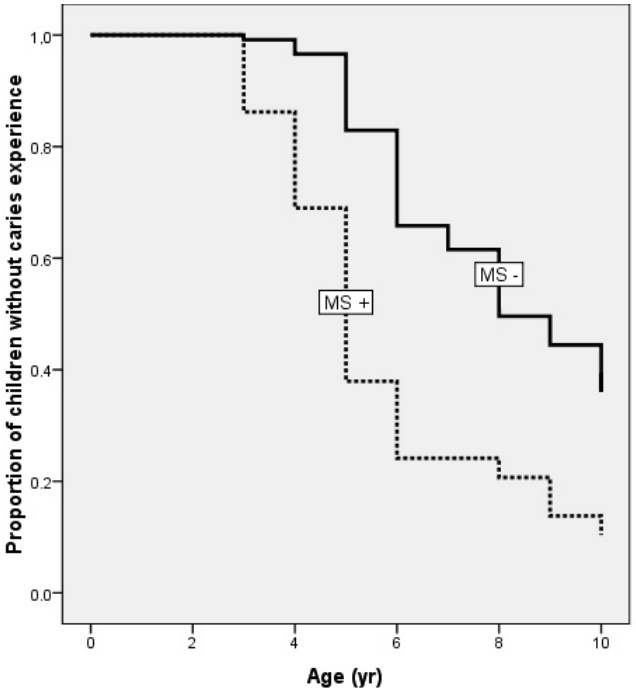
The main results of the study were as follows:

The children who were not colonized with mutans streptococci (MS) at the age of 2 years maintained their primary teeth caries-free for longer, had lower caries experience and less restorative visits up to the age of 10 years, compared with the MS-colonized children. The results in relation to MS colonization were similar in all three experimental groups who were known to have had high maternal MS levels. The MS-colonization figures had been lowest in children of the xylitol group, and they had the first caries occurrence later and fewer restorative visits throughout the study years, in comparison with the children in the chlorhexidine and fluoride varnish treatment groups. The costs of the maternal prevention programme were highest in the xylitol group. The children in the xylitol group had lower caries occurrence figures and needed less restorative treatment than the children of the same age cohorts in the reference group.

5.1 Caries occurrence and dental visits in relation to early MS colonization

5.1.1 Age at first dentinal decay

The children who were not colonized with MS at the age of 2 years maintained their primary teeth healthy for longer and had lower caries experience up to the age of 10 years compared with the MS-colonized children (Figure 4 and Table 3). The median value for the first dentinal caries experience in primary teeth among the MS-colonized children was 4.61 years. Among the non-MS-colonized children, the median value was 7.96 years; the difference between the MS-colonized and the non-MS-colonized children was significant ($p<0.001$). The MS-related hazard ratio (HR) was estimated to be 2.70; 95%CI 1.72-4.25 (Cox regression analysis) (Figure 4).



MS- = not colonized by MS at the age of 2 years (n = 118)

MS+ = colonized by MS at the age of 2 years (n = 29)

MS+ vs MS-, p < 0.001, HR 2.70; 95%CI 1.72-4.25 Cox regression analysis

Figure 4. Proportion of children without caries experience in primary teeth in relation to MS colonization at the age of 2 years (Kaplan-Meier curve)

Table 3. The proportions of children with dentinal caries experience (dmft>0) until 10 years of age in relation to MS colonization at the age of 2 years

		Dentinal caries occurrence in primary teeth		
		until 6 yr	**until 8 yr**	**until 10 yr**
MS-	**%**	39	56	62
	n	118	118	118
MS+	**%**	72	86	90
	n	29	29	29

MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children

5.1.2 dmft index

The children who had been colonized by MS at the age of 2 years had higher dmft values until 10 years of age than the non-MS-colonized children. The differences in the dmft indices between MS-colonized and non-MS-colonized children were significant (Table 4 and Figure a in Appendix).

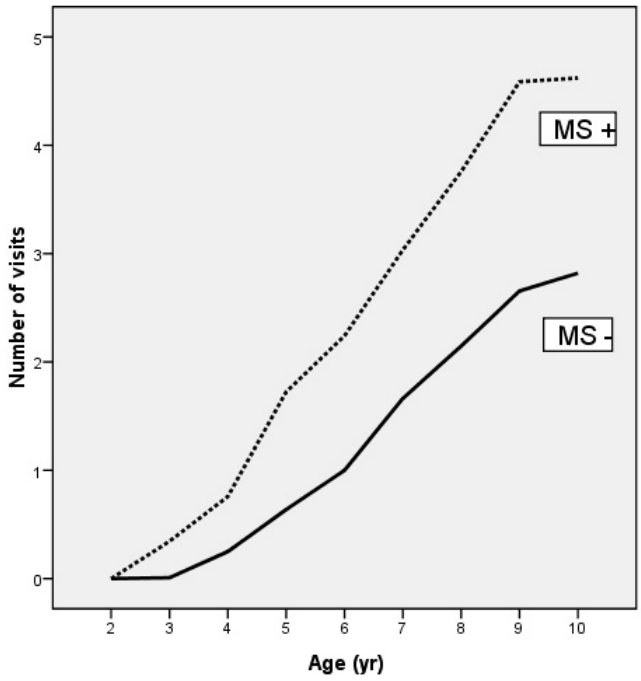
Table 4. dmft indices in relation to MS colonization at 2 years of age, the highest values for MS-colonized and non-MS-colonized children in bold

		dmft6	dmft7	dmft8	dmft9	dmft10
MS-	**mean**	1.29	1.69	1.88	**2.05**	1.41
	SD	2.28	2.48	2.42	2.54	1.96
	n	117	113	118	115	118
MS+	**mean**	**3.68**	3.39	3.66	3.52	2.45
	SD	3.76	3.54	3.02	2.68	2.13
	n	28	28	29	27	29
	p	<0.001		0.001		0.006

MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children
p = p-value of the difference between the MS+ and MS- children, Mann-Whitney U-test

5.1.3 Restorative visits

The children who had been colonized by MS at the age of 2 years needed more restorative treatment for primary dentitions compared with the non-MS-colonized children. At the age of 10 years, the MS-colonized children had made on average 4.6 visits for restorative treatment, while those who were not colonized by MS at the age of 2 years had made 2.8 visits, the difference being statistically significant (Figure 5 and Table 5).



MS- = not colonized by MS at the age of 2 years (n = 116)

MS+ = colonized by MS at the age of 2 years (n = 29)

Figure 5. Mean values of the cumulative number of visits for restorative treatment of primary teeth until 10 years of age in relation to MS colonization at the age of 2 years

Table 5. Mean values of cumulative visits for restorative treatment of primary teeth until 4, 6, 8, and 10 years of age in relation to MS colonization at 2 years of age

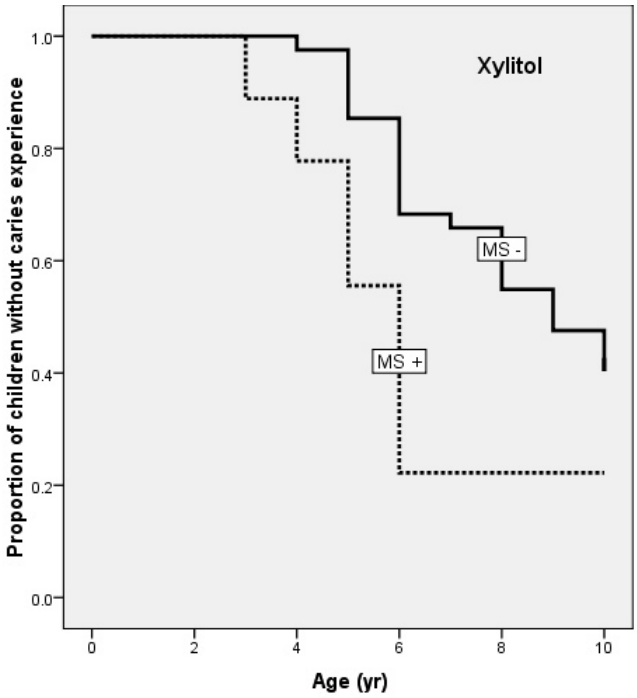
		Cumulative number of visits for restorative treatment of primary teeth			
		until 4 yr	**until 6 yr**	**until 8 yr**	**until 10 yr**
MS-	**mean**	0.3	1.0	2.2	2.8
	SD	0.8	2.2	3.3	4.0
	n	116	116	116	116
MS+	**mean**	0.8	2.2	3.8	4.6
	SD	1.4	3.0	3.6	4.1
	n	29	29	29	29
	p	0.006			0.005

MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children
p = p-value of the difference between the MS+ and MS- children, ANOVA

5.2 Interaction of MS colonization and experimental grouping

5.2.1 Interaction in relation to caries

In all three experimental groups, the children who were not colonized by MS at the age of 2 years maintained their primary teeth caries-free for longer than the MS-colonized children in the same study group (Cox regression analysis; interaction term 'group*MS'; p = 0.85) (Figures 6, 7, 8 and Table 6). In the xylitol group, the median value for the first dentinal caries occurrence in primary teeth for the MS-colonized children was 5.17 years, while for the non-MS-colonized children it was 8.67 years. In the fluoride group, the corresponding values were 4.58 years for the MS-colonized and 6.75 years for the non-MS-colonized children, and in the chlorhexidine group 3.75 years for the MS-colonized and 7.25 years for the non-MS-colonized children.

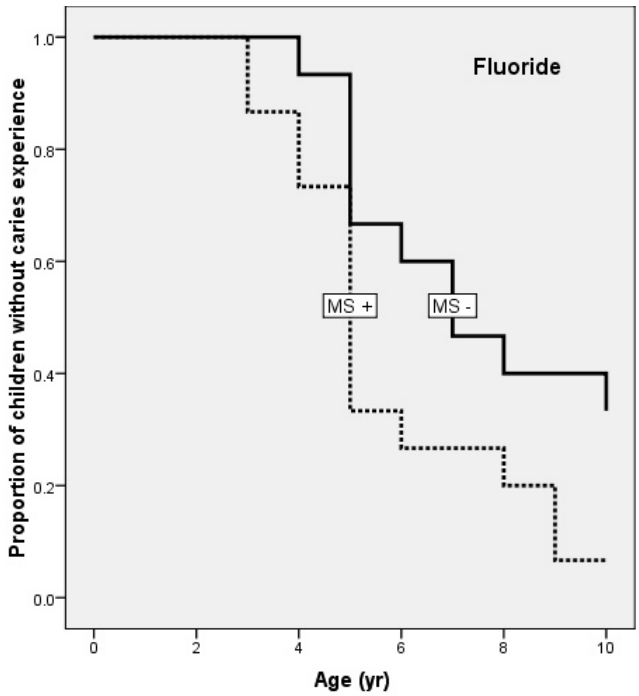


MS- = not colonized by MS at the age of 2 years (n = 83)

MS+ = colonized by MS at the age of 2 years (n = 9)

MS+ vs MS-, p = 0.045, HR 2.26; 95%CI 1.02-5.01 Cox regression analysis

Figure 6. Proportion of children without caries experience in primary teeth in relation to MS colonization at the age of 2 years; xylitol group (Kaplan-Meier curve)

