OULU 2010
D 1078

ACTA
UNIVERSITATIS OULUENSIS

Kaja Leskinen

FISSURE SEALANTS IN CARIES PREVENTION

A PRACTICE-BASED STUDY USING SURVIVAL ANALYSIS

*UNIVERSITY OF OULU,
FACULTY OF MEDICINE,
INSTITUTE OF DENTISTRY*

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A practice-based study using survival analysis

Academic dissertation to be presented with the assent of the Faculty of Medicine of the University of Oulu for public defence in Auditorium 1 of the Institute of Dentistry (Aapistie 3), on 26 November 2010, at 12 noon

UNIVERSITY OF OULU, OULU 2010

Acta Univ. Oul. D 1078, 2010

Supervised by
Professor Markku Larmas

Reviewed by
Professor Heikki Murtomaa
Professor Liisa Suominen

ISBN 978-951-42-6341-5 (Paperback)
ISBN 978-951-42-6342-2 (PDF)
http://herkules.oulu.fi/isbn9789514263422/
ISSN 0355-3221 (Printed)
ISSN 1796-2234 (Online)
http://herkules.oulu.fi/issn03553221/

Cover Design
Raimo Ahonen

JUVENES PRINT
TAMPERE 2010

Leskinen, Kaja, Fissure sealants in caries prevention. A practice-based study using survival analysis
University of Oulu, Faculty of Medicine, Institute of Dentistry, P.O.Box 5281, FI-90014 University of Oulu, Finland
Acta Univ. Oul. D 1078, 2010
Oulu, Finland

Abstract

The purpose of this study was to analyse the effectiveness and cost of fissure sealant treatment in preventing dental caries in children in a practice-based research network using survival analysis.

The survival times of first permanent molars in children were analysed in three countries: in Finland (age cohorts 1970–1972 and 1980–1982), in Sweden (1980–1982) and in Greece (1980–1982), and additionally at two municipal health centres in Finland (age cohorts 1988–1990 in Kemi and 1990 in Vantaa). The study population comprised altogether 8 551 children.

The data were collected manually from paper dental records (Finland, Sweden and Greece), and an automatic data-mining system for collecting data from electronic dental records was used in the case of the two health centres in Finland (Kemi and Vantaa). Comparisons of the survival times of first molars caries-free were performed between sealed and non-sealed individual teeth, and between the subjects in cases where a subject’s all first permanent molars were either sealed or non-sealed before the age of eight years. The cumulative costs of caries risk determination, use of xylitol, fissure sealant treatment, and restorations were calculated based on the data from the digital dental records of the health centres of Kemi and Vantaa.

The results stressed the importance of caries-risk assessment on a tooth and subject level, when estimating the need for sealing treatment. Sealing of first molars of very high caries risk children (caries present in any of the permanent first molars before the age of eight years) seemed to be insufficient to prevent further dental decay later on. Instead, sealants were beneficial in caries prevention in medium-risk children (caries present in any of the permanent first molars between the ages of eight and ten years). Low-risk children (no caries in any of the permanent first molars before the age of ten years) did not benefit remarkably from sealant treatment. When sealant treatment were targeted only at high caries risk children based on risk-determination at the age of two years and all their permanent first molars were sealed (Kemi), their total treatment costs later were higher compared to the low-risk children, who were left unsealed. Significant differences in the survival curves of sealed and non-sealed first molars on a tooth and subject level confirmed that a translational approach is needed to study the effectiveness of preventive dental treatment in practice.

The practice-based study model provides a good overview on the situation in real-life circumstances and helps to incorporate the evidence-based dentistry study results into everyday dental practice.

Keywords: dental caries, fissure sealants, practice-based research, preventive dental care

Leskinen, Kaja, Fissuurapinnoitteet hammaskarieksen ehkäisyssä. Käytäntöön perustuva tutkimus käyttäen elinkaarianalyysimenetelmää
Oulun yliopisto, Lääketieteellinen tiedekunta, Hammaslääketieteen laitos, PL 5281, 90014 Oulun yliopisto
Acta Univ. Oul. D 1078, 2010
Oulu

Tiivistelmä

Tutkimuksen tarkoituksena oli analysoida fissuurapinnoituksen tehokkuutta ja kustannuksia lasten hammaskariesta ehkäisevänä toimenpiteenä käytäntöön perustuvan tutkimusmenetelmän ja elinkaarianalyysin avulla.

Ensimmäisten pysyvien poskihampaiden elinkaarianalyysi tehtiin Suomen (ikäkohortit 1970-1972 ja 1980-1982), Ruotsin (1980-1982) ja Kreikan (1980-1982) aineistojen sekä lisäksi kahden suomalaisen terveyskeskusaineiston (Kemi 1988-1990 and Vantaa 1990) perusteella. Tutkimusaineisto koostui yhteensä 8 551 lapsesta.

Tutkimukseen tarvittavat tiedot kerättiin manuaalisesti potilaspapereista Suomen, Ruotsin ja Kreikan aineistoista sekä elektronisesti suoraan kahden suomalaisen terveyskeskuksen (Kemi ja Vantaa) digitaalisista potilastietojärjestelmistä. Ensimmäisten pysyvien poskihampaiden elinkaarikäyriä verrattiin pinnoitettujen ja pinnoittamattomien hampaiden sekä pinnoitettujen ja pinnoittamattomien henkilöiden (kaikki neljä pysyvää ensimmäistä poskihammasta joko pinnoitettu tai pinnoittamatta kahdeksanteen ikävuoteen mennessä) välillä. Kumulatiiviset kustannukset karieksen riskimäärityksestä, ksylitolin käytöstä, pinnoituksista ja täytteistä laskettiin Kemin ja Vantaan terveyskeskusaineistojen perusteella.

Tutkimuksen tulokset korostavat riskimäärityksen tärkeyttä pinnoituspäätöksen tekemisessä sekä hammaskohtaisesti että potilaskohtaisesti. Korkean kariesriskin lapsille (kariesta yhdessä tai useammassa ensimmäisessä pysyvässä poskihampaassa ennen kahdeksatta ikävuotta) pinnoitusten teho näytti olevan riittämätön estämään karieksen kehittymisen myöhemmällä iällä. Pinnoitukset olivat tehokkaita keskisuuren kariesriskin (kariesta yhdessä tai useammassa ensimmäisessä pysyvässä poskihampaassa kahdeksan ja kymmenen ikävuoden välillä) lapsilla. Matalan kariesriskin lapset (ei kariesta yhdessäkään ensimmäisessä pysyvässä poskihampaassa ennen kymmenettä ikävuotta) eivät hyötyneet merkittävästi pinnoitteiden kariesta ehkäisevästä vaikutuksesta. Kun pinnoitteet kohdennettiin valikoidusti lapsille joilla oli kahden vuoden iässä todettu korkea kariesriski ja heidän kaikki ensimmäiset pysyvät poskihampaat pinnoitettiin (Kemi), heidän osaltaan kokonaishoidosta seuranneet kustannukset myöhemmin olivat korkeampia verrattuna lapsiin joilla oli matala kariesriski ja joiden hampaita ei pinnoitettu. Pinnoitettujen ja pinnoittamattomien ensimmäisten pysyvien poskihampaiden hammas- ja henkilökohtaisten elinkaarikäyrien tilastolliset erot tutkituissa kohorteissa osoittavat, että käytäntöön perustuva tutkimusmenetelmä on suositeltava analysoitaessa hammashoidon tehokkuutta jokapäiväisessä toiminnassa.

Käytäntöön perustuva tutkimusmalli antaa hyvän käsityksen todellisissa hoito-olosuhteissa tehtyjen toimenpiteiden tehokkuudesta ja avaa siihen uuden näkökulman sekä edesauttaa soveltamaan näyttöön perustuvan hammaslääketieteen tutkimustuloksia jokapäiväiseen hammaslääkärintyöhön vastaanotolla.

Asiasanat: ehkäisevä hammashoito, fissuurapinnoitukset, hammaskaries, käytäntöön perustuva tutkimus

To Jessica and
Erik-Kristian

Acknowledgements

This study was carried out at the Department of Cariology, Pedodontics and Endodontics at the Institute of Dentistry, University of Oulu, Finland in 2005-2010.

First of all, I wish to express my deepest respect and gratitude to Emeritus Professor Markku Larmas D.D.S., Ph.D., the supervisor of this thesis. The opportunity to work with you was a great honour for me. Your profound knowledge together with long and extensive experience in the field of caries research has been irreplaceable during all these years. Your endless encouraging and supporting attitude, especially at difficult times, during the study process has been extremely valuable. The moments of sharp-tongued humour we shared made working much more enjoyable.

My co-authors of the original publications, Dr. Agneta Ekman, Dr. Hans Forsberg, Dr. George Vadiakas, Professor Constantine Oulis, Sinikka Salo D.D.S, Ph.D., and Jorma Suni D.D.S., Ph.D., are very warmly thanked for your fruitful counselling, advises, support and help during the whole study period.

I am sincerely grateful to the official reviewers of this work, Professor Heikki Murtomaa D.D.S., Ph.D., and Professor Liisa Suominen D.D.S., Ph.D., for your valuable comments and constructive criticism, which developed and markedly improved the content of the thesis. It was a great pleasure for me to collaborate with you.

I want to express my best gratitude to Hannu Vähänikkilä, M.Sc., and Jari Päkkilä, M.Sc., for your good work on data processing and kind advice in statistical matters. Special thanks are expressed to Outi Hiltunen, M.A., for efficiently reviewing the English language of this thesis.

I wish to thank also Professor Leo Tjäderhane D.D.S., Ph.D., the Head of the Department for your comments and valuable suggestions during the preparation of the final manuscript and for kindly providing the facilities to complete this work. My colleagues at the department: Liisa Seppä, Päivi Ollila, Vuokko Anttonen, and Päivi Rajavaara, and colleagues of the dental clinic of the Oulu Teaching Health Centre, I am grateful to all of you.

My lovely friends in Estonia and in Finland: I wish to thank all of you for your support and encouraging words during these years. Special thanks to my closest friends Lii, Ragne, Tiina and the “panda- girls” Sari and Aura, you carried me over the most difficult moments during this work.

I wish to express my respectful gratitude to my dear parents Ulvi and Jaan Kiho, and my lovely younger sister Katri and your family for your endless love and support throughout these years.

Thank you, Juha, for your help and patience during those difficult years.

Most of all, I can´t thank enough my lovely children, Jessica and Erik-Kristian. You make the life worth of living. You help me to remember every day what is really important in this world.

The financial support from the Finnish Dental Society Apollonia and research grant received from the European Union is gratefully acknowledged.

Tallinn, September 2010 Kaja Leskinen

Abbreviations

BGMA	bisphenol-A-glycidyl methacrylate
CB	cost–benefit
CE	cost-effectiveness
CI	confidence interval
CHX	chlorhexidine
CR	caries reduction
DMF(T)	the number of decayed, missing and filled permanent teeth
EBD	evidence-based dentistry
EBDP	evidence-based dental practice
GIC	glass-ionomer cements
GICS	glass-ionomer cement sealants
ICD	international classification of diseases
OR	odds ratio
PBD	practice-based dentistry
PBRn	practice-based research network
RBS	resin-based sealants
RBSS	risk-based sealing strategy
RCT	randomised controlled trial
RRR	relative risk reduction
RR	the pooled relative risk reduction estimate
QRCT	quasi-randomised controlled trial
SA	seal-all strategy
SM® test	*Streptococcus mutans* salivary test
SN	seal-none strategy
STAKES	National Research and Development Centre for Welfare and Health
WHO	World Health Organization

List of original papers

This thesis is based on the following articles, which are referred to in the text by Roman numerals I–IV.

I Leskinen K, Ekman A, Oulis C, Forsberg H, Vadiakas G, Larmas M (2008) Comparison of the effectiveness of fissure sealants in Finland, Sweden and Greece. Acta Odont Scand 66: 65–72

II Leskinen K, Salo S, Suni J, Larmas M (2007) A practice-based study of the sealant treatment effectiveness in Finns. J Dent 35: 338–342

III Leskinen K, Salo S, Suni J, Larmas M (2008) Comparison of dental health in sealed and non-sealed first permanent molars: 7 years follow-up in practice-based dentistry. J Dent 36: 27–32

IV Leskinen K, Salo S, Suni J, Larmas M (2008) Practice-based study of the cost-effectiveness of fissure sealants in Finland. J Dent 36: 1074–1079

Contents

1 Introduction

Dental caries is a chronic non-communicable disease (Hujoel 2009), and continues to be a major public health problem. It may also be the source of considerable pain and suffering for many. It is one of the few chronic diseases which affect also children, and its management represents a large proportion of the health resources worldwide (Petersen 2003, 2004).