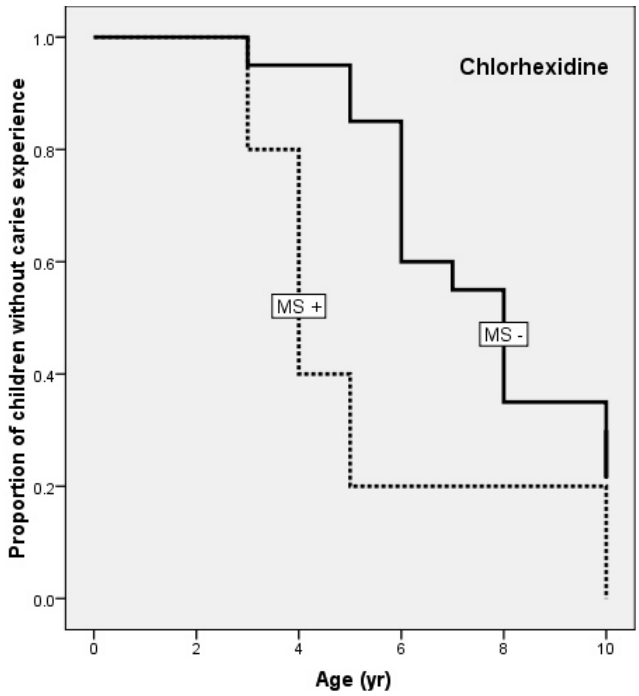


MS- = not colonized by MS at the age of 2 years (n = 15)

MS+ = colonized by MS at the age of 2 years (n = 15)

MS+ vs MS-, p = 0.07, HR 2.14; 95%CI 0.94-4.89 Cox regression analysis

Figure 7. Proportion of children without caries experience in primary teeth in relation to MS colonization at the age of 2 years; fluoride group (Kaplan-Meier curve)



MS- = not colonized by MS at the age of 2 years (n = 20)

MS+ = colonized by MS at the age of 2 years (n = 5)

MS+ vs MS-, p = 0.03, HR 3.22; 95%CI 1.13-9.16 Cox regression analysis

Figure 8. Proportion of children without caries experience in primary teeth in relation to MS colonization at the age of 2 years; chlorhexidine group (Kaplan-Meier curve)

Table 6. Proportions of children with dentinal caries experience (dmft>0) in primary teeth in relation to MS colonization at 2 years of age in xylitol, fluoride, and chlorhexidine groups

Group		Dentinal caries in primary teeth					
		until 6 yr		until 8 yr		until 10 yr	
		MS-	MS+	MS-	MS+	MS-	MS+
Xylitol	**%**	35	78	53	78	58	78
	n	83	9	83	9	83	9
Fluoride	**%**	53	67	60	93	67	93
	n	15	15	15	15	15	15
Chx	**%**	45	80	65	80	75	100
	n	20	5	20	5	20	5

Chx = chlorhexidine
MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children

In all three experimental groups, the children who had been colonized by MS at the age of 2 years had, on average, higher dmft values during the follow-up years than the non-MS-colonized children (Table 7).

Table 7. dmft indices in xylitol, fluoride, and chlorhexidine groups in relation to MS colonization at 2 years of age, the highest values for each group in bold

Group			dmft6	dmft7	dmft8	dmft9	dmft10
Xylitol	MS-	mean	1.17	1.46	1.71	**2.08**	1.36
		SD	2.24	2.30	2.34	2.67	2.03
		n	82	79	83	80	83
	MS+	mean	1.89	1.78	2.33	**3.13**	2.11
		SD	1.97	2.05	1.66	2.30	1.69
		n	9	9	9	8	9
Fluoride	MS-	mean	1.33	**1.60**	1.53	1.47	1.40
		SD	2.02	2.53	2.10	1.92	1.72
		n	15	15	15	15	15
	MS+	mean	4.21	4.14	**4.47**	4.14	2.80
		SD	4.30	4.06	3.36	2.98	2.43
		n	14	14	14	14	14
Chx	MS-	mean	1.75	2.74	**2.85**	2.40	1.60
		SD	2.65	3.02	2.87	2.42	1.88
		n	20	19	20	20	20
	MS+	mean	**5.40**	4.20	3.60	2.40	2.00
		SD	3.96	3.77	3.50	2.30	2.12
		n	5	5	5	5	5

Chx = chlorhexidine
MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children

5.2.2 Interaction in relation to restorative visits

In all three experimental groups, the children who were colonized by MS at the age of 2 years needed more restorative visits due to dental caries in primary dentitions than the non-MS-colonized children (Table 8).

Table 8. Mean values of cumulative visits for restorative treatment of primary teeth in relation to MS colonization at the age of 2 years, and p-values related to differences between the means (ANOVA)

Group		Cumulative number of visits for restorative treatment of primary teeth							
		until 4 yr		until 6 yr		until 8 yr		until 10 yr	
		MS-	MS+	MS-	MS+	MS-	MS+	MS-	MS+
Xylitol	**mean**	0.2	0.2	0.8	1.9	1.9	3.0	2.6	3.9
	SD	0.6	0.4	1.8	2.3	3.1	3.0	3.9	3.6
	n	82	9	82	9	82	9	82	9
Fluoride	**mean**	0.7	0.8	1.9	1.7	2.4	3.7	3.0	4.7
	SD	1.4	1.3	3.5	2.1	3.9	3.0	4.4	3.7
	n	14	15	14	15	14	15	14	15
Chx	**mean**	0.3	1.6	1.3	4.4	3.0	5.2	3.5	5.8
	SD	0.8	2.3	2.4	5.6	3.6	6.3	4.3	6.2
	n	20	5	20	5	20	5	20	5

	p-values related to differences between the means (ANOVA)	
	until 4 yr	until 10 yr
MS colonization at 2 yr	0.006	0.005
Group	0.012	n.s.
Interaction of MS colonization*group	n.s.	n.s.
Xylitol vs Fluoride	0.002	n.s.
Xylitol vs Chx	n.s.	n.s.

Chx = chlorhexidine
n = number of children

5.3 Caries occurrence and dental visits in relation to groups

5.3.1 Caries occurrence

The median value for the age of the first dentinal caries experience in primary teeth was 8.17 years in the xylitol group, 5.00 years in the fluoride group, and 6.50 years in the chlorhexidine group. The hazard ratio (HR) between the fluoride group and the xylitol group was significant, while between the chlorhexidine and the xylitol group it was non-significant (Cox regression analysis). In the reference group, the median value for the age of the first dentinal decay was 8.14 years (Figure 9).

The proportion of children with dentinal caries occurrence in primary teeth was lowest in the xylitol group during all the follow-up years. The absolute risk reduction (ARR) of dentinal caries between the xylitol and the fluoride group was significant at the ages of 6, 8, and 10 years, the corresponding NNT values being 5.0 (95%CI 1709.28-2.48), 4.8 (95%CI 39.03-2.57), and 5.1 (95%CI 42.48-2.69). Between the xylitol and the chlorhexidine group the ARR was significant at the age of 10 years, the corresponding NNT being 5.1 (95%CI 82.26-2.61) (Table 9).

Table 9. Proportions of children with dentinal caries experience in primary teeth (dmft>0) in xylitol, fluoride, chlorhexidine, and reference groups, and absolute risk reduction (ARR) values with 95%CI (significant differences in bold)

Group		Dentinal caries in primary teeth		
		until 6 yr	until 8 yr	until 10 yr
Xylitol	**%**	40	56	60
	n	93	93	93
Fluoride	**%**	60	77	80
	n	30	30	30
Chx	**%**	52	68	80
	n	25	25	25
Reference	**%**	42	57	67
	n	349	349	349
Total	**%**	43	59	67
	n	497	497	497

	ARR(95%CI)		
	until 6 yr	until 8 yr	until 10 yr
Xylitol vs Fluoride	**0.20(0.00-0.40)**	**0.21(0.03-0.39)**	**0.20(0.02-0.37)**
Xylitol vs Chx	0.12(-0.10-0.34)	0.12(-0.09-0.33)	**0.20(0.01-0.38)**

Chx = chlorhexidine
n = number of children

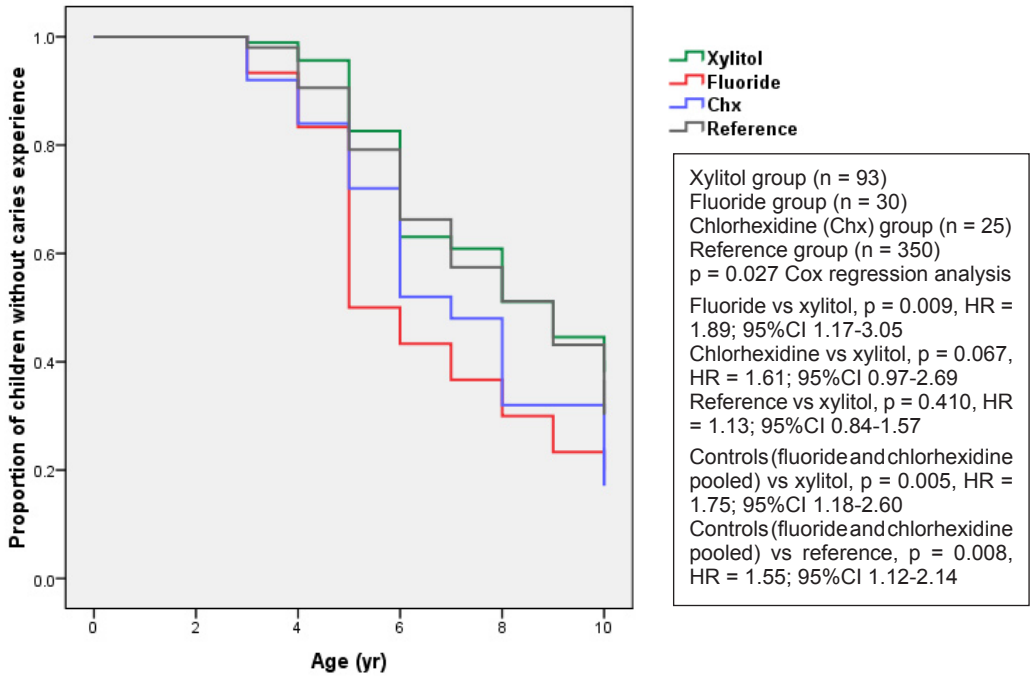


Figure 9. Proportion of children without caries experience in primary teeth in relation to groups (Kaplan-Meier curve)

5.3.2 Mean dmft values

The children in the xylitol group had the lowest dmft values when compared with the children in the fluoride and the chlorhexidine groups throughout the follow-up years. At the age of 6 years, the dmft difference between the xylitol and the fluoride groups was statistically significant (Mann-Whitney U-test) (Table 10). In relation to the reference group, the dmft values of the xylitol group did not show notable difference, the cumulative dmft curve of the reference group lying between the corresponding curves of the xylitol and the control (fluoride and chlorhexidine) groups (Figure 10).

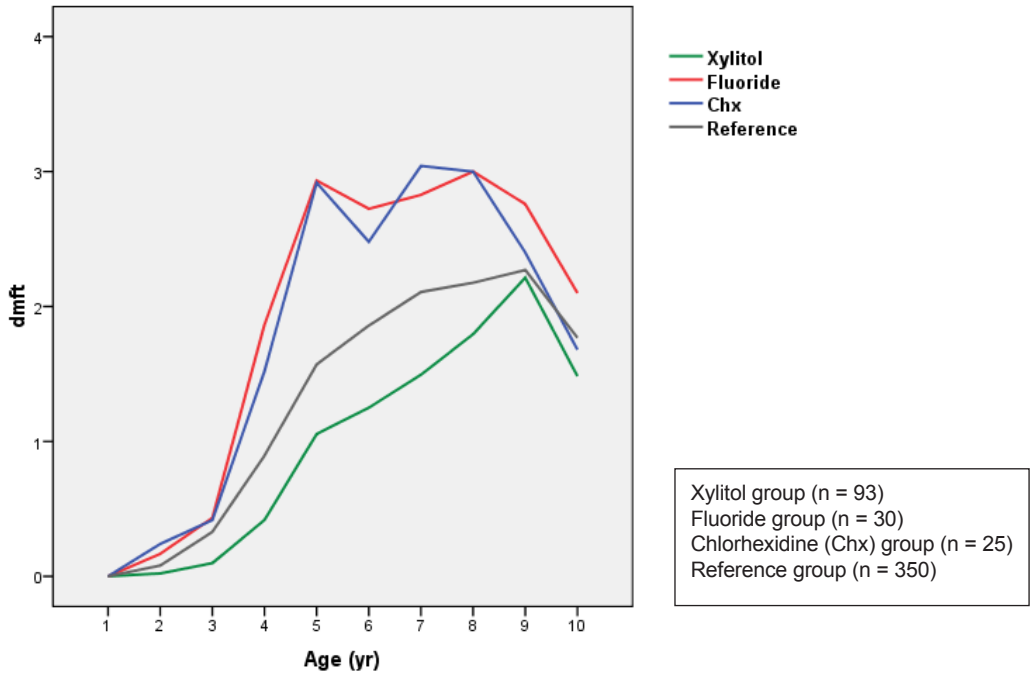


Figure 10. dmft values until 10 years of age in groups

Table 10. dmft values in different groups from 6 to 10 years of age, the highest values for each group in bold

Group		dmft 6 yr	dmft 7yr	dmft 8 yr	dmft 9 yr	dmft 10yr
Xylitol	**mean**	1.25	1.49	1.80	**2.21**	1.48
	SD	2.21	2.25	2.28	2.66	2.05
	n	92	89	93	89	93
Fluoride	**mean**	2.72	2.83	**3.00**	2.76	2.10
	SD	3.58	3.53	3.13	2.80	2.19
	n	29	29	30	29	30
Chx	**mean**	2.48	**3.04**	3.00	2.40	1.68
	SD	3.23	3.16	2.94	2.35	1.89
	n	25	24	25	25	25
Reference	**mean**	1.86	2.11	2.18	**2.27**	1.77
	SD	3.00	2.91	2.59	2.53	2.25
	n	339	344	352	340	358
Total	**mean**	1.83	2.08	2.20	**2.30**	1.73
	SD	2.93	2.87	2.60	2.55	2.20
	n	485	486	500	483	506

	p-value related to the differences between the groups (Mann-Whitney U-test)		
	until 6 yr	**until 8 yr**	**until 10 yr**
Xylitol vs Fluoride	0.035	0.055	n.s.
Xylitol vs Chx	n.s.	n.s.	n.s.
Xylitol vs Reference	n.s.	n.s.	n.s.
Xylitol vs controls (Fluoride and Chx)	0.019	0.018	n.s.
Reference vs controls (Fluoride and Chx)	n.s.	0.055	n.s.

Chx = chlorhexidine
n = number of children

5.3.3 Dental visits due to restorative treatment

During the follow-up period, the children in the xylitol group needed fewest restorative visits due to dental caries in primary dentition. Until 10 years of age, the children in the xylitol group had had on average of 2.8 restorative visits, whereas the corresponding figures were 3.9 both in the fluoride and in the chlorhexidine group. Until 4 years of age, the difference between the xylitol and the fluoride group was significant. In the reference group, the cumulative curve of the restorative visits due to dental decay in primary teeth lay between the corresponding curves of the xylitol and the experimental control (fluoride and chlorhexidine) groups (Figure 11 and Table 11).

Altogether 36 subjects out of 92 (39%) in the xylitol, 8 out of 29 (28%) in the fluoride, and 8 out of 25 (32%) in the chlorhexidine group had made no restorative visits until 10 years of age. In the reference group, 34% of the children had not made restorative visits. The maximum value of the restorative visits was 24 (one child in the reference group); in addition, one child in the xylitol group had made 17 and one child in the fluoride and one child in the chlorhexidine group 16 restorative visits for the restorative treatment of their primary teeth.

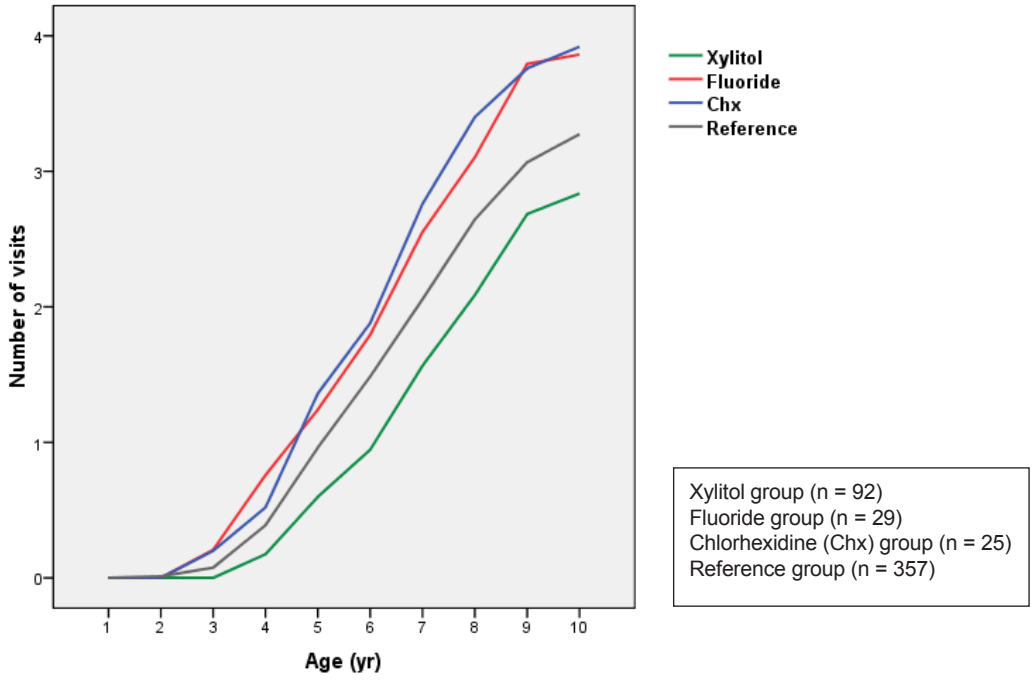


Figure 11. Mean values of cumulative number of visits for the restorative treatment of primary teeth until 10 years of age in the groups

Table 11. Mean values of cumulative visits for restorative treatment of primary teeth until 4, 6, 8, and 10 years of age in the groups

Group		Cumulative number of visits for restorative treatment of primary teeth			
		until 4 yr	until 6 yr	until 8 yr	until 10 yr
Xylitol	**mean**	0.2	1.0	2.1	2.8
	SD	0.6	1.9	3.1	3.9
	n	92	92	92	92
Fluoride	**mean**	0.8	1.8	3.1	3.9
	SD	1.3	2.8	3.5	4.1
	n	29	29	29	29
Chx	**mean**	0.5	1.9	3.4	3.9
	SD	1.3	3.4	4.2	4.7
	n	25	25	25	25
Reference	**mean**	0.4	1.5	2.7	3.3
	SD	1.2	2.6	3.6	4.0
	n	358	358	358	357
Total	**mean**	0.4	1.4	2.6	3.3
	SD	1.1	2.6	3.5	4.0
	n	504	504	504	503

	p-values related to differences between the groups (ANOVA)	
	until 4 yr	until 10 yr
Xylitol vs Fluoride	0.002	n.s.
Xylitol vs Chx	n.s.	n.s.
Xylitol vs Reference	n.s.	n.s.
Xylitol vs controls (Fluoride and Chx)	0.006	n.s
Reference vs controls (Fluoride and Chx)	n.s.	n.s.

Chx = chlorhexidine
n = number of children

5.4 Other dental visits

The numbers of caries-preventive visits, consisting of fluoride varnish treatments and counselling on oral hygiene and diet, until 10 years of age between the MS-colonized (mean 1.0, SD 1.3) and non-MS-colonized (mean 0.7, SD 1.3) children did not differ significantly. The maximum value was 4 in MS-colonized children, and 6 in non-MS-colonized children.

The number of preventive visits was highest in the chlorhexidine group, on average 1.9 visits throughout the follow-up years. The corresponding figures were 0.4 in the xylitol group and 0.9 in the fluoride group. In the reference group, the children had had 0.6 caries-preventive visits until the age of 10 years (Table 12).

Until 10 years of age, the mean number of all dental visits was 20.2 in the xylitol group, 22.4 in the fluoride group, and 21.2 in the chlorhexidine group. Besides the annual examinations, which accounted for half of the total number of visits, the preventive visits and the visits for caries treatment of the primary teeth, these visits included caries treatment of permanent teeth, and trauma-related visits, as well as orthodontic treatment. Of all dental visits until 10 years of age, 18% were made for the restorative treatment of the primary teeth: 14% in the xylitol group, 17% in the fluoride group, and 18% in the chlorhexidine group. In the reference group, 18% of all dental visits were made for restorative treatment of the primary teeth.

Table 12. Mean values of the cumulative preventive treatment visits of children until 4, 6, 8, and 10 years of age by group

Group		Cumulative number of children's preventive treatment visits			
		until 4 yr	until 6 yr	until 8 yr	until 10 yr
Xylitol	**mean**	0.0	0.1	0.2	0.4
	SD	0.1	0.3	0.5	0.7
	n	91	91	91	91
Fluoride	**mean**	0.2	0.4	0.6	0.9
	SD	0.5	0.8	1.0	1.4
	n	29	29	29	29
Chx	**mean**	0.3	0.5	0.9	1.9
	SD	0.7	1.3	1.6	2.0
	n	25	25	25	25
Reference	**mean**	0.1	0.2	0.3	0.6
	SD	0.2	0.5	0.7	1.1
	n	358	358	358	358
Total	**mean**	0.1	0.2	0.4	0.7
	SD	0.3	0.6	0.8	1.2
	n	504	504	504	504

Chx = chlorhexidine
n = number of children

5.5 Permanent teeth at 10 years of age

As regards the permanent teeth, the association of dentinal caries occurrence and MS-colonization was not similar to that observed in primary teeth. At the age of 10 years, 45% of the children who had been colonized by MS at the age of 2 years had had dentinal caries in their permanent teeth. The corresponding value was 42% among the non-MS-colonized children. The DMFT indices, the numbers of erupted permanent teeth and the numbers of sealed permanent teeth, as well as the cumulative number of preventive visits for MS-colonized and non-MS-colonized children at the age of 10 years, are given in Table 13.