Although the overall caries rate in terms of DMF-index values has fallen in industrialized countries, the rate of caries lesions in pits and fissures has not decreased at the same time (Marthaler 2004). Almost 90% of all dental caries occurs on occlusal, buccal and lingual tooth surfaces with pits and grooves, making these surfaces most susceptible to decay in children and adolescents (Ripa 1993).

World Health Organization (WHO) developed oral disease surveillance systems several years ago, particularly in relation to dental caries in children (Petersen 2003). According to the WHO data from the 1970s, Finland had one of the highest caries index values among European countries (WHO Global Oral Data Bank, Renson 1986). Pursuant to the Finnish Primary Health Care Act, which entered into force in 1972, the municipal health centres all around the country must provide dental care to everyone and free of charge to children and adolescents under the age of 17 years. Therefore, Finland has access to follow-up data on oral health and oral health care services of the population provided by health centres throughout the country since the 1970s (Nordblad *et al.* 2004).

The nation-wide follow-up system has been a significant tool in the assessment of the effectiveness of operations and also a factor guiding the operations of health centres (Nordblad *et al.* 2004). The Primary Health Care Act emphasized the use of different preventive methods in dental treatment of children and adolescents. Routine measures in the 1970s and 1980s involved not only annual dental examinations, use of fluoride in different forms in homes and schools and at dental offices, and health education at dental offices and in schools, but also the use of fissure sealants, even routinely, at many dental health centres. Fissure sealant placement became popular in Finland compared to other Nordic countries and the USA, where it was originally developed (Widström *et al.*1997). All these caries-preventive measures resulted in a favourable development in the decreasing of caries level in the developed countries in 1980–1998 (Petersen 2003, Honkala 2008).

However, the dental health of children and adolescents has not much enhanced since the beginning of the 1990s in Finland. In 2000, almost half of the 6-year-olds had or had had caries in their teeth, while a good third of the 12-year-olds had not needed any treatment for caries in permanent teeth (Nordblad *et al.* 2004, Suominen-Taipale *et al.* 2009). In the 1970s and 1980s, systematic care and full annual coverage of dental health for children and adolescents was emphasized. A new national legislation on public dental health care in 2001 extended the system to cover the entire population, which limited the resources available for younger age groups.

Fissure sealants have been recognized as an effective approach in preventing pit and fissure caries in children (Llodra *et al.* 1993, Mejáre *et al.* 2003, Ahovuo-Saloranta *et al.* 2004 & 2008, Beauchamp *et al.* 2008, Oong *et al.* 2008) when used carefully according to the recommendations. However, plenty of clinical questions remain on the indications of placing sealants, the criteria for their placement over enamel caries, technique to optimize retention, and effectiveness in real-life circumstances.

Caries level as well as criteria for sealant placement varies at different health centres in Finland. Nowadays, sealing is recommended primarily to high caries-risk children and teeth (Weintraub 2001, Ahovuo-Saloranta *et al.* 2004). However, identifying caries risk with sufficient accuracy in high-risk individuals is difficult since prediction of caries development is still an obscure method (Hausen 1997, Hausen *et al.* 2000).

The purpose of this work was to estimate the effectiveness of fissure sealant treatment in real-life settings at two health centres in Finland using different sealant placement criteria and to compare the results to data sets from Finland, Sweden and Greece and also to different sealant treatment strategies and dental care organizations.

2 Review of the literature

2.1 Dental caries as a process and a disease

G.V. Black, the father of modern cariology, defined caries in the following way in 1914: *Caries in its simplest expression consists in a chemical dissolution of the calcium salts of the tooth by lactic acid, followed by the decomposition of the organic matrix, or gelatinous body, which, in the dentin, is left after the solution of the calcium salts*. Black (1914) precisely stressed that the process that dissolves dental hard tissues occurs as a result of dental plaque bacteria, which stick to tooth surfaces, particularly at stagnant sites around the dentition. Today, almost a century later, dental plaque has gradually been replaced by the concept of biofilms (Marsh 2004), as it is evident that the biofilms in the mouth display similar properties to those found elsewhere in nature.

The caries process occurs across time as an interaction between the biofilm and the tooth surface and the subsurface (Pitts & Stamm 2004). The bacteria in biofilm are metabolically active, which causes fluctuations in the plaque fluid pH. These fluctuations may cause a loss of mineral from the tooth when the pH level is decreasing (Manji *et al.* 1991, Kidd & Fejereskov 2004). Progression occurs when the equilibrium between demineralization and remineralization is in imbalance, leading to a net mineral loss. In clinical care settings, diagnosis of caries means not only determining whether caries is present but also determining if the disease is arrested or active and, if active, progressing rapidly or slowly (Kidd & Fejereskov 2004, Kidd 2004).

The *International Classification of Diseases* (ICD-10) of WHO (WHO 1992) determines dental caries as a disease as follows: caries limited to enamel (K02.0), caries extending into dentin (K02.1), caries of cementum (K02.2), arrested caries (K02.3), other specified dental caries (K02.8), and dental caries, unspecified (K02.9). WHO also recommends that all diagnoses must be recorded on an appropriate level, i.e. with 3, 4 or 5 character codes (WHO 1992). This means that physicians diagnose dental caries with three characters, whereas dentists, the experts in treating the disease, should be more precise and use four character codes.

2.2 Evidence-based dentistry (EBD)

Systematic clinical reviews of diseases demonstrating causality normally evolve from laboratory studies through animal studies to case series and thereafter to controlled clinical trials (Niederman & Leithch 2006). These studies demand strict scientific rules (good laboratory practice, good clinical practice, etc.) for providing information for each of these steps. Based on the systematic clinical reviews, the evidence-based dental practice (EBDP) was created for epidemiological purposes.

The concept of evidence-based care have been brought into discussion for a solution to the problem of large variability between dentists and inappropriate dental care (Grace 1998, Niederman 1998, Tinanoff & Douglas 2001, Marinho *et al.* 2001, Sheiham 2002, Goldstein & Preston 2002, Elderton 2003, Ismail & Bader 2004, Pitts 2004 a-c, Gordon & Dionne 2005, Innes *et al.* 2005).

The epidemiology of dental caries should base on evidence-based research, which means that caries is diagnosed by calibrated examiners with standardized criteria which do not change over time, so that the results are exact and can be reproduced.

Most articles on the subject of evidence-based dental care are based on controlled clinical trials. This might constitute an ideal for dental academics, but it is an entirely unrealistic and inefficient method in the context of clinical dental practice. The task of acquiring and maintaining a solid evidence base for all the interventions and procedures that are carried out by the average dental practitioner is overwhelmingly large.

Clinical trial information is published at a rate that makes it practically impossible for anyone to have the latest information about all subspecialities relevant to general dental practice (Russo *et al*. 2000, Kim *et al.* 2001, Yang *et al*. 2001, Park & Niederman 2002, Nishimura *et al.* 2002). With about 500 clinical trials per year in dental speciality, increasing by 10% each year (Niederman *et al.* 2002), clinicians and educators are overwhelmed with clinical information. Moreover, the scientific information provided is often conflicting, leaving it to the users and patients to work out what to believe. Dentists therefore often lack the know-how to critically appraise and appropriately distil the information (Ismail & Bader 2004, Niederman & Leitch 2006), and they therefore resort to doing what they have always done and felt comfortable with (Redelmeier & Shafir 1995, Grace 1998). As it has been seen in the health care sector, it can take more than 15 years for clinical systems to incorporate new and effective concepts into routine practice (Lau *et al*. 1992).

2.3 Practice-based dentistry (PBD)

Almost 100% of clinical research is performed in an evidence-based fashion in academic centres, on very selected disease entities, and on a very homogenous subset of patients (0.1% of patients) (explicit knowledge of efficacy). However, this homogenous patient population is very different from the very heterogeneous 99.9% of patients, and primary care clinicians see problems where effectiveness is truly measured (Green 2001). A trivial question highlights the problem (Niederman & Leitch 2006): Is a disease cure with an efficacy of 100% truly 100% effective if it can be delivered to only 10% of the population?

An evidence-based approach to create knowledge may not be enough: translational research (know-how) is also needed in addition to the classical laboratory and clinical studies (Niederman & Leitch 2006, Zerhouni 2009) to show how science works in practice. The new scientific approach to supplement the EBD is referred to as practice-based dentistry (PBD). Data collected from ordinary dental records may result in PBD data and show, how science and theoretical treatment prescriptions work in everyday practice (Mjör *et al.* 2005, Mjör 2007 & 2008). While data collected from public health records are not decisively inferior to those obtained from examinations by trained examiners (Hausen *et al.* 2001), changing the dentist often predicted more caries lesions diagnosed and to be treated in adults (Korhonen *et al.* 2009).

During the last decade, many PBD studies concerning the effectiveness of pit and fissure sealants have been published (however, the earliest of these studies do not use the term PBD in the sense defined in this research) (Kuthy *et al.* 1990, Weintraub *et al.* 1993, Dennison *et al.* 2000, Weintraub 2001, Zabos *et al.* 2002, Bhuridej *et al.* 2005, Tickle *et al.* 2007, Hevinga *et al.* 2010).

2.4 Principal caries prevention strategies

Disease control in dentistry concerns influencing biofilm formation and growth or modifying the dissolution kinetics of the apatites, or both. The levels of disease prevention can be classified as primary, secondary and tertiary prevention.

The goal of *primary prevention* is to inhibit the development of a disease before it occurs. It includes also dental sealants to prevent tooth decay (Rose 2001). The goal of s*econdary prevention* is to identify and detect the disease in its earliest stages – as regards dental caries, in the enamel caries stage (Rose 2001). It also includes prevention of the progression of an existing lesion (in enamel, by chemical means; in dentin, using restorative procedures). If the disease has advanced to an outcome which involves a loss or impairment of a function, then *tertiary prevention* with treatment measures seeks to limit the loss and restore the function if possible (Riordan 1992).

In general, preventive strategies in health promotion are divided into two distinct groups: strategies aimed at the entire population and those aimed at people or individuals at risk (Rose 2001).

The *population strategy* seeks to control common causes of caries (disease) incidence, whereas the *high-risk strategy* seeks to protect susceptible individuals (Fejereskov 1995). The population strategy has become questionable in most industrialized countries today, because of the skewed caries distribution in their populations (Fejereskov 1995). The problem of skewed distribution in terms of disease prevalence (experience) or incidence is two-fold: the prevalence of most diseases is skewed unfortunately. Most chronic diseases affect only a small fraction of population, and therefore "healthiness" is dominating, but acute diseases may have epidemic or even pandemic nature. In the latter cases, the presence of disease is dominating.

According to the *individual (high-risk) strategy*, individuals with a high risk for caries are identified and preventive measures are taken to diminish their risk (Rose 2001, Hausen 1997).

Unfortunately, there are no tests with sufficient predictive power to identify individuals at "high risk" (Hausen 1997, Hausen *et al.* 2000). A series of randomized controlled trials have revealed the relatively low value of non-operative treatment in terms of reduced caries incidence in high caries-risk subjects (Seppä *et al.* 1991, Hausen *et al.* 2000, Blinkhorn *et al.* 2003, Kallestål 2005). These studies appear to show that preventive interventions targeted only at high-risk individuals may not be cost-effective. However, a recent work on a child population with overall low caries experience (Hausen *et al.* 2007) showed that targeting caries control in all children to an area with an active lesion recorded a significantly reduced increment in dental decay. Indeed, the prevented fraction was similar to studies on non-operative caries management conducted in areas of high or moderate levels of dental caries (Ekstrand *et al.* 2000, Curnow *et al.* 2002). In spite of the skewness in the distribution of disease in the population, most lesions are still found in individuals with moderate or low DMF index values. One consequence of this is that the high-risk strategy aimed at *individuals* will be limited on the *population* level.

Prevention of dental caries can also be divided into two groups based on the operator: *individual prevention* performed by the patient itself, including mechanical/chemical removal of plaque (oral hygiene), use of fluoridated toothpaste, choosing an appropriate dietary composition (dietary control), and using sugar substitutes such as xylitol; and *professional prevention*, including regular dental examinations, professionally applied fluorides (varnishes, gels and rinses), antimicrobial modification of plaque (chlorhexidine), and fissure sealing at a dental office.