Table 13. DMFT indices, numbers of permanent teeth, numbers of sealed permanent teeth, and cumulative numbers of preventive visits of 10-year-old children in relation to MS colonization at 2 years of age

			Until 10 years		
		DMFT10	number of permanent teeth	number of sealed permanent teeth	cum number of preventive visits
MS-	**mean**	0.97	17.0	3.3	0.7
	SD	1.33	4.8	2.0	1.3
	n	118	118	117	116
MS+	**mean**	1.21	17.9	3.6	1.0
	SD	1.76	5.0	1.6	1.3
	n	29	29	29	29

MS- = not colonized by MS at the age of 2 years
MS+ = colonized by MS at the age of 2 years
n = number of children

5.6 Oral-health-related behaviour of children at 10 years of age

The habits concerning tooth-brushing and usage of xylitol, sucrose sweets, or soft drinks did not differ between the experimental groups (Tables 14 and 15). The amount of visible plaque was similar in all three experimental groups (Table 16): 82% of the children in the xylitol, 90% in the fluoride, and 92% in the chlorhexidine group used fluoridated toothpaste.

Table 14. Tooth-brushing habits of the children at 10 years of age in different study groups

Group	Tooth-brushing habits		
	twice a day or more % (n)	once a day % (n)	less often than once a day % (n)
Xylitol	26 (23)	65 (58)	10 (9)
Fluoride	37 (11)	57 (17)	7 (2)
Chx	13 (3)	67 (16)	21 (5)

p = 0.201
Chx = chlorhexidine
n = number of children
p = p-value of the difference between the xylitol, fluoride and chlorhexidine groups, Chi-Square test

Table15. Usage of xylitol, sucrose sweets and soft drinks among the children at 10 years of age in different study groups

Group	Usage of xylitol		
	daily % (n)	twice a week % (n)	less often than twice a week % (n)
Xylitol	29 (26)	50 (45)	21 (19)
Fluoride	30 (9)	33 (10)	37 (11)
Chx	21 (5)	46 (11)	33 (8)

p = 0.347

Group	Usage of sucrose sweets		
	daily % (n)	twice a week % (n)	less often than twice a week % (n)
Xylitol	7 (6)	56 (50)	38 (34)
Fluoride	3 (1)	60 (18)	37 (11)
Chx	4 (1)	63 (15)	33 (8)

p = 0.932

Group	Usage of soft drinks		
	daily % (n)	twice a week % (n)	less often than twice a week % (n)
Xylitol	9 (8)	39 (35)	52 (47)
Fluoride	7 (2)	33 (10)	60 (18)
Chx	13 (3)	42 (10)	46 (11)

p = 0.861
Chx = chlorhexidine
n = number of children
p = p-value of the difference between the xylitol, fluoride and chlorhexidine groups, Chi-Square test

Table 16. Visible plaque amount among the children at 10 years of age in different study groups

Group	Visible plaque		
	not at all % (n)	a little % (n)	a lot % (n)
Xylitol	42 (37)	46 (40)	13 (11)
Fluoride	43 (13)	40 (12)	17 (5)
Chx	38 (9)	58 (14)	4 (1)

p = 0.569
Chx = chlorhexidine
n = number of children
p = p-value of the difference between the xylitol, fluoride and chlorhexidine groups, Chi-Square test

5.7 Economic evaluation

5.7.1 Costs of programmes

The costs of the maternal prevention programmes were highest in the xylitol group, 116 euros. The corresponding figures were 74 euros in the fluoride group and 112 euros in the chlorhexidine group. In the fluoride and chlorhexidine groups, the costs of maternal prevention included not only the material costs, but also the costs of varnish treatment visits. The costs of altogether three varnish treatments visits were 73 euros in the fluoride group and 110 euros in the chlorhexidine group. The additional costs of the maternal prevention programme in the xylitol group were 42 euros when compared with the fluoride group, and 4 euros when compared with the chlorhexidine group.

5.7.2 Costs of additional caries-free year of life

The children in the xylitol group maintained their primary teeth caries-free on average 3.17 years longer than the children in the fluoride group, and 1.67 years longer than the children in the chlorhexidine group. The additional costs for one additional caries-free year were 13 euros when maternal xylitol use was compared with the maternal fluoride varnish treatments, and 2 euros when compared with the maternal chlorhexidine varnish treatments. The costs of xylitol in relation to one additional caries-free year were 37 euros.

5.7.3 Costs of one saved restorative visit

Until the age of 10 years, the children in the xylitol group needed 1.1 fewer restorative visits due to caries occurrence in their primary teeth when compared with the children in the fluoride and chlorhexidine groups. The additional costs for one saved restorative visit were 38 euros when the prevention in mothers was carried out with maternal xylitol chewing gum when compared with maternal fluoride varnish treatment, and 4 euros compared with maternal chlorhexidine varnish treatment. The costs of xylitol in relation to one saved restorative visit were 105 euros.

6. DISCUSSION

The study consisted of two elements: first, the long-term follow-up of the experimental mother-child transmission study and, secondly, the comparison of the outcomes in these experimental groups with those of the other children of the same age cohort. The ten-year follow-up suggested that the results of the Ylivieska mother-child study had not been temporary and that the prevention of MS transmission in assumed high-risk families can be economically reasonable. Compared with the average levels of the age group, the prevention of early MS colonization in assumed high-risk families may improve dental health and reduce the need for restorative treatment in primary teeth.

6.1 Methodological considerations

6.1.1 Study subjects

None of the children in the experimental or reference groups was excluded from the present study because of sickness or diseases such as asthma, diabetes, leukaemia, or rheumatoid arthritis. Some of these conditions might have had an influence on diet, cooperation, or oral hygiene. No information about the possible changes in the diet of the children during the follow-up period was available. The children with very poor cooperation during early childhood had been randomly distributed in all groups.

6.1.1.1 Children in original Ylivieska mother-child study (experimental groups)

Practically all mothers-to-be in Finland come into contact with public well-baby clinics during their pregnancy. In the area of the Ylivieska Public Health Care Centre, there are no private well-baby clinics. From the beginning of 1990 until spring 1991 (i.e. about 18 months) all the pregnant mothers who had visited the well-baby clinics at the Ylivieska Public Health Care Centre had been invited to the screening for salivary MS for the Ylivieska mother-child study. Altogether 338 women had been screened. The reason for the larger size of the xylitol group had been the aim to study the effect of xylitol also on the transmission of *S. sobrinus* (Söderling *et al.* 2000). As the birth rate in the beginning of the 1990s in the area of the Ylivieska Public Health Care Centre was on average 320 babies per year, the participation among the pregnant women in the screening of the Ylivieska mother-child study had been comprehensive. It is possible that those mothers-to-be were, on average, already interested in taking care of their

children's dental health. This may have had a slight influence on the results; in real life, the cooperation of mothers might not be as good as in the study conditions. The examination with screening, as well as the xylitol chewing gum and the fluoride and chlorhexidine varnish treatments, had been announced to be free-of-charge. Therefore, low socio-economic status should not have had an influence on the participation of the mothers. The screening for high-caries-risk mothers had been carried out with the MS strip saliva test (CFU ≥ 100 000/ml). Of those screened, 58% had had high MS levels. In comparison, in the Swedish mother-child study carried out a few years later than the Ylivieska study, the mothers were screened when their infants were 3 months of age, the threshold value of MS being CFU ≥ 150 000/ml. Altogether 416 mothers were screened, and 46% of them showed high MS levels (≥ 150 000/ml) (Thorild *et al.* 2003).

The dropout rate (24%) after the beginning of the Ylivieska mother-child study in the early 1990s can be regarded as very low and similar in each study group. After eleven years, 93 (73%) of the original 127 xylitol group children, 30 (83%) of the 36 fluoride group children, and 25 (78%) of the 32 chlorhexidine group children were still available. Of those children who had not been colonized by MS at the age of 2 years, 91% were available at the age of 10 years, while 85% of those who had been colonized by MS were available. The proportions of the MS-colonized subjects in the xylitol and fluoride groups were similar among the dropouts and among the children who were included in the analyses. In the chlorhexidine group, all three dropouts were MS-colonized children. The only reason for dropouts was relocation. During the study period, there was not much movement in rural communities in central Finland. Two children had lived outside the Ylivieska Public Health Care district for a short period in their early childhood and their dental visit registrations were incomplete. They were both included in the annual analyses but excluded from the cumulative analyses, although it was highly probable that they had not had dental treatment in their earliest childhood. The dmft-values at 5 years of age in the present study were in line with the earlier results of the Ylivieska mother-child study (Isokangas *et al.* 2000) although the subjects in the groups were not exactly the same.

The fact that the experimental grouping was not totally blinded can be considered a weakness of the original study design. However, as regards MS colonization, the blinding was complete throughout the original and the present study. This considerably strengthens the present study.

In a clinical study, the size of the study material has a relevant effect on the results and conclusions. To calculate the adequate size of a study group, a clinically significant difference in relation to the main variable has to be determined. The smaller the difference determined the greater the size of material is required (Uhari and Nieminen 2000). In the present study, in a cross-sectional analysis, a 20% absolute risk reduction was estimated to have clinical significance and the size of the material available was considered appropriate. Within the group size of the present study, a 10% reduction in caries-free subjects could not have been found statistically significant, but, on the other hand, a 10% reduction would not have considerable clinical significance in the high-caries-risk children. In comparison with the cross-sectional analyses, the longitudinal data used in the survival analyses increase the statistical power as well as the reliability. This can be considered a strength of this study. However, in some comparisons between the subgroups, the number of subjects was quite low. This has weakened the statistical power, and therefore, these figures have to be interpreted with caution. Due to the original Ylivieska mother-child study design, it was not possible to increase the number of subjects for the present study.

6.1.1.2 Children in reference group

The Finnish Population Register is comprehensive, so it was possible to list all the children born in 1991 and 1992 who lived in the area of the Ylivieska Public Health Care Centre and whose data on dental health and visits from birth until 10 years of age could be found from the dental health care registers.

6.1.2 Data

The data in the Finnish public dental care registers can be regarded as exhaustive, and public dental records have been used as a source of information in several longitudinal studies (Seppä *et al.* 1989, Vehkalahti *et al.* 1997, Virtanen 1997, Varsio *et al.* 1999, Korhonen *et al.* 2003, Leskinen *et al.* 2007, Ollila and Larmas 2007). In Finland, it is ordered by law (Act on the Status and Rights of Patients 785/1992 and Personal Data File Act 523/1999) that all dental visits and treatments, as well as materials, must be documented in the files. In addition, the salary of the dentists partially depends on the measures, which ensures that data are thoroughly registered. In the present study, one of the main variables was the number of restorative visits, and the reliability of data concerning this variable can be assumed to be high. When dental health is measured using a dicotomic scale and as the first dental caries occurrence, the reliability of the data in public dental records is better than using dmft or dmfs indices. However, Hausen *et*

al. (2001) have suggested that the data collected from Finnish public health records are not decisively inferior compared with the data obtained from examinations by trained examiners.