Since 1972, all caries prevention strategies have been tested alone or in combination in several municipal health centres in Finland. Each health centre stressed different aspects in preventive dental care. Re-call intervals have been determined individually for each patient since the 1990s, taking into account the patient's caries activity, age, possible general diseases, medical history, possible fear of dentist, oral hygiene, and dietary control.

Annual dental examinations for children under the age of 17 years can be classified also as *secondary preventive method* since these resulted in the elimination of open carious lesions in the lesions' early non-transmissible stages. Annual examinations enable the use of sophisticated survival analysis in measuring the changes and impact of different preventive methods in dental health.

The ability of fluorides to inhibit or even reverse the initiation and progression of dental caries is well documented (Ten Cate 2004, Marinho *et al.* 2002, 2003, 2004 and 2009). According to the WHO, long-term exposure to fluoride at an optimal concentration leads to a reduction in dental caries in all populations (WHO 2003).

Systematic review of reviews by Rozier (2001) covering the period from 1980 to 2000 revealed good evidence for the effectiveness of professionally applied fluoride (gels and varnishes), chlorhexidine and sealants as regards caries prevention in children and adolescents.

A meta-analysis of eight studies concerning professionally applied fluorides reported a reduction of 38% in dental caries (Helfenstein & Steiner 1994). In a systematic review including 22 studies (Bader *et al.* 2001), the strength of the evidence for fluoride varnishes to reduce dental caries was judged to be fair.

Professionally applied fluorides (varnishes, gels) could be effective for individuals who have lately erupted teeth or active caries lesions (Marinho *et al.* 2004, Käypä hoito 2009). Fluoride varnish prevents dental caries in deciduous and permanent teeth when applied at three to six months intervals in high caries-risk children (Marinho *et al.* 2002, Käypä hoito 2009).

Any additional benefit of fluoride toothpastes used in combination with other topical methods, such as mouthrinses, gels and varnishes, is less conclusive, and only modest caries reduction might be anticipated (Marinho *et al.* 2004). It has also been stated that if the bacterial challenge is too high, it is not possible for fluoride to overcome the challenge completely (Brathall *et al.* 1996, Featherstone 2004).

Although dental caries is clearly a multifactorial disease, and caused not only due to lack of fluoride, the problems with fluoride relate generally to compliance with appropriate product use rather than to clinical effectiveness. While caries of smooth surfaces can be reduced by fluorides (Warren *et al.* 2006) and by xylitol (Virtanen *et al.* 1996), the problem of defending occlusal fissures remains as a challenge. However, there is some insufficient evidence of the superiority of pit and fissure sealants over fluoride varnish application in the prevention of occlusal decays (Bravo *et al.* 2005, Hiiri *et al.* 2006, Käypä hoito 2009).

Since adequate self-performed mechanical control of dental biofilms is difficult and often inadequate, antimicrobials may offer an adjunct. There are some antimicrobial agents with a documented anti-caries effect, owning to either a lack of properly controlled clinical trials or the lack of efficacy of the agents. The main caries preventive agents are chlorhexidine and triclosan.

In a recent review of chlorhexidine intervention studies performed between 1995 and 2003, chlorhexidine varnish seemed to have an inhibitory effect on fissure caries development in children with low exposure to fluoride (Twetman 2004). In elderly people and in fluoride-exposed caries-active children and adolescents, evidence for an anti-caries effect of chlorhexidine was inconclusive (Twetman 2004). The inconclusive results from studies on the anti-caries effect of chlorhexidine are also reflected in two recent publications reporting a caries-inhibiting effect of 40% chlorhexidine varnish in Chinese children: in one study, the authors conclude that the effect is questionable and only transient (Zhang *et al.* 2006), whereas as high as 37.3% caries reduction in terms of dmf(s) values was found in the other study (Du *et al.* 2006). Autio-Gold (2008) suggested that chlorhexidine rinse (0.12%) should not be recommended for caries prevention in children because its effect is questionable. In Finland, chlorhexidine supplements (0.8–1.0% gel and 1.0% varnish) are suggested to be used periodically as a supplement for individual prevention only in patients with general diseases that involve low salivary flow (Käypä hoito 2009).

2.4.1 Fissure sealants

History and types of fissure sealants

The idea of occluding pits and fissures, in the first phase by minimal operative preparation of sound fissures and restoration with amalgam, dates from the 1920s (Hyatt 1923). The mechanical adhesion of composite material to enamel was first reported by Buonocore (1955), who showed that treatment of enamel with phosphoric acid allowed the resin materials to penetrate into the microspaces of this etched enamel surface. The first work describing the adhesive system in caries preventive applications was carried out by Buonocore (1963). The materials investigated fell into three categories: the cyanoacrylates (Swanson & Beck 1960), the polyurethanes (Lee & Swartz 1971) and the bisphenol-A-glycidyl methacrylate (BGMA) (Buonocore 1970), which were the most effective in clinical trials.

Pit and fissure sealants (ultraviolet activated, autopolymerized or light-cured resin-based sealants (RBS) and glass-ionomer cement sealants (GICS)) were first developed in the 1970s and 1980s, and their effectiveness in preventing dental caries has now been established by randomized clinical trials (Llodra *et al.* 1993, Ripa 1993, Mejáre *et al.* 2003, Ahovuo-Saloranta *et al.* 2004).

Glass-ionomer cements (GIC) used as fissure sealants are available in two forms, both of which contain fluoride: conventional and resin-modified (Pardi *et al.* 2003). However, the clinical effect of fluoride release from GIC is not well-established. The reason why GICS have prevented caries even after they appear to be lost is that the material was still left on the bottom of the fissures (Torppa-Saarinen & Seppä 1990). Clinical studies have provided conflicting evidence as to whether these materials significantly prevent or inhibit caries and affect the growth of caries-associated bacteria compared with materials not containing fluoride (Donly *et al.* 1999, Mjör *et al.* 2000, Pardi *et al.* 2005, Wiegand *et al*. 2007).

It is generally accepted that RBS are retained longer than low-viscosity GICS (Simonsen 2002, Locker *et al.* 2003) and that they are more effective in preventing dental caries in permanent molars (Ahovuo-Saloranta *et al.* 2004, Pardi *et al.* 2005). However, which of the two types of sealant material is more able to prevent caries development is not clear (Beiruti *et al.* 2006a). However, in an *in vitro* study, high-viscosity GICS with the finger pressure technique had a four times higher chance of preventing caries development in re-exposed pits and fissures on occlusal surfaces of first molars than can be achieved using light-cured composite resin sealant material over a 1–3-year period (Beiruti *et al.* 2006b).

Effectiveness of sealants in caries prevention

Sealants are placed to prevent pit and fissure caries initiation and to arrest caries progression by providing a physical barrier that inhibits micro-organisms and food particles from collecting in pits and fissures. Early clinical studies with sealants date back to the 1970s, when applying the half-mouth technique to non-carious contralateral teeth was selected for study controls. Sealant was applied to one tooth, while the other was monitored for caries activity as an untreated control. Three years after the application of sealants to the homologous test-control tooth pairs in the clinical study in Finland, the effectiveness of the method was found to be 88.1%. When evaluated on an individual basis, the sealant treatment was found to have benefited 60.2% of the subjects (Meurman 1977). Fifteen years after a single application of sealants to the permanent first molars, 27.6% were still completely retained, carious or restored surfaces made up 31.3% of the surfaces in the sealed group, and 82.8% in the unsealed group (Simonsen 1991).

Llodra *et al.* (1993) performed a meta-analysis on evaluation studies of sealant programmes. The results indicated that the autopolymerized sealants were more effective (caries reduction 71.4%) than light-polymerizing sealants (caries reduction 45.9%). Moreover, they found that the effectiveness of sealants decreased over time and was higher in populations exposed to fluoridated water (82.7% *vs* 72.3%) (Table 1).

Evidence from systematic reviews of randomized controlled trials shows that placement of resin-based sealants on the permanent molars of children and adolescents is effective for caries reduction (Ahovuo-Saloranta *et al.* 2004, 2008). Reduction of caries ranged from 86% at 12 months to 57% at 48 to 54 months (Ahovuo-Saloranta *et al.* 2004). The review by Mejáre *et al.* (2003) contained 13 Cochrane library studies (involving 3 897 children/adolescents) from 1966–2003, with follow-up time at least two years. The pooled relative risk reduction estimate (the number of decayed occlusal surfaces in the controls minus the number of decayed surfaces in sealed teeth divided by the number of decayed surfaces in the controls) was 33% for the first permanent molars for resin-based sealants after 2–5 years follow-up (Table 1).

There are a number of factors potentially modifying the caries-preventive effect of fissure sealing, such as caries prevalence in the population under study, single or repeated sealant applications, type of sealant material, quality of sealant placement technique, retention of sealant, cooperation of patient, follow-up time, type of tooth and jaw, and the operator and the content of fluoride in the drinking water (Llodra *et al.* 1993, Mejáre *et al.* 2003). In general, also dietary, oral hygiene and the socioeconomic factors influence the effectiveness of sealants.

Because dental caries causes fissures so frequently, sealants seem to offer an alternative in preventing occlusal caries in societies with good dental health in children. On the contrary, if the level of approximal caries is high, there is no point trying to save only the occlusal surfaces with sealants (Alanen *et al.* 2000).

Some evidence has been found on the superiority of pit and fissure sealants over fluoride varnish application in the prevention of occlusal decays. However, it remains unclear to what extent there is difference between the effectiveness of

Table 1. The effectiveness of fissure sealants in preventing dental caries according to different studies.

Author(s)	Year of publication	N	Treatment effect	Study method	Follow-up time
Meurman	1977	150 children	88.1–93.0% E[1]	test–control tooth pairs	6 months–1.5 years–3 years
Simonsen	1991	200 children	68.7% CR[2]	sealed *vs* non-sealed children	15 years
Llodra	1993	24 studies	45.9–71.4% CR	meta-analysis	1 year
Mejáre *et al.*	2003	13 studies/ 3 897 children	33% RRR[3] 0.67 RR[4]	review, sealed *vs* non-sealed teeth	2–5 years
Ahovuo-Saloranta *et al.*	2004	8 studies	86% CR 57% CR 0.14–0.43 RR	systematic review of RCT[5]s	1 year 4–4.5 years
Bravo *et al.*	2005	120 children	65.4% CR	randomized trial, sealant *vs* control	9 years
Ahovuo-Saloranta *et al.*	2008	16 studies	60–87% CR 0.13–0.40 RR	systematic review of RCTs or QRCT[6]s	1–4.5 years

[1]E – effectiveness

[2]CR – caries reduction

[3]RRR – relative risk reduction = the number of decayed occlusal surfaces in the control minus the number of decayed surfaces in sealed teeth divided by the number of decayed surfaces in the controls.

[4]RR – the pooled relative risk reduction estimate

[5]RCT- randomised controlled trial

[6]QRCT- quasi-randomised controlled trial

these two preventive methods (Hiiri *et al.* 2006). The median survival times over 48 months for both sealed and varnished molars (hazard ratio of 0.177 for the sealant *vs* control; 0.463 for varnish *vs* control, and 0.382 for sealant *vs* varnish) were found using survival analysis (Bravo *et al.* 1997). In a randomized trial (Bravo *et al.* 2005), after nine years, caries reduction was 65.4% (SE=8.5%) for sealants *vs* control and 27.3% (SE=10.2%) for varnish *vs* control (Table 1). Furthermore, the varnish programme was not effective during the discontinuation period.

Folke *et al.* (2004) studied the success of occlusal sealants at a private practice over a period of ten years and reported that the cumulative survival probability is 87%. The factors associated with an increased risk of failure included: (1) age ($p < .001$), (2) dmft ($p < .003$), (3) no fluoride ($p < .001$), and (4) operator ($p < 00.1$). The no fluoride group showed almost twice the risk of failure as compared to the to the optimal fluoride group. Dental assistants and dental hygienists were equal or better than the dentists as regards long-term sealant effectiveness.

Sealing caries-susceptible enamel and dentin

Several studies have examined the consequences of sealing carious enamel and dentin. Earlier prospective studies have demonstrated that sealed carious lesions appeared to arrest both clinically and radiographically (Handelman *et al.* 1976, Going *et al.* 1978, Mertz-Fairhurst *et al.* 1979a and 1979b, Handelman *et al.* 1981, Mertz-Fairhurst *et al.* 1986). Investigations of the fate of the sealed bacteria showed a decrease of micro-organisms over time or their complete elimination in these lesions after sealant treatment (Handelman *et al.* 1976 and 1987, Going *et al.* 1978, Mertz-Fairhurst *et al.* 1979a and 1986). No pulpitis was reported in sealed teeth, but lesions were progressed where sealants were lost and in unsealed teeth. However, the results of these studies should be reviewed with caution because their evaluation periods were short or the carious status of the fissures was unclear.

A retrospective study showed that cariogenic micro-organisms (*lactobacilli*, *mutans streptococci* and *non-mutans streptococci*) were found in 50% of teeth despite of sealants (Weerheijm *et al.* 1992). Going *et al.* (1978) and Weerheijm *et al.* (1992) found that cariogenic micro-organisms were (still) present and the dentin was often soft and moist in sealed teeth after a follow-up time of five years. Since there were no pre-operative samples, it is impossible to know whether sealing had changed the numbers or the distribution of the microflora. In a recent *in vitro* study (Hevinga *et al.* 2008), sealed carious fissures showed significantly more microleakage and insufficient sealant penetration depth than sound fissures.

Celiberti & Lussi (2007) reported also higher microleakage scores in sealants placed over natural enamel caries lesions.

Oong *et al.* (2008) found in their review that when placed over existing caries, sealants lower the number of viable bacteria by at least 100-fold and reduce the number of lesions with any viable bacteria by 50 percent. These findings do not support the reported concern on poorer outcomes associated with inadvertently sealed caries. Also Griffin *et al.* (2008) and Kervanto-Seppälä (2009) recommended that sealing incipient caries lesions is both effective and practical – dental care professionals should be encouraged to use sealants more in an interceptive manner rather than in a preventive or operative manner.

Several studies have examined the consequences of simply sealing carious dentin (Handelman *et al.* 1987, Weerheijm *et al.* 1992, Feigal & Donly 2006). Caries activity was assessed in a number of ways, including clinical observation, lesion depth measurement, radiographic lesion depth measurement, and microbiological sampling. The observation period varied from two weeks to five years. The controls were unsealed lesions or sound teeth. The results of these studies could be concluded as follows: 1) sealed lesions appeared to arrest both clinically and radiographically, 2) micro-organisms were decreased or completely eliminated over time, 3) no pulpitis was reported in sealed teeth, 4) lesions progressed where sealants were lost and in unsealed (control) teeth. However, the observation time in these studies was limited, and the caries status of the sealed teeth was not documented sufficiently enough.

Effect of sealing approximal caries

Because the dental flossing habit is generally poor in populations (e.g. 18% floss regularly in Denmark, Martignon *et al.* 2006), it is important to look for other treatment possibilities than the traditional flossing instructions and topical fluoride preventive measures to arrest approximal lesion progression. Gomez *et al.* (2005) performed a two-year clinical evaluation on sealed non-cavitated approximal posterior carious lesions in adolescents. In the split-mouth study, 92% and 88% of the surfaces with enamel caries respectively showed no progression after sealant or fluoride varnish treatment, the difference being statistically non-significant. The results showed the potential of sealants to act as a non-invasive treatment of early approximal enamel lesions (Gomez *et al.* 2005). In a scanning electron microscope analysis of sealant penetration in posterior approximal enamel carious lesions *in vivo*, it was found that the use of a bonding system prior to the application of a pit and fissure sealant on lesion and sound enamel areas does not increase the sealant penetration length under non-contaminated conditions (Gomez *et al.* 2008). However, Meyer-Lueckel *et al.* (2008) and Paris *et al.* (2007) have experimentally studied sealing of approximal caries lesions and analysed the influence of penetration time and application frequency on the penetration of dental resins into artificial enamel lesions. In an 18-month clinical split-mouth design study (n=82), the approximal sealing technique was found to be superior to instructing patients to floss their teeth. Using subtraction radiography, it was found that 44% of the test group (sealed lesions) and 84% of the control group (non-sealed lesions) had progressed (Martignon *et al.* 2006). There is a need, however, for defining more precise criteria for selecting the lesions to be sealed, for developing better materials in terms of penetration ability and retention rate, and for clinical investigations that evaluate the long-term effect of sealing approximal lesions (Martignon *et al.* 2006).

Indications of sealant treatment

Originally, routine application of sealants was recommended for all posterior teeth, because it was believed to be the only realistic way to prevent occlusal decay. On the basis of more recent understanding of occlusal caries initiation and progression and the costs associated with routine application of sealants, it has become increasingly common to recommend selective criteria for the sealing of occlusal surfaces (Mitchell & Murray 1989, Llodra *et al.* 1993, Dennison *et al.* 2000, Weintraub 2001, Simonsen 2002, Bhuridej *et al.* 2005, Bravo *et al.* 2005, Ahovuo-Saloranta *et al.* 2004, 2008).

The decision to place sealants on a sound surface should be based on age (eruption stage of the tooth) and oral hygiene of the patient, individual history of dental caries, dietary habits, patient cooperation and reliability in keeping re-call appointments, as well as tooth type and tooth morphology. Because the time from tooth emergence to full occlusion is the most critical period for caries initiation (Carlos & Gittelsohn 1965, Carvalho *et al.* 1991, Carvalho *et al.* 1992), adequate timing of sealant application is important (Vehkalahti *et al.* 1991). Pit and fissure sealants should be placed on early (non-cavitated) carious lesions in children, adolescents and young adults to reduce the percentage of lesions that progress (Griffin *et al.* 2008). Sealing is indicated in cases where fissures are deep and narrow and the caries risk is increased because of difficulties to clean the tooth (Kallestål 2005, Locker *et al.* 2003, Weintraub *et al.* 2001).

Even though sealants have been used in Finland since 1970 (Nordblad *et al.* 2004), neither uniform criteria for sealant application nor a trend regarding sealant policy could be found among the responses in the survey study of Kervanto-Seppälä *et al.* (2009). The placement of sealants has shown a declining trend in Finland since 1988 (Nordblad *et al.* 2004) (Table 2).

Table 2. The number of fissure sealants per treated child in 1985–2000 (modified from: Nordblad *et al.* 2004).

Age	Sealants/ treated child				
	1985	1988	1994	1997	2000
5	0.1	0.2	0.2	0.1	0.1
6	0.9	1.2	1	0.9	0.8
9	0.2	0.3	0.3	0.3	0.2
12	0.7	1.2	1	0.8	0.7

The criteria for applying sealants and the actual strategies seemed to vary locally between the dentists and the health centres nationwide in Finland. The health centres choosing to seal detected or suspected enamel caries lesions had a DMFT value of 1.0 at the age 12 compared to the value 1.2 for those health centres applying sealants based on alternative criteria (Kervanto-Seppälä *et al.* 2009). Moreover, opening a susceptible fissure is no longer considered necessary, since sealants have been shown to be effective when placed in a cariostatic manner, thus arresting the progression of the eventual enamel lesion (Handelman *et al.* 1976, Mertz-Fairhurst *et al.* 1986, Griffin *et al.* 2008, Beauchamp *et al.* 2008).

Occlusal caries management may be improved by shifting the sealant policy from the traditional approach of prevention to interception, i.e. applying sealants over detected or suspected enamel caries lesions instead of sealing sound teeth (Kervanto-Seppälä 2009).

According to studies (Weintraub 2001, Locker *et al.* 2003, Kallestål 2005, Käypä hoito 2009), first and second permanent molars should be fissure sealed if on the occlusal surface there is an active enamel caries lesion and if the fissure is deep or its cleaning is difficult.

Despite of over 30 years of routine use, the specific diagnostic criteria for when to seal and when not to seal are not clear either, because they ultimately depend on the clinical judgement of the individual dentist for that special patient.

2.5 Cost-effectiveness of oral health care

2.5.1 General aspects of economic evaluation

Oral diseases are the fourth most expensive diseases to treat in industrialized nations (Petersen *et al.* 2005). In the year 2000 alone, the European Union spent in total EUR 54 billion on oral health care (Widström & Eaton 2004). It has been documented that preventive programmes targeted at the reduction of dental caries have resulted in substantial savings of dental expenditure (Petersen *et al.* 2005).

Dental health is easier to measure than the output of most other health programmes is. The concept of economic efficiency stresses that the decisions must be made in the health-care sector for the allocation of the goods and services that will result in the maximum total benefit for the members in the community (Drummond *et al.* 1997).

The basic tasks of any economic evaluation are to identify, measure, value, and compare the costs and consequences of the alternatives being considered (Drummond *et al.* 1997). There are four main types of cost analyses: *Cost-minimization* analysis means economic evaluation searching for the least cost alternative. Analyses in which costs are related to a single, common effect that may differ in magnitude between the alternative programmes are referred to as *cost-effectiveness* analyses. The results of such comparisons may be stated either in terms of cost per unit of effect, or in terms of effects per unit of cost (life-years gained per terms of money spent). Analyses that measure both the costs and consequences of alternatives in terms of money are called *cost–benefit* analyses. The results might be stated in the form of a ratio of monetary costs to monetary benefits, i.e. cost–benefit ratio, or as a simple difference of these two factors, i.e. net benefit. *Cost–utility* analysis allows for quality of life adjustments to a given set of treatment outcomes and comparison of costs and outcomes in different programmes. There are two generic outcomes, quality adjusted life-years and healthy years equivalent (Drummond *et al.* 1997).

Considering the tremendous quantity of resources allocated to the health care sector, the discipline of health-care economics was created to ensure that the maximum benefit can be derived from the recourses available (Folland *et al.* 2004). Economics does not provide a set of rigid guidelines that must be followed in the decision-making process, but rather, a set of principles that allow decisions to be based on the efficient allocation of recourses. Economic assessment methods, such as cost-effectiveness analyses, are used to determine the efficient treatment action based on alternative treatments that meet a common objective (Drummond *et al.* 1997).

In the oral health care system, the benefit gained from the prevention of dental caries is relative to the value one places on a healthy tooth. Unfortunately, many studies concerning the economic evaluation of dental treatment attach a financial value to a healthy tooth in terms of treatment costs averted. However, according to Mitchell & Murray (1989), it is ”virtually impossible“ to set a financial price for the benefit gained from a healthy unfilled tooth when comparing it to a healthy filled tooth, since future restoration and replacement needs are extremely difficult to measure. Commonly, most dental caries-preventive measures are cost-effective methods of eradicating tooth decay when compared to restorative dentistry approaches (Griffin *et al.* 2001). In a recent RCT study conducted in Finland (Hietasalo *et al*. 2009), the experimental caries control regimen was found to be more effective but also more costly than the standard dental care provided for the control group. However, the total costs of the experimental method decreased year after year.

In an economic evaluation of preventive programmes based on 17 studies (Kallestål *et al.* 2003), the results were contradictory. A review published on cost evaluations of caries prevention showed that all preventive measures, except fluoride gels, gave lower cost compared to fillings, and that water fluoridation was the most cost-effective measure (Kallestål *et al.* 2003).

Joensuu (2009) showed that in Finland, early prevention and control of caries performed by dental hygienists is associated with lower cumulative costs and better or equally good dental health as conventional prevention. Vehmanen (1993) concluded that caries-preventive test methods (fluoride varnish and chlorhexidine-fluoride solution) are recommendable in economic terms, especially if the preventive measures are carried out by dental nurses. The risk-based strategy proved to be of a moderate benefit to dental health in comparison with the cost of normal preventive and restorative care, but it cannot be recommended as such for the target population with a high risk of caries (Raitio *et al.* 2001). The cost of the xylitol regimen during two to three years was roughly the same as the cost of the restorations avoided during the following decade, and the cost of xylitol was covered by savings in restorations after the ten years of follow-up (Virtanen *et al.* 1996).

It has also been pointed out that there are relevant differences in caries prevention programmes between countries (Seppä 2001). In countries with a high caries rate, a low level of basic prevention and an unorganized dental care system, any preventive programme seems cost-effective, but in economically developed (high-income) countries, the effectiveness of preventive programmes seems to have diminished. The reduced prevalence of caries has rendered earlier model calculations of cost-effectiveness outdated (Kallestål *et al.* 2003).