Data for the study were collected retrospectively; all the dental treatments had been carried out before the personnel were informed about the follow-up study, and all the children had received equal dental health care, regardless of whether their mothers had participated in the mother-child study or not. The data from the files were collected by one person (author) to avoid possible differences in interpretation of the used notes and concepts. The data were checked and compared case by case in order to confirm all the details of the first collection. The control of the logical consistency of the notes in the files increased the reliability of the data.

The dental personnel in the Ylivieska Public Health Care Centre were permanent and experienced, and the dental care and treatment procedures were well established. Even among experienced dentists, caries diagnoses are subjective (Baelum *et al.* 2008) and there might have been inaccuracies in diagnostics. A possible error in diagnosis and treatment decision has, however, less impact on the results of long follow-up studies than on the results of cross-sectional studies. Due to the practise-based approach, the absence of calibration of the dentists can be accepted. In fact, because the personnel were not calibrated for the present study, the results may reflect even better the authentic situations in Finnish public dental care. Low numbers of restorations in the children's dentition typically make the diagnosing of dental decay easier and decrease the probability of underestimations. There are no indications to suggest that the first dental decay had been detected, registered or treated in a systematically biased way. In adults, who usually have more restorations, the probability of errors in diagnosis would be higher than in children.

All the dentists had examined and treated children from all three study groups during the ten-year period. It is unlikely that diagnoses and treatment decisions would have favoured any of the groups even if there had been variations in the criteria for caries diagnosis and treatment decision among the dentists. Because of the original Ylivieska mother-child study programme, the same dentist examined the same children annually until the age of 6 years. From then on, these children were examined like others of the same age, and neither the dentists nor the dental hygienists and assistants knew for sure whether the children had been participants in the mother-child study or not. However, even if the personnel had remembered in which study group the children were included, they were blinded with regard to MS colonization during the whole follow-up period.

There are no indications to suspect that the dentists would have been treating the children in a different way due to the earlier study grouping.

6.1.3 Outcome measures

6.1.3.1 Dental health

Since the 1930s, dental decay has most commonly been measured using DMFT/DMFS and dmft/dmfs indices. However, these indices have limitations; e.g. caries incidence, activity, or severity cannot be measured by these indices. The same teeth may have been filled several times, treated endodontically, and extracted during several visits without any changes in the index. In addition, the DMFT/DMFS and dmft/dmfs indices are inadequate for measuring new decay in teeth which have already been restored (Alanen 1991). Concerning dental health in primary teeth, the exfoliation causes inaccuracy in the dmft/dmfs index. In addition, the lower the caries level in the population the more problematic is the use of mean values as a measure of health or disease. The influence of one individual with a high number of decayed, filled or extracted teeth on the mean values of the group may be considerable. This problem becomes more pronounced with the increasing proportion of individuals without caries experience (DMFT/DMFS and dmft/dmfs = 0). The dmft index values in the present study facilitate comparisons with other studies and demonstrate the association of the dmft level and the timing of the first dental decay. During the data collection, it was noticed that there were inaccuracies in the number of affected tooth surfaces concerning primary teeth. Therefore, it was relevant to use the dmft index.

In the present study, the dental health of primary teeth was also measured by the children's age at first caries occurrence. This measure and the survival analysis used do not suffer from the limitations of the dmft index, e.g. exfoliation does not lead to inaccuracy. Instead, this measure enables the use of longitudinal data analyses, thus increasing the validity of the data and outcomes. Furthermore, the statistical power is improved (Mancl *et al.* 2004).

The data on enamel caries were not included in the analyses. At the beginning of the 1990s, enamel caries was not systematically registered in the files. The probability of differences in the diagnoses of enamel caries between the examiners is higher than in the diagnoses of dentin caries (Isokangas *et al.* 1987). The criteria for caries were those used in real decision-making situations for restorative treatment in public dental care. X-rays had been taken on an individual basis. The systematic use of X-rays would probably have increased

the number of lesions and, consequently, the number of restorative treatments. However, there is no reason to believe that this influence had differed between the groups.

During the Ylivieska mother-child study and the present study in the Ylivieska Public Health Care Centre, no sealants were applied to primary teeth. The dental personnel had been advised to seal the first permanent molars according to individual need. However, almost all the first permanent molars had been sealed (Table 13, p. 65). Furthermore, the application of sealants – or repeated sealants – may have been carried out more often in children with more decay in primary teeth, thus biasing the comparisons between the groups. Therefore, the information about the dental health of the permanent teeth has to be interpreted with great caution, and no statistical testing was performed. Accordingly, no conclusions about the effect of maternal prevention of MS transmission on permanent teeth can be drawn.

6.1.3.2 Restorative treatment visits

One of the key variables in the analyses was the number of restorative treatment visits up to 10 years of age. The figures for the restorative treatment visits were in good agreement with the figures of caries occurrence in each study group, also when the children were studied in relation to the early MS colonization. The data were collected retrospectively and all the treatment decisions had been carried out before the onset of the present study. There is no reason to presume that the method used to measure the need for restorative treatment would have favoured any study group.

In addition to dental health, the DMFT/DMFS and dmft/dmfs indices may also be used to measure the need for restorative treatment (Davies *et al.* 1973, Spencer 1981). In the present study, the practical consequences of the preventive measure for the health care organisation were studied. For this purpose, the number of restorative visits offered a more proper measure than the dmft index. Measuring differences in the numbers of restorative treatment visits facilitates easy interpretation of the outcomes from a clinical point of view. In primary teeth, the exfoliation further complicates the use of the dmft/dmfs index. This absence of correlation between the figures for mean dmft values and restorative visits can be clearly observed in the curves of the dmft and the cumulative restorative treatment visits of the groups, shown in Figures 10 and 11 (pp. 60 and 62). In all groups, the dmft curve starts to descend at the age of 7 to 9 years, while the cumulative curves of restorative visits are still ascending. The number of treatment visits needs to be evaluated to assess the economic outcomes of caries prevention and to develop cost-effective health care in public dentistry.

6.1.3.3 Costs

The prices for the prevention materials, xylitol chewing gum, fluoride varnish, and chlorhexidine varnish, were the true market prices for the year 2002. As this study was intended to inform the decision-makers for the 2000s, it was more valid to use the prices of the year 2002. It is possible that the changes in the market prices of these three preventive measures had not been similar during the study period. In fact, the ratio between the material costs was different in the beginning of the 1990s; the wholesale price of a 10 kg box of xylitol chewing gum (Xylifresh®) had risen from 185.01 euros in 1990 to 243 euros in 2002 (according to the registers of Leaf), while the price of fluoride varnish (Duraphat®) remained practically the same (Pharmaca Fennica® and the registers of the Ylivieska Health Care Centre). The chlorhexidine varnish (EC40®) had varied in the (retail) price of a 1.7 ml cartridge from 11.34 euros in 1990 to 9.07 euros in 2002, being at its highest, 22.69 euros, in 1999 (registers of Biodent). Moreover, the quantity discounts for public health care institutions may have varied during the follow-up. If the material costs had been calculated using the prices from the year 1990, the results would have favoured xylitol.

The data on the costs of dental visits were collected from the files of the Ylivieska Public Health Care Centre. In 2002, the wage costs in the Ylivieska Public Health Care Centre were 74% of the total costs. This is in line with other studies concerning public dental health care in Scandinavia where the wage costs have been 65–75% of the total costs (Wang 1994, Oscarson *et al.* 1998, Pienihäkkinen *et al.* 2005). The costs of the dental visits were strongly related to the times reserved for the visits. The application of 40% chlorhexidine varnish demanded more time than the fluoride varnish application. According to the directions of the producer, the application of chlorhexidine varnish was carried out with a special needle, and after the treatment the removal of the varnish was time-consuming, whereas the application of fluoride varnish was carried out with a brush and the fluoride varnish was left on the tooth surfaces. The mothers in the study, like all other patients in the Ylivieska Public Health Care Centre, visited the dentist or the dental hygienist according to a prearranged schedule, the times reserved for the visits following the established protocols of the Ylivieska Public Health Care Centre. The times reserved for the dental visits also included the preparation and the cleaning of the surgery room, as well as the possible waiting time for the next patient. Even if the fluoride or chlorhexidine varnish treatment did not always require all the time reserved for it, the next patient may not have been available before his or her scheduled appointment. In addition, the time needed for varnish treatment may have occasionally exceeded the time reserved. The true cost of a dental

appointment depends on the length of the reserved time, not on the 'true' length of the treatment itself.

6.1.3.4 Oral-health-related habits of children

The children were interviewed by the dentist during the examination at the age of 10 years, and none of the children refused to answer the questions. It may be presumed that children of this age might give answers they think are acceptable in order to please the dental personnel. It is not, however, likely that there would have been differences in overrating or underrating between the groups.

6.1.4 Statistical procedures

The Cox regression model helps to determine the explanatory variables in the event – in the present study, the first dentinal caries occurrence in the primary teeth – during the follow-up period. This analysis is recommended for use in clinical studies to demonstrate the proportion of the subjects who experience the event – symptom or disease – in the given time (Uhari and Nieminen 2001, reviewed by Spruance *et al.* 2004). The survival analysis can be considered valid to test the caries-free time in the primary teeth. Exfoliation does not affect the survival time, but may have an effect on the dmft indices.

As the number of restorative visits is a scale variable, the parametric univariate analysis of variance was used to test the differences between the groups. When evaluating the effectiveness of inhibition of early MS colonization, additional caries-free time and saved restorative visits can be considered valid, reliable, and easily understood measures.

The differences in the dmft indices between the groups were tested with nonparametric Kruskal-Wallis and Mann-Whitney U-tests, which are not dependent on the skewed values of the variables.

As in the original Ylivieska mother-child study, xylitol had had a strong effect on the occurrence of MS in the 2-year-olds, the analyses in the present study included additional modelling to test whether the association of MS and the outcome variables was similar in all experimental groups. As the interaction term was not significant, the effect of early MS colonization is suggested to be similar in each group. Unfortunately, in this modelling, the statistical power of the present analyses was quite low. However, when analysed in detail, the data indicated similar MS patterns in every experimental group.

6.2 Outcomes

The systematic reviews reveal a lack of studies concerning caries prevention in primary teeth (Rozier 2001, Marinho *et al.* 2002, 2003, SBU 2002, SIGN 2005). Clinical studies, especially on infants and young children, have to be carried out with critical care, and testing the new preventive materials might sometimes be even ethically questionable (WMA Declaration of Helsinki 1964, WMA Declaration of Ottawa 1998). With preventive measures targeted only to mothers, maternal caries prevention models avoid this problem.

The confounding factors have to be considered when interpreting the outcomes of a study. In long-term follow-up caries prevention studies, there can be several possible confounders, e.g. changes in dietary and oral hygiene habits, diseases, and possible differences in access to dental care. In the present study, there was no indication to believe that there were group-related differences in the confounders. Dental care was similar and free-of-charge to all the subjects. In the experimental groups, the interventions had been targeted only to the mothers. None of these interventions decreased the plaque levels of MS in mothers, only the transmission of MS to children was reduced (Söderling *et al.* 2000). Even if the mothers in the xylitol group had continued the use of xylitol or the mothers in the fluoride and chlorhexidine groups had started to use xylitol, it is not likely that the daily xylitol dosages would have been large enough or the use regular enough to have clinical significance (Milgrom *et al.* 2009). All the outcomes in the present study concerned the children and their dental health.