2.5.2 Cost-effectiveness of fissure sealants

The main drawback to the use of sealants is that this technique calls for specific materials and educated personnel to apply the fissure sealant individually into each single tooth in question. It is also time consuming and normally requires dental-office equipment. An ideal micro-costing approach to the placement of pit and fissure sealants would include the cost of the resin-based material, all brushes/applicators used, the cost of the operator's time, loss of wages of the parents, and travel costs. Of the costs incurred to the dental professional, the main cost in sealant application is the opportunity cost of their time. Since pit and fissure sealants are applied to individual teeth by oral health-care professionals, they are considered to be a resource-expensive preventive measure. Undoubtedly, the cost-effectiveness of sealants would be improved through their application by trained dental auxiliaries instead of dentists (Burt 1984; Mitchell & Murray 1989, Deery 1999).

Other factors that would enhance the cost-effectiveness of sealants include improved sealant retention rates, increased sealant resin durability, and use with other caries preventive measures such as water fluoridation or fluoride dentifrices. Lastly, the economics viability of pit and fissure sealants would be dramatically enhanced if sealants were placed on only teeth that are destined to become carious (Mitchell & Murray 1989).

The cost of a sealant application has been estimated to be half as much or less than the cost of a small, one-surface restoration. However, dental restorations and sealants should not be regarded as alternative methods since sealants are meant for only prevention of decay and restoration with amalgam or composites is used to restore carious teeth.

The value of health maintained is difficult to assess solely on a monetary basis. Mitchell & Murray (1989) noted that despite the large number of clinical trials on the effectiveness of sealants in preventing occlusal caries, valid information is still lacking on the cost-effectiveness of this technology. Further, Mitchell & Murray stressed that the median survival time of sealants and amalgam restorations in first permanent molars of 5- to 8-year-olds was only about two years, which further complicates valid estimation of the cost-effectiveness of preventive techniques based on the application of dental materials (Mitchell & Murray 1989).

There has been a shift in the recent literature of the economics of pit and fissure sealants towards sealant delivery based on risk development of dental caries. Two theory-based studies demonstrated this, and concluded that risk-based sealant delivery is less costly than sealing all teeth or sealing no teeth (Griffin *et al.* 2002, Quinonez *et al.* 2005). It was pointed out that depending on an individual patient's evaluation of his or her oral health, the increased delivery of sealants with associated increase in effectiveness and costs may still be worth the investment if the other alternative is a restored occlusal surface (Griffin *et al.* 2002). Sealing was generally found to be cost-effective and the risk-strategy to be preferable to either the seal-all or the seal-none strategy in a moderate caries increment situation (Virtanen *et al.* 2003). On the other hand, in a higher annual caries increment situation, the seal-all strategy was superior to the risk strategy (Griffin *et al.* 2002). Weintraub *et al.* (1993) concluded that the strategy of identifying children with prior restorations and sealing the remaining molars showed cost-savings within four to six years (Table 3).

Donaldson *et al.* (1986) compared the cost-effectiveness of a preventive dental health programme with the ordinary restorative treatment of carious teeth. The preventive programme consisted of personal health education, oral fluoride supplements, applications of fluoride gel, and pit and fissure sealants. The cost per unit improvement in DMFS was higher for the preventive programme than for the restorative treatment. Once the quality differences between the restored and healthy teeth were taken into account, however, the ranking changed. Given that a healthy tooth has the value 1, if the value of a restored tooth is less than 0.85, the preventive programme is more cost-effective.

As sealant integrity, and thus the regular maintenance of sealants and sealed teeth, is necessary to the successful outcome with the sealant approach, a method having low retention rates and time-consuming application procedures may add to the final costs of a sealant programme (Kervanto-Seppälä 2009). Caries risk evaluation on a tooth and an individual level may improve the effectiveness of a sealant programme and render the sealant approach more economically attractive (Kervanto-Seppälä 2009).

Table 3. Comparison of cost-effectiveness of different sealant treatment strategies.

Author(s)	RBSS[1] more cost-effective than SA[2]	RBSS more cost-effective than SN[3]	SA more cost-effective than RBSS
Weintraub 1993	cost savings within 4–6 years	cost savings within 4–6 years	not studied
Weintraub *et al.* 2001	yes	yes	not studied
Griffin *et al.* 2002	yes	if annual caries increment is 0.05	if annual caries increment is 0.095
Virtanen *et al.* 2003	in a moderate caries situation	in a moderate caries situation	no
Quinonez *et al.* 2005	yes	yes	no

[1]RBSS– risk-based sealing strategy

[2]SA – seal-all strategy

[3]SN – seal-none strategy

2.6 Survival analysis

2.6.1 Main principles

The first study applying survival analysis methods by calibrated examiners to dentistry is the classic study by Carlos & Gittelsohn (1965). Their report was based on a clinical trial conducted in two towns in the state of New York in the USA in the 1940s. They applied life-table estimates of logarithmic failure intensities to different teeth. They were among the first who determined tooth-specific caries and did not use the severity of caries in the oral cavity as the measure.

A survival curve is a summary curve of individuals (with dates of birth and failure), not the means of cohorts. Survival methods combine the values of individuals as long as they have been under the follow-up during the analysis.

A standard survival analysis requires independent data for significance testing (Hannigan 2004). The lifetime must correspond to a specific individual who is independent of the others. Because each tooth in the oral cavity is dependent on other teeth, and the dependence further increases when active caries affects the dentition, independence is a special problem in dental research. In recent years, it has been recognized that survival analysis could also be applied to dependent data, for example in repeated observations of the same individual (Aalen *et al.* 1995).

For each tooth, the survival time should be measured from either the tooth's emergence or the birth of the subject. The latter time point can be regarded as the "birth" of that event. The mouth of a patient may contain teeth of greatly varying durations, and therefore survival analysis of molar teeth as caries-free under the age of twelve, for example, will give different outcome for first and second molars due to different eruption times between these teeth. Because a standard survival analysis demands independent data, which is not the case between the individual teeth inside the mouth, an analysis should be made on a tooth-specific level, e.g. the upper right canine should be compared to its counterpart in another mouth only (Korhonen *et al.* 2007).

The use of survival time as the outcome measure is an approach that can be understood easily by everyone. When the methodology proposed here is either subject- or tooth (surface)-based, it uses all the data collected during the clinical treatment of the patient during his or her lifetime in the PBD study approach. It includes data collected during clinical examinations and data from subjects in intermediate examinations, as long as the subjects keep visiting that dental office. Survival analysis stresses the importance of time and includes possible variables such as eruption time of the tooth, time to decay, and length of exposure to treatment like restoration, sealant treatment, etc. The results of the analysis can easily be interpreted with the use of survival curves and median survival times.

2.6.2 Censoring in survival analysis

The observed timing of an event is not always exact because of censoring (Lindsey & Ryan 1998, Bogaerts *et al.* 2002). All cohort studies have always used censored data, which means that each subject is followed for a certain period of time, and the event must be censored if it did not occur at the completion of the follow-up or it happened before the follow-up. *Censoring* means that the observation time is not known exactly.

If a tooth has already erupted or been restored at the first examination, no exact date can be recorded for these events before that time. In statistical analyses such survival data are *left-censored*. If the observation period is terminated at a certain point, the failure times of those teeth/restorations are *right-censored* after that time. *Interval-censored* observations are recorded as having occurred at the first examination following the event or alternatively, at the midpoint of the two last examinations (Lindsey and Ryan 1998). If, for example, the first examination at seven years of age reveals that the first permanent molar has emerged, there is a possibility that interval-censoring (from the birth of the subject) at that examination (instead of left-censoring) is used, because the eruption is so close to the mean tooth eruption times in the population and the statistically correct left-censoring diminishes the N value unnecessarily. In this case, interval-censoring at the first examination instead of the midpoint of birth and the first examination seems appropriate.

3 Aims and background of the present study

General aim of the study was

- to estimate the effectiveness of sealant treatment of first permanent molars in caries prevention in a real-life setting (PBRn) applying survival analysis methodology.

Specific objectives of the study were

- to compare the cumulative survival rates of first molars remaining caries-free in three European countries with different sealant strategies in children born in 1970 and 1980 (I);
- to evaluate the effectiveness of risk-sealing strategy to prevent dental caries compared to routine sealant application at two health centres in Finland (II,III);
- to compare retrospectively the cost-effectiveness of sealants and restorative treatment in two municipal dental health centres in Finland (IV).

Working hypotheses:

- sealant treatment prevents fissure caries of first permanent molars.
- different sealant strategies lead to different outcomes.
- the total cost of treatment (preventive treatment, sealants and restorative treatment) of sealant-treated subjects is higher than the total costs for non-sealed subjects.

Background of the study

In Finland, the Primary Health Care Act of 1972 reformed the planning of primary health services by establishing a network of health centres funded by municipalities, which are independent in organizing services in their own way and in deciding on, for example, different treatment lines (Nordblad *et al.* 2004, Widström & Eaton 2004, Kravitz & Treasure 2009).

In the 1970s–1980s, dentists examined schoolchildren annually and treated those with diagnosed oral problems. In the 1990s, annual examinations were recommended to replace by individually determined examination intervals. Additionally, oral hygienists examined children under the age of six years, and referred those with signs of illness to dentists. The information on general health, medical history, oral health status of a patient as well as preventive measures, fluoride therapies, and restorative, prosthetic and surgical procedures was documented in standard paper dental records.

In Sweden, the Public Dental Service Act (1973) provided free care for children 0–19 years of age (Bolin 1997, Kravitz & Treasure 2009). The county councils assumed the responsibility for providing this service, which included regular annual visits to a dental clinic from the age of three (Bolin 1997). Dental care for children below this age concentrated on guidelines for health promotion and disease prevention at Child Welfare Centres; the target group being pregnant mothers and mothers of children under three. Counselling comprised hygiene measures, information and recommendation on the use of fluorides and dietary habits. The information was given by dentists, dental hygienists, or specially trained dental nurses of the public dental health service. Children at high risk of developing caries were entitled to dental care at specialist paediatric dental clinics. About 50% of the practicing dentists in Sweden were employed in the Public Dental Service, and the rest were private practitioners. During the late 1980s and the early 1990s, many pilot projects were conducted in attempts to improve general cost-effectiveness and also to seek methods for identifying children at greater risk of developing caries (Bolin 1997). For fissure sealing, clinical and microbiological caries risk evaluations were used, and only the high caries risk molars were sealed.

In Greece, health care is provided by a complex mixture of social security organizations and since 1983, a basic framework of state-funded national health services has been established (Kravitz & Treasure 2009). About 400 Public Health Centres were organized geographically to cover the entire population. They provided prevention and treatment for children only, and were organized as urban or rural (Bolin 1997). In urban regions, up to 80% of restorative dental care was provided by private practitioners, while in rural regions, the Health Centres also provided restorative treatment for children. The main task for all Health Centres was to provide oral health prevention to the entire child population of 0–18 years of age, and the preventive programme included the entire spectrum of prevention, with special emphasis on dental health education. Furthermore, the law allows for a link between the Health Centres and schools (nurseries, elementary and high schools). Both the rural and the urban Health Centres were entirely financed by the Government. The responsibility for bringing the children to the Health Centres lied with the parents, but a re-call system was under way. The uneven distribution of dentists was the reason why private dentists performed most of the treatment for urban children.

Dental care in private practice had a fee, and there was only a nominal fee in the Health Centres. Restorative treatment provided by private practitioners was paid for by the children's parents. Dental health insurance covered anywhere from 20%

to 50% of the treatment cost, depending on the policy of each insurance scheme and the premium paid by the insured persons for coverage. There were different health insurance organizations according to the occupation of the insured person. Use of dental auxiliaries differed. The majority of dentists were working without assistance, but some had assistance from a "self-educated nurse". There were no formally trained dental hygienists in Greece until 1993, when the first formal two-year education for dental nurses started (Bolin 1997).

4 Material and methods

4.1 Caries preventive methods in different study locations

4.1.1 The study in Finland, Sweden and Greece in the 1970s–1980s (I)

In Finland, the preventive methods in dentistry have largely been based on the administrative guidelines of the National Board of Health. Standard preventive procedures included fluoride varnish application, oral hygiene instructions, and dietary counselling once in every one or two years in the 1970s–1980s. Enamel caries was followed or treated by preventive methods, including the sealing of occlusal fissures. Application of sealants was performed by dentists, and the fissures of the first and second permanent molars (in the 1970s also premolars) were sealed. The criterion for restorative treatment due to caries was performed when caries had reached dentin. This practice concerns the age cohorts born in 1960–1980.

In Sweden, in the 1980s, the preventive programme was similar to Finland's, including topical applications of fluoride varnishes and diet counselling. For fissure sealing, clinical and microbiological caries risk evaluations were used, and only the high caries risk molars were sealed (Virtanen *et al.* 2003).

In Greece, in the 1980s, a regular re-call system was implemented in private paediatric dental clinics and in the Health Centres. The same dentists who worked in the private practices served also in the Public Health Centres on a part-time basis, and the treatment criteria and the re-call interval in the public and private practices were the same. Sealants were placed on ”molars at risk for caries” based on individual selective criteria (i.e. past caries experience, deep fissure anatomy). Sealants were applied only after a parent's consent; therefore, parents' subjective evaluation of cost of sealants was another factor to be considered. Applying these criteria, approximately 40% of the first molars from private practice and 20% from the Health Centre were sealed (respective values for second molars were 60% and 30%). As regards caries diagnostics, tooth surfaces were considered carious when there was a definite caries diagnosis at the dentin level. If a surface was diagnosed as questionable, a sealant was placed or replaced when necessary.

4.1.2 The study in Finland (Kemi and Vantaa) in the 1990s (II–IV)

There were some principal differences between the treatment lines at the two health centres as regards the analysed 1990s age cohorts.

In Kemi, children born in the early 1990s were classified as a high caries risk subjects once they were clinically evaluated and had signs of dental caries and high *Streptococcus mutans* level in dental plaque, which was determined at the age of two years by a chair-side dip slide test (Dentocult® SM Strip Mutans, Orion Diagnostica, Espoo, Finland). Xylitol chewing gum was delivered to children once a day in day care centres. In addition, a recommendation was made to the parents to give xylitol chewing gum to their children after every meal. Application of sealants was performed by dentists and oral hygienists, and the fissures of permanent molars of all high caries risk children were sealed. Low-risk subjects were left unsealed. The decision to seal or not to seal each particular subject/child was made by dentists on the basis on the individual caries risk of each child.

In Vantaa, toothbrushes were provided free of charge in day care centres, and oral hygienists supervised children's toothbrushing. Fluoride rinses (0.2%) were performed in day care centres and in elementary schools. The strategy of routine sealing of all first molars soon after their eruption without caries risk determination was followed, and the sealing procedure was performed mainly by dental hygienists.

Application of resin-based sealant (Delton, Light Curing Clear, Dentsply De Trey, Germany) was performed at both Kemi and Vantaa health centres.

4.2 Datasets

4.2.1 The study in Finland, Sweden and Greece following the tooth age (I)

Data for this study were collected from the dental records in Finland and in Sweden (age cohorts 1970–72 and 1980–82), Sweden (cohorts 1980–82) and Greece (cohorts 1980–82) (Table 4).

Table 4. The representative sample of subjects born in 1970–72 in Finland and in Sweden and in 1980–82 in Finland, Greece and Sweden (I).

Country	Gender	1970–72 n	1980–82 n	Total n
Finland	Boys	694	734	1 428
	Girls	747	760	1 507
Greece	Boys	–	267	267
	Girls	–	292	292
Sweden	Boys	312	335	647
	Girls	297	297	594
Total		2 050	2 685	4 735

For this study, the examiners compiled data manually from the paper records, after which the data were transferred into an electronic form. Dentists recorded the findings in dental charts on a tooth-surface level, and the treatment was recorded in progress notes. The timing of the emergence of permanent molars, placement of the fissure sealant, dental caries, and restorative procedures were recorded in the dental records. The ages of the subjects were recorded with an accuracy of one day and the dates of examination with an accuracy of one month. The interval of annual oral examinations was observed to be 12–18 months in practice, with some no-show subjects. If the follow-up intervals were longer than 18 months, the subject was excluded from the study.

Because the time of the eruption of first permanent molars into full occlusion varies and caries does not affect un-erupted teeth, the tooth emergence (the time point when the tooth was registered the first time to penetrate through *gingival mucosa* by a dentist) was taken as the baseline for the analysis. The emergence of the tooth and the onset of the caries process were interval-censored as having occurred at the first examination following the event. If the sound tooth was attacked by dental caries (or was restored because of caries) at the first examination after the eruption, it was interval-censored to have happened at that examination. This resulted in the practice that in the first examination after the tooth eruption, some of the first molars were registered as both erupted and affected by caries. Previously, this was defined as a ”post-eruptive step” (Larmas *et al.* 1995). Most teeth were sound at the end of the follow-up, and carious stages of these teeth were hence right-censored.

If fissures were sealed within the first 12 months after the tooth emergence, this was identified as ”early sealing”. All other sealant placements were recorded as ”late sealing”. Dental caries was recorded and interval-censored at the stage when the dentist made the decision to restore the lesion.

4.2.2 The study in Finland following the chronological age of patients (II, III)

Data were collected at two health centres in Finland, Vantaa (age cohort 1990) and Kemi (cohorts 1988–90) (Table 5).

Table 5. The representative sample of subjects born in 1990 in Vantaa and in 1988–90 in Kemi divided into subgroups based on the sealant treatment statuses of their first molars in the first examination after tooth eruption (II, III).

Town	1990 n (total)	1988–90 n (total)	all-sealed n (%)	partly sealed n (%)	non-sealed n (%)
Vantaa	2 851	–	1 472	895	484
	(100%)		(52%)	(31%)	(17%)
Kemi	–	965	251	328	386
		(100%)	(26%)	(34%)	(40%)

Electronic dental records were available, and the information was automatically compiled from children born in 1988–90 in Kemi and in 1990 in Vantaa. An electronic patient record system (Denting, Kemi TT Center, Kemi, Finland) has been used since 1989 in Kemi and (Winhit, Novogroup, Helsinki, Finland) since 1994 in Vantaa. The birth of the subject was taken as the baseline for the survival analysis, and if caries was diagnosed in permanent teeth, it was interval-censored to have occurred at the first examination after the subject had turned six years of age. The data collected included the date of birth, gender, and in every examination, the number of cavitated carious lesions, restorations on each tooth surface, application of fissure sealants, and presence of fractured, extracted or missing teeth. The following surface-specific information of each tooth was registered: sealant treatment and enamel/dentin caries. The dates and codes of this information and treatment procedures were compiled into an intermediate file.

Each subject was followed for a certain period of time and censored if the event (caries onset, restoration) did not occur at the completion of the follow-up (right-censored). Up to the age of 16 years, the accepted interval between examinations was 10–13 months. If the interval was longer, the subject was excluded. Thereafter, the examination interval was based on the clinical determination of individual caries risk of a subject, and varied from one to three years. At least one annual dental examination was carried out in the early 1990s, and later, almost 70% of the age cohort was examined once a year.

Because tooth emergence was not carefully registered in the electronic dental records, caries onsets were interval-censored, i.e. recorded to have occurred at the first exam following the diagnosed event in patients who had to visit the health centre at the age of 6–8 years. If they had visited another health centre (no information available), they were left-censored. The exact dates of sealant treatment or restorations were also recorded. Enamel caries was followed and treated using non-operative preventive methods, including the sealing of occlusal fissures. Restorations placed due to crown fractures and resealing procedures were excluded from this analysis. With these data, left-censoring was used in all subjects not attending dental care in the health centre before the age of eight years. Right-censoring was used for the teeth which were sound at the end of the follow-up.

For this analysis, the non-sealed and all-sealed subjects at both health centres were retrospectively classified into two subgroups based on their caries susceptibility: caries-prone subjects were those with at least one of their first molars carious/restored before the age of eight years, and caries-resistant were the subjects without any restoration in any of their first molars under the age of ten years. Subjects with caries experience in any of their first molars between the ages of 8 and 10 years were censored.

4.2.3 Cost-effectiveness analysis (IV)

The cost-effectiveness analysis was performed to compare the total costs of fissure sealing and restorative treatment by means of targeted fissure sealant treatment for high caries risk subjects at the Kemi health centre *vs* routine sealing at the Vantaa health centre. Second, this analysis may provide an idea how the cost of sealant treatment in different countries or health centres could be measured.

The study population consisted of all children born in 1988-1990 in Kemi (n=965) and in 1990 in Vantaa n=2851) (Table 5). All subjects were retrospectively divided into two subgroups based on the sealant treatment status of their first permanent molars: (1) all-sealed group consisted of subjects who had all their first permanent molars sealed at the onset of follow-up. (2) the non-sealed group consisted of subjects who had none of their first molars sealed/restored at the onset of follow-up (Table 5). Premolars, canines and second molars were not included into the study because only a few of these teeth were erupted at the end of the follow-up on subjects who were 12 years old.

The costs considered here were the costs of preventive procedures, such as fissure sealant treatment, SM® tests, and xylitol chewing gum. The measure of effectiveness was the cost of caries risk determination by SM® tests, caries prevention by xylitol, sealing and restorative treatment of first permanent molars and incisors per subject in euros after the entire follow-up period in the two towns with different preventive treatment strategies.

Cost of sealants and restorative treatment

The costs of sealants and restorations, including the costs of materials and the labour cost of the oral hygienist or dentists, were calculated based on the 2008 level in Finland, using the same scheme as Virtanen *et al.* 1996 and Raitio *et al.* 2001. It was not possible to find out the fee for single restoration or treatment from health centre statistics (treatment of children was free). Therefore, we used the fees for restorations charged in private dental clinics in the calculations, and assumed that the costs of restorations and sealants are nearly equal in the health centres, including the filling material and working time of the operators.

The average fee for sealants was calculated to be EUR 21 for a mouth quadrant. For all-sealed subjects, the EUR 21 was multiplied by four, even if the cost of sealing first molars only was analysed. The total cost of occlusal restoration was estimated to be EUR 60, and each additional surface increased it by EUR 30 in the same restored permanent molar/premolar. All restored surfaces of the first and second incisors were calculated to cost EUR 60. The cost analysis was conducted comparing the sum of restored teeth surfaces (i.e. surface-specific filling increment) in children in a cross-section at the age of 12 years in the non-sealed and all-sealed groups. The cost of sealing treatment of all first molars (EUR 84) was added to the cost of the restorations in sealed patients. The measure of effectiveness was the total cost of restorations in the targeted sealant treatment group (Kemi) as compared to the routine sealant treatment group (Vantaa) at the end of the follow-up period.

Cost of xylitol

One piece of xylitol chewing gum a day was delivered to children in day care centres in Kemi. The retail price of one chewing gum was two cents (= EUR 0.02). The maximum total cost of xylitol delivered in the day care centres per child was thus on average EUR 6 in one year (EUR 0.02 × 300 day-care days = EUR 6) from the age of three years onwards, thus in total EUR 18 in three years per child.

Cost of SM® tests

The SM® test was performed once per child at the age of two years. The costs of one test per child (EUR 5) and the labour costs/working hours of oral hygienists were counted. The time required to perform the SM® test was estimated to be five minutes per subject. The salary cost of one working hour for a hygienist was calculated to cost EUR 12. Thus the SM® test and five working minutes for hygienist were counted to cost altogether EUR 6 (EUR 5 + 1).

The early caries risk determination by SM® test and prevention by xylitol per one child were counted to cost in total EUR 18 + 6 = 24 in three years.

4.3 Statistical analyses

The data were entered into a computer, and the SAS statistical software program version 9.1.3 (SAS Institute Inc., Gary, N.C., USA) was used for the analysis of tooth survival individually for each tooth, applying the Kaplan–Meier method.

Survival time was defined as the time that elapsed between the eruption of the tooth (= tooth-age) and placement of restoration due to caries (I), and between the birth of subject (= chronological age) and placement of restoration due to caries (II, III). Survival times of first molars were measured on a subject level [all-sealed subjects (all four first molars sealed) *vs* unsealed subjects (none of their first molars sealed) I, II] and on a tooth level (sealed *vs* non-sealed teeth, III). Separate analyses were done from all these data sets. Mean survival times and confidential intervals (95% CI) were counted separately for each first molar in the subject-specific analysis (II).

Survival curves for homologous teeth on the left and right sides were found to be similar and were combined in the figures, but not in the statistical analysis, in which the child was the unit of analysis. The significance of the differences between the survival curves for each tooth in each group were compared by means of the log-rank test, and a p-value of less than 0.001 was taken to indicate statistical significance (I, II, III).