6.2.1 Dental decay

The high impact of the delayed MS colonization on caries experience was clearly seen in the present study. Of the children who were not colonized by MS at the age of 2 years, 60% had not had caries experience until the age of 6 years, whereas only 30% of the MS-colonized children were caries-free at the same age. At the age of 10 years, the difference in the timing of the first dental decay was still notable, 30% of the non-MS-colonized children and 10%of the MS-colonized were caries-free. If early MS colonization was inhibited, the timing of the first dentinal caries experience was delayed by more than three years. It can be assumed that avoiding inconvenience and pain increases the quality of life. Concerning very young children, this point has to be emphasized. Lower caries occurrence figures could be observed in the primary teeth until exfoliation, when compared with the MS-colonized children. Besides being statistically significant, these

findings have clinical significance, which is also an important aspect to recognize in clinical trials (D'Agostino and Massaro 2004).

The results are in good agreement with the results of other MS transmission studies (Köhler *et al.* 1984, 1994, Günay *et al.* 1998, Gomez *et al.* 2001, Türksel Dülgergil *et al.* 2004, Ercan *et al.* 2007, Thorild *et al.* 2006). In the present study, the follow-up period was longer than in these studies. The decrease in caries occurrence achieved by inhibiting the early MS colonization of children can have effects far into the future. Earlier studies have shown that if there is no or minimal caries experience in the primary dentition, it is highly probable that there will also be low caries experience in the permanent dentition (Alaluusua *et al.* 1987, Seppä *et al.* 1989, Raadal and Espelid 1992, Steiner *et al.* 1992, Skeie *et al.* 2006). Secondary (recurrent) caries has been shown to be a major problem among adults (Goldberg *et al.* 1981), thus by avoiding the first restorations, the problem with secondary caries may also be reduced.

The Ylivieska mother-child study demonstrated that the inhibition of MS transmission from mother to child can be achieved with maternal use of xylitol chewing gum (Söderling *et al.* 2000). In the Swedish study (Thorild *et al.* 2003, 2004, 2006), all the mothers used chewing gum with different xylitol concentrations, and the daily xylitol dose (from 0.9 g to 2.0 g) was also lower in Sweden. The duration of xylitol chewing gum usage was 21 months in Ylivieska, whereas it was only 12 months in Sweden. The results of Thorild *et al.* (2006) are in line with the results of the Ylivieska mother-child study; the MS colonization and caries figures were lower in the high-concentration xylitol group than in the comparison groups even in those with lower daily xylitol dosages and a shorter usage period.

It has been claimed that the caries preventive effect of xylitol chewing gum is principally based on the salivary-flow-stimulating effect of chewing (Scheie and Fejerskov 1998, Imfeld 1999). This does not, however, explain the decrease in caries occurrence of the children in the original Ylivieska mother-child study (Isokangas *et al.* 2000) and in the present study. Because the children themselves did not use chewing gum or other caries-preventive measures during the intervention, no saliva stimulation was present in the children. Additionally, the results of the study of Thorild *et al.* (2003, 2004, 2006) are in line with the suggestion that xylitol does have a special effect on MS transmission and caries occurrence. In that study, the mothers in all the study groups used chewing gum, thus the saliva-stimulating effect of chewing gum can not primarily explain the differences in the MS transmission or in the caries figures.

At the age of 5 years, the mean dmft figure of the xylitol group (0.83) had been reported to differ significantly from the corresponding figures of the fluoride (2.87) and chlorhexidine (3.22) groups (Isokangas *et al.* 2000, Table b in Appendix). The results of the present study are in line with the earlier results; at the age of 6 years, the mean dmft index was 1.25 in the xylitol group, 2.72 in the fluoride group, and 2.48 in the chlorhexidine group. The lower dmft values in the fluoride, and especially in the chlorhexidine group at the age of 6 years compared with the indices at 5 years may have been caused by dropouts among the MS-colonized children in these groups, but may also have been due to earlier exfoliation of the decayed primary teeth.

The low NNT value of 5 between the xylitol and the fluoride or the chlorhexidine groups at the age of 10 years can be regarded as good for such a long follow-up. This NNT value indicates that five mothers with high levels of MS should regularly use xylitol chewing gum from the 3rd to the 24th month of their infant's life to have one child without dental decay in primary teeth up to the age of 10 years. In the study of Thorild *et al.* (2006) the NNT by 4 years of age was 5.5. Oscarson *et al.* (2006) showed clearly higher NNT values with xylitol lozenges and very low daily xylitol dosages, the NNT being 13.9 by the age of 4 years, the higher NNT value indicating the lower effectiveness of the caries prevention model. In the study with Finnish high-caries-risk infants, two children had to receive intensive caries prevention care for three years to avoid restorative treatment of caries by the age of 5 years, the overall NNT figure of the prevention programme in the study being 8.3 (Pienihäkkinen and Jokela 2002). When the xylitol chewing gum was used instead of tooth-brushing at day-care centres for one year, the NNT by 9 years of age was reported to be 11 (Kovari *et al.* 2003). Due to the original study design, it was not possible to calculate ARR and NNT values between the experimental groups and the reference group.

When evaluating the outcomes of health care strategy, the side effects of the given prevention or therapy should also be considered (Weinstein *et al.* 1996). With maternal use of preventive measures, the children themselves were not exposed to possible side effects of xylitol, fluoride, or chlorhexidine at all. When interviewed, none of the mothers had reported any side effects during the use of the preventive measures (Isokangas, personal communication).

Even if the prevention strategy is effective in high-risk groups, the results may not be observed in the mean values of the whole population (Rose 2001). The original Ylivieska mother-child study aimed to investigate the effect of MS transmission in high-caries-risk families, and the favourable microbiological and clinical outcomes are considered

practical and typically represent a risk-based prevention strategy. If these results, as well as the results of the present study, are related to the whole age cohort in a population with low caries levels, it can be noticed that the results concerning the high-risk groups do not have a remarkable effect on the figures of the total age cohort (seen in Tables 9, 10 and 11).

6.2.2 Amount of restorative treatment

The children who were not colonized by MS at the age of 2 years needed significantly fewer visits for restorative treatment during the follow-up period. This phenomenon could be observed in all experimental groups. The strong association of early MS colonization with caries occurrence and need for restorative visits suggests the importance of the prevention of the MS transmission from mother to child.

The avoidance of any kind of discomfort in childhood is valuable; unpleasant experiences in dental care can have regrettable consequences (Low *et al.* 1999, Filstrup *et al.* 2003), and may lead to recurrent neglect of oral hygiene and dental care even in adulthood. If the dental decay can be prevented, the quality of the dental care is automatically high, whereas the quality of restorative treatment varies; the value of the intact tooth is higher than the value of the restored tooth. Generally, the earlier the teeth must be restored the poorer is the prognosis, and the need for renewing restorations is more likely because of the poor cooperation of toddlers. Lack of cooperation may lead to the need for extra measures such as nitrous oxide sedation or general anaesthesia, both of which raise caries treatment costs significantly.

The children in the xylitol group needed the fewest restorative treatment visits for their primary teeth. The figures were lowest in the xylitol group, even though the children in the fluoride and chlorhexidine groups had made more caries prevention visits. In the fluoride and chlorhexidine groups, most of the restorative treatment was needed in early childhood before school age, when the treatment is more demanding and takes more time, and thus generally increases the costs. Dental decay in early childhood may lead to extractions of primary molars and cause lack of space for the permanent teeth. The possible increased need for orthodontic treatment among the children with high caries prevalence could not be observed in the present study because the follow-up of the children ended at 10 years of age, and treatment with fixed appliances is often carried out in the teenage years. In addition, the number of children needing orthodontic treatment, especially in the fluoride and chlorhexidine groups, was too small for reliable comparisons.

6.2.3 Oral-health-related habits

The dental health of the study children does not necessarily reflect only the effect of maternal caries prevention and early MS colonization. Oral hygiene habits, diet, and use of dental care facilities have a prominent impact on caries experience. The mothers had been interviewed about the type of day care, changes in the diet, illnesses and medications of the child, possible medications of the mother, oral hygiene procedures, and use of xylitol and fluorides by either the child or the mother when the children were 3 and 6 years old. No significant associations between MS colonization and diet, use of fluoride products or antibiotics, or type of day care had been detected. At the age of 6 years, the study children were reported to have similar xylitol usage habits in each study group (Söderling *et al.* 2001). As regards the xylitol use of the mothers, during the intervention period, the mothers in the fluoride and chlorhexidine groups had followed the instructions of the study protocol and had not used xylitol chewing gum. The mothers had been interviewed about the post-intervention use of xylitol when the children were 4 years old. No significant differences between the groups had been detected; 35% of the mothers in the xylitol and chlorhexidine groups, and 16% in the fluoride group, had reported that they were daily users of xylitol chewing gum. (Isokangas *et al.* 2000)

In the interview carried out during the examination when the children were 10 years of age, no significant differences between the study groups in relation to the oral-health-related habits of the children were detected. The finding on the similarity of oral-health-related habits after the intervention is in line with earlier studies (Isokangas *et al.* 1989, 1993). Surprisingly, less than one third of the children in all three groups reported regular use of xylitol products. As the parents and especially mothers are known to be the principal examples and transmitters of health habits to their children (Rossow and Rise 1994, Mattila *et al.* 2005), it was expected that after the trial, the use of xylitol would have continued and been regular not only in the xylitol group families, but also that other families in the Ylivieska region would have adopted the xylitol usage. The knowledge about the encouraging results of the Ylivieska mother-child study did not seem to have essentially increased xylitol gum chewing. This finding was, however, in line with the suggestion by Poutanen *et al.* (2006), that the oral-health-related behaviour among Finnish 11–12-year-olds is more strongly associated with their parents' behaviour than with their parents' knowledge. In the previous interview carried out by Söderling *et al.* (2000) during the Ylivieska mother-child study, a similar level of xylitol usage in children can be noticed (Questionnaire 2 in Appendix, based on the reanalysis of the original data with the permission of the authors). Until 10 years of age, the children's use of xylitol was similar in all three experimental groups, thus the xylitol usage did not have

a significant influence on the dental health differences between the groups. As the xylitol was not widely used after the study period, it can be presumed that xylitol used by the children themselves did not have an extensive effect on their dental health.

The questionnaire revealed that the study children were at high risk for caries when evaluated on the basis of their oral-health-related behaviour. Only one third of the children in all three study groups reported using sucrose sweets less often than twice a week, and half of the children consumed sucrose-containing soft drinks more often than twice a week. A minority of the children brushed their teeth at least twice a day as generally recommended (Löe 2000), the children in the chlorhexidine group brushed the least. In fact, only the tooth-brushing habits of the children in the fluoride group reached the average frequency of Finnish schoolchildren of the same age (Kuusela *et al.* 1997, Honkala *et al*. 2009).