Cost-effectiveness analysis was performed from the electronic data set of the 1988–1990 age cohort in Finland (IV). The data from the patient documents were transferred to the SAS survival procedure and the cumulative cost of restorations and sealing treatment was calculated. The chi-squared test was used for statistical comparison of surface-specific filling increments between Kemi and Vantaa (IV).

4.4 Ethical aspects

The health centres and private dental clinics involved from Finland, Sweden and Greece granted their permission for the study, which was a part of the EUDENT research network project (I). The Committee of Ethical Affairs of the Oulu University Hospital and corresponding committees at each health centre granted their permission for this study (II, III, IV). The data were collected from copies of the patient dental records. In the copies, the last names and social security codes were removed in order to make the data anonymous for the purpose of data analysis processes. The children in this study were examined in connection to regular dental health controls, and the data were confidential; i.e. it is not possible to match a certain health status with an individual child. Automatic data mining was performed to ensure that individuals could not be identified.

5 Results

5.1 Preventive effect of sealants on dental caries in Finland, Sweden and Greece (I)

In Finland, half of the molars and 20–30% of the premolars were sealed in the 1970 age cohort.

In Sweden, very few teeth were sealed in that cohort, and therefore no comparisons between sealed and non-sealed teeth/subjects could be performed for that country. In Greece, the 1970 cohort was unavailable.

In the 1980 cohort in Finland, routine fissure sealing resulted in 80–90% of all molars being sealed. In Sweden, the sealing only in high caries risk subjects resulted in 20–30% of molars and a low percentage of premolars being sealed. In Greece, the prevalence of sealant placement for first molars was at the same level as in Sweden, but second molars were sealed twice as often as the first molars, and a relatively high percentage of premolars was also sealed (Figure 1).

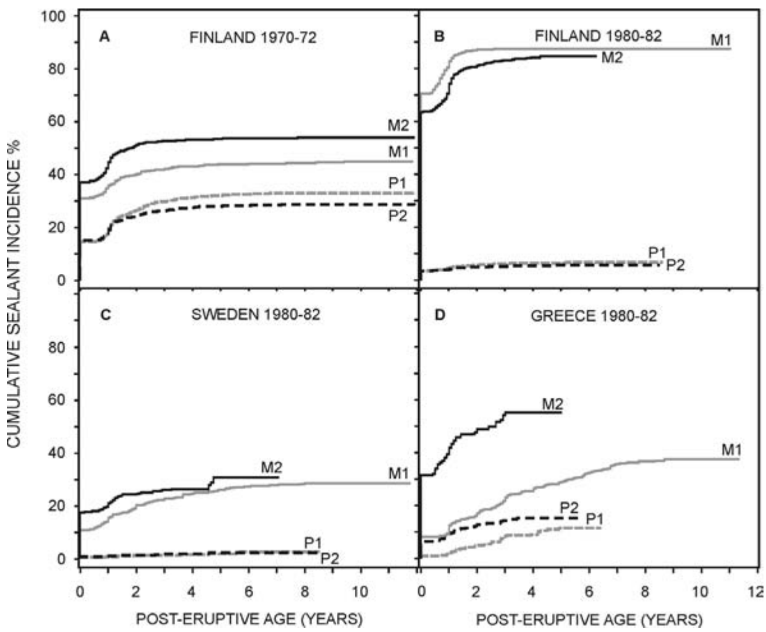

Figure 1. Cumulative sealant incidence of permanent first (M1) and second (M2) molars and first (P1) and second (P2) premolars in subjects born in 1970–1972 and 1980–1982 in Finland, Sweden and Greece (I).

No differences were noted between the survival curves of molars and premolars of boys and girls in any country or between the left and right sides of the mouth, therefore the data were combined in the analyses. The maxillary first molars were chosen to represent the survival curves of first molars.

Sealing of any first molar resulted in a significant reduction ($p < 0.001$) of restoration placement in these teeth compared to their non-sealed counterparts. Approximately 30–40% of sealant-treated molars and 60–80% of non-sealed molars were restored after the seven-year follow up in all these countries. Sealing in the year of tooth emergence (early sealing) was not significantly ($p > 0.05$) more effective than sealing later on (late sealing). This outcome was similar in all countries (Figure 2).

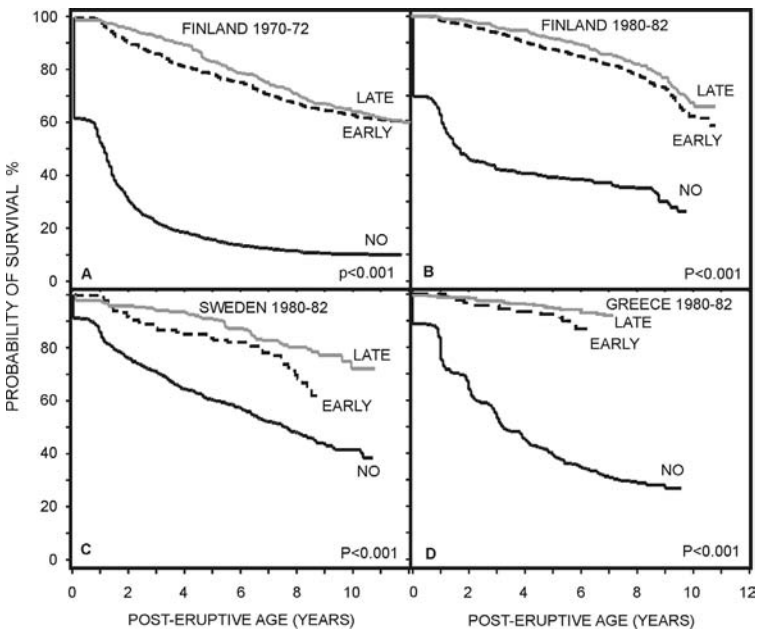

Figure 2. Survival rates of maxillary permanent first molars with early, late or without any sealant treatment in subjects born in 1970–1972 in Finland and 1980–1982 in Finland, Sweden and Greece. The log-rank model p-value is listed between early/late sealed and non-sealed first molars (I).

In subject-specific analysis, the subjects with all their first molars sealed had less restorations than the unsealed subjects did, and the difference was significant (p < 0.001) between the sealed/unsealed subjects in all cohorts, except in Sweden in the 1980 cohort (Figure 3).

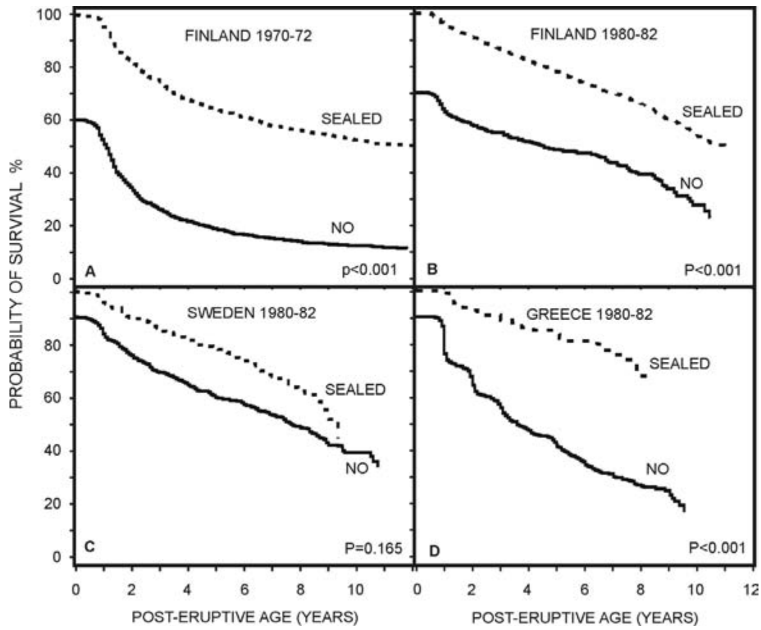

Figure 3. Survival rates of maxillary permanent first molars in subjects with no sealant treatment in any of their first molars ("no") and in subjects with all their first molars sealed ("sealed") during the first post-eruptive year in Finland, Sweden and Greece. The log-rank model p-value listed between sealed and non-sealed first molars (I).

The number of teeth/subjects participated in the study and differentiated the amount of "failed" (carious) and "censored" teeth/subjects are presented in Tables 6 and 7.

Table 6. The number of permanent first molars divided into failed (carious) and right-censored (healthy) groups at the end of follow-up. OR[1] illustrates the instantaneous risk for first molars to become cavitated at tooth level.

	Finland 1970–72				Finland 1980–82				Sweden 1980–82				Greece 1980–82			
The sealing status of first molar	Failed	Right-censored	Total	OR[1] (95%CI[2])	Failed	Right-censored	Total	OR (95%CI)	Failed	Right-censored	Total	OR (95%CI)	Failed	Right censored	Total	OR (95%CI)
Early	373	494	867	1.0	548	1526	2074	1.0	42	95	137	1.0	14	77	91	1.0
Late	178	214	392	1.1 (0.9–1.4)	122	380	502	0.9 (0.7–1.1)	45	168	213	0.6 (0.4–1.0)	30	261	291	0.6 (0.3–1.3)
No	1390	153	1543	12.0 (9.7–14.9)	244	120	364	5.7 (4.5–7.2)	469	440	909	2.4 (1.6–3.5)	492	225	717	12.0 (6.7–21.7)

[1]OR- odds ratio

[2]CI- confidence interval

Table 7. The number of subjects divided into failed and right-censored groups at the end of follow-up. OR[1] illustrates the instantaneous risk for first molars to become cavitated at subject level.

	Finland 1970–72				Finland 1980–82				Sweden 1980–82				Greece 1980–82			
The sealing status of subjects	Failed	Right-censored	Total	OR[1] (95%CI[2])	Failed	Right-censored	Total	OR (95%CI)	Failed	Right-censored	Total	OR (95%CI)	Failed	Right censored	Total	OR (95%CI)
Sealed subjects[3]	604	320	924	1.0	1073	1435	2508	1.0	78	114	192	1.0	35	79	114	1.0
Unsealed subjects[4]	1378	220	1598	3.3 (2.7–4.0)	188	216	404	1.2 (0.9–1.4)	497	563	1060	1.3 (0.9–1.8)	615	349	964	4.0 (2.6–6.0)

[1]OR- odds ratio

[2]CI- confidence interval

[3]Sealed subjects – all first molars sealed

[4]Unsealed subjects- not any of first molars sealed

The highest risk for first molars to become cavitated (= failed) on a tooth level was found to be in non-sealed molars in Finland (cohort 1970–72) and in Greece (OR 12.0) (Table 6). On a subject level, the same tendency was found: unsealed subjects in Finland (cohort 1970–72) (OR 3.3) and in Greece (4.0) had the highest risk for developing caries (Table 7). In the tooth-specific analysis, the differences in ORs between sealed and non-sealed teeth were higher than in the subject-specific analysis between the subjects (Tables 6 and 7).

5.2 Preventive effect of sealants in Finland (Kemi and Vantaa) (II, III)

5.2.1 Subject-specific analysis (II)

The proportion of unsealed subjects at the first examination after the emergence of first molars was twice as high in Kemi (40%) compared to the respective group in Vantaa (17%). In Vantaa, 52% of the subjects and in Kemi only 26% belonged to the all-sealed group (Figure 4).

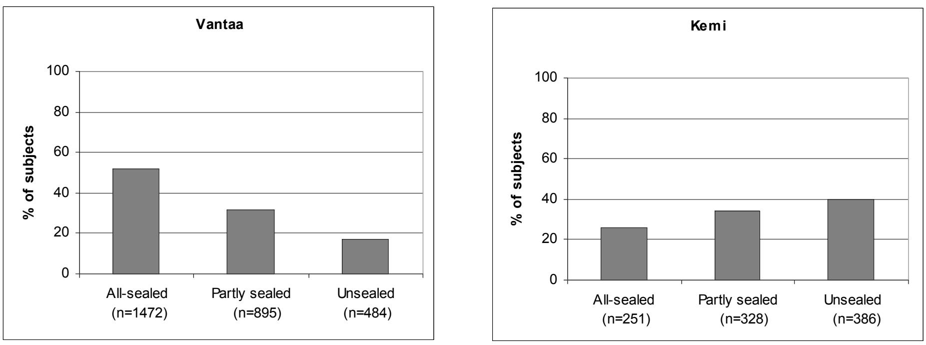

Figure 4. Cumulative incidence of all-sealed, partly sealed and unsealed subjects at the Vantaa and Kemi health centres based on the sealant treatment statuses of their permanent first molars in the first examination after tooth emergence (II).