6.2.4 Evaluation of costs in relation to benefits

In the literature, several maternal caries prevention strategies have resulted in lower caries experience of children. Besides the clinical effectiveness, the cost of prevention has a major significance for the cost-effectiveness of a prevention strategy. The trials in Sweden (Köhler *et al.* 1984, 1994), Germany (Günay *et al.* 1998), Chile (Gomez and Weber 2001, Gomez *et al.* 2001), and in Turkey (Türksel Dülgergil *et al.* 2004, Ercan *et al.* 2007) did not include economic evaluation of the maternal prevention. Although they were clinically effective, the strategies were also highly resource-demanding, resulting in high costs for the public dental care.

As a measure of maternal caries prevention, xylitol chewing gum differs from the other presented strategies, as the demand for public dental care resources is minimal. Besides the price of the xylitol chewing gum, also the length of the treatment period had a significant effect on the costs. The maternal use of xylitol chewing gum had continued for altogether 21 months, while in the study of Thorild *et al.* (2003, 2004, 2006) in Sweden, the figures for caries occurrence at 4 years of age were lower even with a 12-month xylitol chewing period and smaller daily dosages. In Sweden, the material costs for the recommended xylitol chewing gum consumption would have been 25% of the costs in Ylivieska (at Finnish prices). However, the caries occurrence of the children up to 10 years of age is not known.

The results of the present study are in line with the suggestion by Thorild *et al.* (2006) that xylitol chewing-gum-based maternal caries prevention might be cost-effective even

in low-caries communities. The additional caries-free year, as well as the decreased need for restorative visits achieved by the maternal use of xylitol chewing gum, were attained at relatively low costs. According to the files of the Ylivieska Public Health Care Centre, the costs of a dental visit to a dentist with a dental assistant were 37 euros per half hour, which is the typical appointment time reserved for a restorative visit for toddlers and young children. This cost is practically the same as the cost of xylitol in relation to one additional caries-free year.

The results concerning the costs of one saved restorative visit and one additional caries-free year of life are highly sensitive to the changes in the material costs of the maternal prevention. The value-added taxes (VAT) of xylitol chewing gum (17% as foodstuff) were higher than those of fluoride or chlorhexidine varnish (8% as pharmaceuticals). In addition, xylitol chewing gum, as well as fluoride and chlorhexidine varnishes, could be purchased at considerable quantity discounts by the Ylivieska Public Health Care. If the prevention costs were calculated with VAT or at retail prices, the differences in prevention costs would be greater, and the costs for the saved restorative visit and the additional caries-free year would rise. Purchasing the xylitol chewing gum at wholesale discounts and without value-added taxes, the daily costs of xylitol chewing gum to the public health care were 0.18 euros. If the mothers had bought the xylitol chewing gum themselves, the cost of the chewing gum would have been 192 euros, the daily cost for the mothers being 0.31 euros at retail prices. If this kind of targeted maternal prevention strategy is to be applied in the public dental health care, all pregnant mothers should be screened for their MS levels. The cost of screening to find one high-caries-risk mother would be about twice the price of the test, because about half of the pregnant mothers have high MS levels. On the other hand, the screening itself brings savings when the prevention and public recourses can be efficiently targeted to those most in need.

The wage costs had a strong effect on the evaluation of costs in relation to inputs. If the fluoride and the chlorhexidine varnishes had been applied by a dental hygienist, the costs of maternal prevention would have been lower in both groups because of the lower wage costs, although with a dental hygienist working alone the appointment time would have been longer. The chlorhexidine and fluoride varnish could also be applied by an experienced and trained dental assistant, and then the wage costs would be even slightly lower. On the other hand, if the costs of transportation to the dental clinic or loss of time of the mothers had been calculated the costs of maternal prevention in the fluoride and chlorhexidine groups would have been higher.

Opportunity costs (Weinstein 1981, Forbes and Donaldson 1987) were not included in the calculations of the maternal prevention costs. The alternative use of resources instead of the varnish treatments of mothers or preventive and restorative treatment of children could bring monetary benefits to the public health care institution. As the children need fewer dental visits, more resources are available for the dental care of adults, leading to increased monetary profits for the health care institution.

All the costs of maternal prevention were accrued at the beginning of the Ylivieska mother-child study at the beginning of the 1990s, while the health benefits of the prevention programmes were achieved during the ten-year follow-up period. In health economics, discounting is commonly used to compare benefits and costs occurring in different years, the difference between the future value and the present value is determined by the rate of discount (Drummond 1980, Tuominen 1994, Sintonen *et al.* 1997). In the present study, the maternal prevention costs occurred at the same time in each group and health benefits were not measured by monetary values, so the costs did not need to be discounted.

The costs of dental caries are not caused by caries itself, but by the treatment decisions. The data of the study were observed retrospectively and all the treatments were carried out before the data collection. In the economic evaluation of the preventive strategy, the long-term effects and the need and costs of renewing fillings should also be considered (Donaldson *et al.* 1986). In this study, primary dentitions were actually followed until exfoliation, and practically all the restorative treatments of the primary teeth, including the renewing of fillings, were included.

6.2.5 Outcomes of experimental groups in relation to reference group

All the children in the experimental groups were at high risk of caries, whereas the average risk for caries in the reference group was lower, because a remarkable proportion of the high-risk children in these age groups had been included in the experimental groups. Due to the larger proportional representation of low-caries-risk subjects, it could have been assumed that the dental health of the children in the reference group would have been better than the dental health in the experimental groups. However, in the xylitol group, the outcomes concerning all the main variables were at about the same level as the reference group. On the contrary, the other two intervention groups, the fluoride and chlorhexidine groups, maintained their higher levels until the end of the follow-up period. It seems that by maternal use of xylitol, it might be possible to improve the dental health of high-caries-risk children to the same level as that of the whole age cohort. Particularly if the timing of the first dental decay is delayed, the clinical significance is

considerable. These findings concerning the dental health and the number of restorative visits of the children in the reference group are not, however, strictly comparable with the corresponding outcomes of the experimental groups, so the results have to be interpreted as only suggestive. When interpreting the statistical analyses between the reference group and the experimental groups, the baseline difference concerning the MS levels of the pregnant mothers must be kept in mind. Therefore, too strict conclusions cannot be drawn.

6.3 General discussion

It has been suggested that caries prevention programmes among high-caries-risk subjects have been unsuccessful because the timing of the preventive strategy has been too late (Hausen 2000, Meriläinen 2004). Maternal preventive strategies target the inhibition of early MS colonization. As the first oral microbiota influence the consistency of later microbial colonization, the optimal non-caries-promoting homeostasis in dental biofilm can be achieved in childhood. According to the 'ecological plaque hypothesis' (Marsh 2003), the microbial consistency of the oral biofilm has a significant role in the balance of demineralization and occurrence of dental decay.

In health care, the evaluation of costs in relation to benefits should help politicians and other decision-makers to compare different health care strategies (Russell *et al.* 1996, Siegel *et al.* 1996). Politicians and other decision-makers in public health care have to evaluate the costs of the dental health of children and decide how much society is willing to pay for caries-free primary teeth. The relative costs of caries prevention are higher in communities where caries prevalence is low. However, inputs in prevention are still necessary because of caries-causing factors such as high sucrose consumption in snacks and beverages. In low-caries communities, caries-preventive strategies have either achieved limited success (Hausen *et al.* 2000, Källestål and Fjelddahl 2007), or the improved dental health has required huge efforts (Hausen *et al.* 2007). The results of the present study demonstrated that better dental health of children can be achieved using less of the resources of public dental care. Maternal use of xylitol chewing gum does not call for specific equipment, health care facilities or dental personnel, and the gum chewing can easily be done during leisure time or working hours. The wage costs have the greatest effect on the costs of dental visits, and thus, if the number of visits, especially to the dentist, can be reduced, savings for public health care are achieved. In Finland, during the study period, the children started school at 7 years of age. Before school age, the children are usually accompanied to the dental clinic by their parent or

caregiver. The loss of the parent's time and the costs of transportation to the dental clinic could be decreased if the early MS-colonization is inhibited.

The results of the study suggest that inhibition of early MS transmission with the maternal use of xylitol chewing gum may offer a new strategy for caries control in public dental care. In the original Ylivieska mother-child study, the fluoride group was regarded as a control, it was expected that fluoride varnish would not have an inhibitory effect on MS transmission (Schaeken *et al.* 1991). In a real life situation, the biannual fluoride varnish treatments for pregnant mothers do not follow the established oral-health-care procedure. Therefore, the realistic costs of the MS transmission inhibition are 116 euros, not the incremental costs of xylitol chewing gum compared with the fluoride varnish treatments. The decision-makers have to consider the cost of the inhibition of early MS transmission; is the public health care institution willing to pay the price of xylitol for the improved dental health and avoidance of discomfort of a child?

The quantity discounts in the price of xylitol are crucial in the cost-effectiveness of the maternal use of xylitol chewing gum. Public health care institutions can purchase xylitol in large amounts, and if the xylitol chewing gum is delivered by a public institution, the costs are lower than when purchased by each mother herself. In addition, if this kind of caries prevention model with relatively high material costs is offered by the public health care, the health benefit can be achieved equally in all socio-economic classes. By reducing the value-added tax on xylitol products the costs for the mothers would decrease, but probably this prevention model would not reach the mothers most in need and with the poorest compliance.

The costs of fear, pain and anxiety can not be calculated in monetary values. If they are evaluated, and if health benefits could be discounted, the importance of the delay in caries occurrence in the evaluation of costs in relation to health benefits would become more significant (Yule *et al.* 1986). Furthermore, the superiority of xylitol in the prevention of early childhood caries would be more obvious. If the health benefits can not be discounted, this may significantly bias the cost-effectiveness analysis (Keeler and Cretin 1983, Weinstein *et al.* 1996). Discounting costs at a higher rate than benefits may lead to delayed investments by policy-makers. According to Drummond (1980), 'if a preventive programme used less resources than a curative programme, then the avoidance of any pain, suffering, or discomfort associated with the latter would serve to reinforce the view that the preventive programme should be chosen'. The results of the present study clearly show that caries prevention targeting the inhibition of early MS colonization saves children from pain and discomfort especially in earliest childhood.

According to Akehurst and Sanderson (1993), positive messages to 'do something' are in general better received by the public than negative 'give up' messages. In their statement given at The Conference on the Efficacy of Caries-preventive Strategies 1992 in the Netherlands, Pollard and Curzon (1992) reported that it was extremely difficult to influence behaviour by diet counselling. Especially high-caries-risk individuals are likely to be poor compliers with caries-preventive therapies requiring dental visits. Xylitol chewing gum and lozenges provide alternatives to sucrose-containing products; the consumers do not have to give up gum chewing, and snacking with xylitol sweets is allowed. Compliance with the xylitol chewing gum is already high in Finland and gum chewing is regarded as a 'smart habit' (Nordblad *et al.* 1995, Honkala *et al.* 1996, 1999). The sweet taste of xylitol is generally well accepted and xylitol gum chewing is regarded as a pleasurable experience. The bitter taste of chlorhexidine varnish decreases its compliance, and also the taste of fluoride varnish is often disliked. The feasibility and acceptance of xylitol chewing gum as a prevention method among toddlers and school children have been reported to be good or excellent (Isokangas 1988, Autio and Courts 2000, Mäkinen *et al.* 2005). Also South Korean parents and personnel in day-care centres regarded the xylitol chewing gum programme as an important procedure in oral health promotion (Mäkinen *et al.* 2005), whereas in the United States, the acceptance of teachers in pre-school classes was poor (Autio and Courts 2000). The message that people themselves can do a great deal to maintain good dental health should be emphasized by dental care professionals. The role of xylitol in caries prevention is complementary; in addition to regular tooth-brushing with fluoridated dentifrices, and avoidance of snacking, also xylitol chewing gum could be included in everyday dental home care, as recently recommended by Deshpande and Jadad (2008).

One well-known problem with targeted high-caries-risk prevention applied by dental personnel is that individuals who are most in need are likely to be least exposed because of their unfavourable oral-health-related lifestyles and poor compliance, and their dental care may never be cost-effective. The advantage of xylitol chewing gum is that it reaches even those who occasionally neglect their regular visits to a dentist. The daily usage of xylitol chewing gum reminds people of the significance of dental health and may have a positive effect on other health-related attitudes. Of course, the compliance of xylitol chewing gum as a caries-preventive measure is not complete. In real life conditions, the use of xylitol may have similar problems to any other caries prevention method. Unfortunately, individuals at the highest risk of caries are not usually motivated to follow any guideline for self-care.

The Ylivieska mother-child study was the first study on the use of xylitol in maternal caries prevention. It showed that caries occurrence in children can be effectively decreased by the maternal use of xylitol chewing gum. The ability of xylitol in maternal caries prevention was most probably due to its good ability to prevent MS colonization. The important result of the present study was that if early MS colonization in children can be inhibited, the need for restorative treatment of the primary teeth is significantly lower when compared with children who have been colonized by MS in early childhood. There are no other long-term studies on maternal caries prevention where the follow-up of the children extends so far. The results of the present study are in good accordance with the suggestion by Thorild *et al.* (2006) that this type of targeted mother-child intervention can be cost-effective even in low-caries communities. However, we still do not know what is the optimal dosage, the best timing of usage, or length of usage for the best cost-effectiveness of maternal use of xylitol chewing gum in caries prevention.

The results of the present study indicate that early MS colonization has a strong long-term effect on caries prevention and need for restorative treatment. Moreover, the results suggest that further analyses of the different procedures of xylitol use and its cost-effectiveness in caries prevention are justified. Any other caries-preventive strategies aiming at the inhibition of MS colonization are interesting subjects for future studies.

7. CONCLUSIONS

Within the limitations of the study, the following conclusions are drawn:

- If a maternal caries prevention strategy effectively inhibits mutans streptococci (MS) transmission from mother to child, this strategy seems to have long-term effects on the dental health of the children's primary teeth. The children's primary teeth remain healthy longer, the number of decayed teeth is lower, and the need for restorative treatment decreases, which consequently reduces the costs of treatment.

- The long-term results concerning the children of the original Ylivieska mother-child study suggest a need for further studies on caries-preventive strategies aiming at the inhibition of early MS colonization. If the maternal use of xylitol chewing gum significantly reduces MS transmission, this prevention strategy may have long-term effects on the health of and on the need for restorative treatment in children's primary teeth.

- The prevention of MS transmission may reduce caries occurrence figures in assumed high- risk children to the same level as the average figures for the whole age cohort.

- The costs of achieving caries-free years in childhood by preventing MS transmission can be considered reasonable.

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APPENDIX

Table a. Isokangas *et al.* 2000, by permission of the copyright owner and the authors

Table 1. Proportion of Children without Caries Experience (Caries-free) at the End of Every One-year Age Interval by Presence of Mutans Streptococci at the Age of 2 Years and the Mothers´ Treatment Group

	MS Not Detected at 2 Years of Age						MS Detected at 2 Years of Age					
Age Interval	Xylitol		Chlorhexidine		Fluoride		Xylitol		Chlorhexidine		Fluoride	
	n[a]	Caries-free[b]	n	Caries-free	n	Caries-free	n	Caries-free	n	Caries-free	n	Caries-free
0-1	93	1.000	20	1.000	17	1.000	10	1.000	8	1.000	16	1.000
1-2	93	1.000	20	1.000	17	1.000	10	0.900	8	0.750	16	0.813
2-3	92	0.957	19	0.947	17	0.882	8.5	0.582	6	0.500	13	0.688
3-4	85	0.867	16	0.770	15	0.706	5	0.466	4	0.375	10.5	0.360
4-5	72	0.746	11.5	0.636	11	0.642	4	0.233	3	0.250	5	0.288

[a] Person-years followed during the given age interval.
[b] The effects of the MS colonization and the treatment group on the survival times (= the age of the child at the first caries attack; 1.000 = all children caries-free) were tested according to the Cox relative hazard model. Risk ratio for MS colonization was statistically significant (3.60; 95% CI, 1.99-6.49), and for the treatment group, differences were not significant.

Table b. Isokangas *et al.* 2000, by permission of the copyright owner and the authors

Table 2. Annual Mean dmf Figures in the Xylitol, Chlorhexidine, and Fluoride Groups

	Years of Age											
	2			3			4			5		
Group	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
Xylitol, all	0.02	0.20	103	0.17	0.72	97	0.41	1.15	92	0.83c	1.63	90
[a]MS-	0.00	0.00	93	0.09	0.49	88	0.31	1.07	83	0.68	1.52	81
[b]MS+	0.20	0.63	10	1.00	1.66	9	1.33	1.50	9	2.22	1.99	9
Chlorhexidine, all	0.21	0.83	28	0.77	2.03	26	1.91	3.40	21	3.22	4.10	23
MS-	0.00	0.00	20	0.06	0.24	18	0.71	1.90	14	1.67	2.74	15
MS+	0.75	1.49	8	2.38	3.20	8	4.29	4.57	7	6.13	4.79	8
Fluoride, all	0.21	0.70	33	0.55	1.18	33	1.69	2.38	32	2.87	3.48	30
MS-	0.00	0.00	17	0.41	1.18	17	1.06	1.78	17	1.33	1.84	15
MS+	0.44	0.96	16	0.69	1.20	16	2.40	2.80	15	4.40	4.08	15
Total n			164			156			144			143

[a] MS- = MS not detected in children at the age of 2 years.
[b] MS+ = MS detected in children at the age of 2 years.
[c] The group differs significantly from the chlorhexidine and fluoride groups, $p < 0.001$.

Table c. Mean DMFT values of the 10-year-olds born 1990-1994 in the area of Ylivieska Public Health Care Centre (Annual reports of Ylivieska Public Health Care Centre).

Year of birth	DMFT 10 yr
1990	0.91
1991	1.02
1992	0.94
1993	0.93
1994	1.04

Table d. The proportions of the costs of dental care in Ylivieska Public Health Care Centre in 2002

	Euros	Proportion of costs (%)
Wage costs	1,478,424	74
Material costs	149,840	7.5
Allocated	229,986	11.5
Services		~ 5
Others		~ 2
Total	1,997,870	100

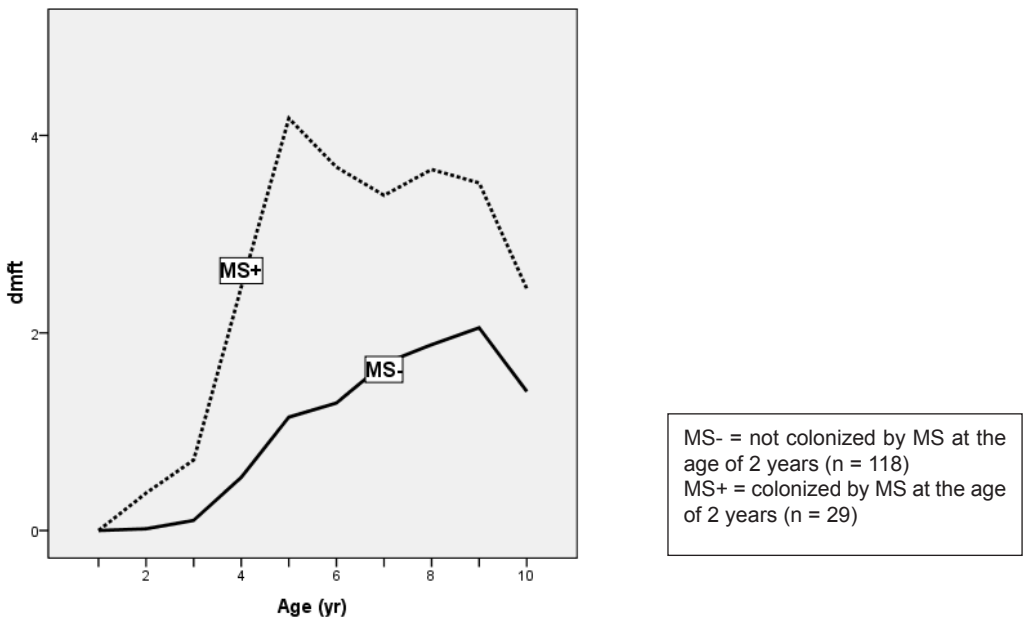

Figure a. Cumulative dmft values until 10 years of age in relation to MS-colonization at 2 years of age

Questionnaire 1

MOTHER-CHILD STUDY / 10 yr

date

1.

- Name of the child……..
- Age (yrs)…….
- Locality……...
- ID of the saliva sample ☐☐☐

2.

- Number of permanent teeth……
- DMF ☐☐
- Amount of plaque…….....
- Tooth-brushing
  - ≥ twice a day ☐
  - once a day ☐
  - less than once a day ☐
- Tooth-paste
  - common fluoride paste ☐
  - children's paste ☐
  - special paste ☐
    - which ?……

3.

- Use of xylitol
  - daily ☐
  - two-three times a week ☐
  - less or never ☐
- Most commonly used xylitol product……

4.

- Use of sweets and soft drinks
- Sucrose sweets
  - daily ☐
  - two-three times a week ☐
  - less ☐
- Soft drinks
  - daily ☐
  - two-three times a week ☐
  - less ☐
  - regular ☐
  - light drinks ☐

5.

- Other aspects concerning the study

…….

Questionnaire 2

MOTHER-CHILD STUDY / 6 yr

1. CHILD – Name:……Number of children in the family

Age (yrs) ☐

d ☐☐	m ☐☐	f ☐☐	dmf ☐☐	DMF ☐☐

saliva sample taken ☐ MS-strip index ☐ sample ID ☐

MS total saliva CFU ☐ ☐ ☐ ☐ dilution ☐

S. Sobr. saliva CFU ☐ ☐ ☐ ☐ dilution ☐

2. USE OF XYLITOL

Child has used xylitol after the examination at 5 yrs

daily (> 5 times a week)	
two-three times a week (≤ 5 times a week)	
not at all	

Type of xylitol, if has used

Xylifresh® chewing gum	
other xylitol chewing gum	
other xylitol product	

3. USE OF FLUORIDE TABLETS AFTER THE EXAMINATION AT 5 YRS

regularly ☐ irregularly ☐ not at all ☐

(≥3 times a week) (<3 times a week)

Type of fluoride tablet Fludent® ☐ Fluorilette® ☐

4. OTHER ASPECTS CONCERNING THE STUDY, medication, diseases, diet

……
……