The mean survival times of the first molars in the all-sealed, partly sealed and in unsealed subject groups varied at the two health centres over the eight-year study period (Table 8).

Table 8. Mean survival time (95%CI) of permanent first molars in years (starting at birth of subject) in two health centers in all-sealed, partly sealed and unsealed subject group (II).

Subject group Tooth number	Vantaa	Kemi
All-sealed		
16	13.2 (13.1–13.3)	13.6 (13.3–13.8)
26	13.2 (13.1–13.3)	13.2 (13.0–13.4)
36	12.9 (12.8–12.9)	13.4 (13.2–13.7)
46	12.8 (12.8–12.9)	13.3 (13.0–13.6)
16–46	13.1 (13.0–13.1)	13.5 (13.3–13.6)
Partly sealed		
16	11.8 (11.6–12.0)	12.9 (12.7–13.1)
26	11.7 (11.5–11.9)	12.8 (12.6–13.1)
36	11.6 (11.4–11.7)	12.6 (12.4–12.9)
46	11.5 (11.3–11.7)	12.6 (12.4–12.8)
16–46	11.7 (11.6–11.8)	12.8 (12.6–12.9)
Unsealed		
16	12.6 (12.4–12.8)	12.3 (12.2–12.4)
26	12.6 (12.4–12.8)	12.9 (12.7–13.0)
36	12.5 (12.3–12.6)	13.3 (13.2–13.5)
46	12.4 (12.3–12.6)	12.8 (12.7–12.9)
16–46	12.5 (12.4–12.6)	12.9 (12.7–13.0)

[1]CI- confidece interval

The mean survival times of first molars were higher in all three groups in Kemi compared to Vantaa, except for the non-sealed tooth 16.

The probability of survival of first molars in all-sealed subjects was at the same level in both health centres, where 80% of teeth had survived without restorations at the 12 years of age of subjects (Figure 5).The survival time of first molars was the highest in the unsealed group in Kemi and the lowest in the partly-sealed group in both towns. The difference in the survival probability of first molars of unsealed subjects between the health centres was statistically significant ($p < 0.001$) (Figure 5).

For the present analysis, the all-sealed and unsealed subjects were retrospectively divided into two extreme subgroups based on their estimated caries susceptibility (caries-prone and caries-resistant). Caries-prone were the subjects with at least one of their first molars carious or restored before the age of eight, and caries-resistant those without any restoration in their first molars under the age of ten. The first molars of the caries-resistant subjects were restored at 13.4–14.0 years of age in both towns regardless of the patients' sealant treatment statuses. All first molars were restored at the age of 6.8–7.7 years in the caries-prone subjects regardless of their sealant treatments (Table 9).

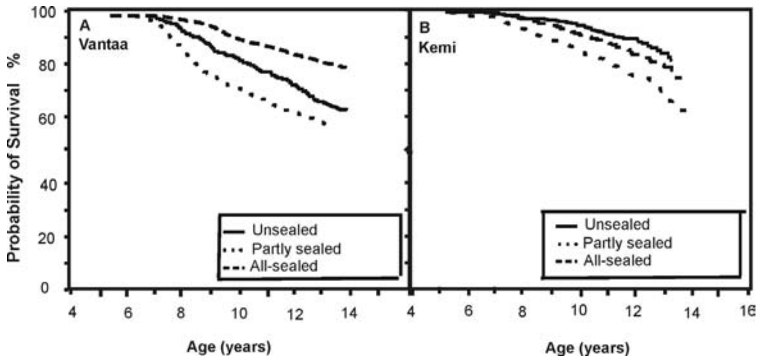

Figure 5. Survival curves illustrating the probability of survival of permanent first molars in subjects with no sealants in any of their first molars before the age of eight years (unsealed), subjects with sealants in their 1–3 first molars (partly sealed) and subjects with all their first molars sealed (all-sealed) (II).

Table 9. Mean survival time (95%CI) of permanent first molars in years (starting at birth of subject) in two health centers in caries-prone and caries resistant all-sealed and unsealed subjects (II).

Subject group	Vantaa	Kemi
All-sealed subjects		
caries-prone	7.4 (7.2–7.6)	6.8 (6.7–6.9)
caries resistant	13.4 (13.3–13.4)	14.0 (13.9–14.1)
Unsealed subjects		
caries-prone	7.3 (7.2–7.5)	7.7 (7.6–7.8)
caries resistant	13.5 (13.4–13.5)	13.6 (13.5–13.7)

[1]CI- confidence interval

5.2.2 Tooth-specific analysis (III)

Sealant placement on the first permanent molars started at about six years of age of the subject, soon after the tooth emergence. In Vantaa, nearly 80% of first molars were sealed before the age of eight years. In Kemi approximately 50–60% of first molars were sealed at that age, in girls more frequently than in boys, the difference being statistically significant ($p < 0.001$) (Figure 6).

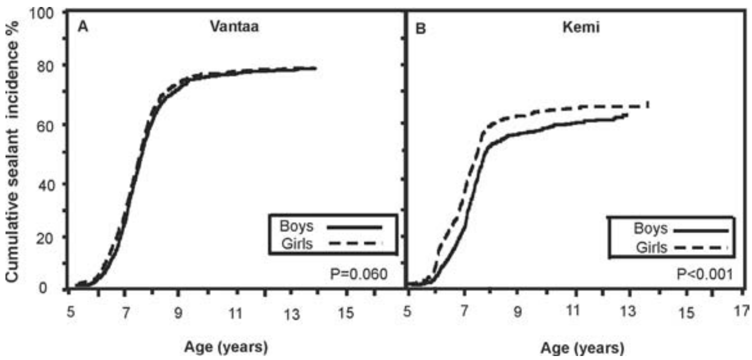

Figure 6. Cumulative sealant treatment incidence of permanent first molars for boys and girls in Vantaa and in Kemi. The log-rank model p-value is listed between boys and girls for both towns (III).

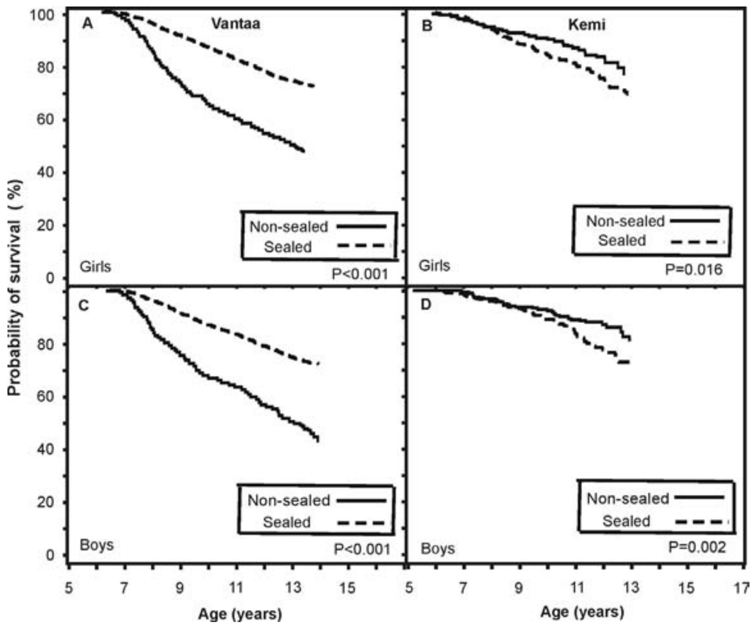

Figure 7. Survival curves for sealed and non-sealed mandibular permanent first molars by genders in Vantaa and in Kemi. The log-rank model p-value is listed between sealed and non-sealed first molars (III).

Sealing of the first mandibular permanent molars after their emergence resulted in a reduced number of restorations compared to their non-sealed counterparts in Vantaa, both in boys and girls the difference was statistically significant ($p < 0.001$). In Kemi, sealant treatment of first mandibular molars resulted in a similar rate of restorative treatment need compared to sealed mandibular molars in Vantaa, but the non-sealed first mandibular molars were restored at the lowest level in Kemi (Figure 7).

The respective curves for maxillary permanent first molars were nearly identical (data not shown).

The variation between mean survival times of sealed and non-sealed first mandibular molars was 11.3–12.9 years in Vantaa and 12.0–12.5 years in Kemi (Table 10).

Table 10. Mean survival time (95%CI) of sealed and non-sealed first permanent mandibular molars in two health centers at 7 years of follow-up (III).

Status of first permanent mandibular molars	Vantaa	Kemi
Sealed (boys)	12.9 (12.8–13.0)	12.2 (12.1–12.4)
Non-sealed (boys)	11.6 (11.4–11.9)	12.5 (12.4–12.6)
Sealed (girls)	12.7 (12.6–12.8)	12.0 (11.9–12-1)
Non-sealed (girls)	11.3 (11.1–11.5)	12.2 (12.0–12.4)

[1]CI-confidence interval

5.3 Cost-effectiveness analysis of fissure sealants in Finland (IV)

The surface-specific filling increments of permanent first molars and incisors and their cumulative costs were expressed per 100 subjects at the age of 12 years in Kemi and Vantaa (Tables 11 and 12 respectively).

Table 11. The surface-specific filling increments of permanent first molars and maxillary incisors per 100 subjects in all-sealed and unsealed subjects (in parenthesis) at the age of 12 years in Kemi.

Tooth	Occlusal	Mesial	Buccal	Distal	Lingual	Total
6	48 (30)	10 (6)	20 (7)	1 (2)	6 (6)	85 (51)
2	–	2 (1)	1 (0)	0 (0)	1 (1)	4 (2)
1	–	4 (3)	1 (1)	3 (1)	1 (0)	9 (5)
Total	48 (30)	16 (10)	22 (8)	4 (3)	8 (7)	98 (58)

The highest number of restorations was on the occlusal surfaces of first permanent molars both in all-sealed and in unsealed subjects in both towns (Tables 11 and 12). Unsealed subjects had more fillings in all surfaces of the first molars but also in maxillary incisors in Vantaa than they did in Kemi (Table 11 and 12).

Table 12. The surface-specific filling increments of permanent first molars and maxillary incisors per 100 subjects in all-sealed and unsealed subjects (in parenthesis) at the age of 12 years in Vantaa.

Tooth	Occlusal	Mesial	Buccal	Distal	Lingual	Total
6	50 (100)	14 (16)	19 (29)	4 (7)	11 (17)	98 (169)
2	–	1 (3)	1 (1)	0 (1)	2 (2)	4 (7)
1	–	4 (5)	4 (4)	3 (5)	3 (3)	14 (17)
Total	50 (100)	19 (24)	24 (34)	7 (13)	16 (22)	116 (193)

The costs of restorative treatment in different teeth and surfaces in all-sealed and in unsealed groups are presented in Tables 13 and 14.

Table 13. The calculated cost of restorations by tooth surfaces per one subject in euros in all-sealed and in unsealed (in parenthesis) subjects at the age of 12 years in Kemi.

Tooth	Occlusal	Mesial	Buccal	Distal	Lingual	Total
6	28.80 (18.00)	3.00 (1.80)	6.00 (2.10)	0.30 (0.60)	1.80 (1.80)	39.90 (24.30)
2	–	1.20 (0.60)	0.60 (0.00)	0.00 (0.00)	0.60 (0.60)	2.40 (1.20)
1	–	2.40 (1.80)	0.60 (0.60)	1.80 (0.60)	0.60 (0.00)	5.40 (3.00)
Total	28.80 (18.00)	6.60 (4.20)	7.20 (2.70)	2.10 (1.20)	3.00 (2.40)	47.70 (28.50)

The total cost of restorations of permanent first molars and incisors per one sealed subject was EUR 47.70 and per one unsealed subject EUR 28.50 in Kemi, and EUR 55.20 and EUR 95.10 respectively in Vantaa (Tables 13 and 14).

Table 14. The calculated cost of restorations by tooth surfaces per one subject in euros in all-sealed and in unsealed (in parenthesis) subjects at the age of 12 years in Vantaa.

Tooth	Occlusal	Mesial	Buccal	Distal	Lingual	Total
6	30.00 (60.00)	4.20 (4.80)	5.70 (8.70)	1.20 (2.10)	3.30 (5.10)	44.40 (80.70)
2	–	0.60 (1.80)	0.60 (0.60)	0.00 (0.60)	1.20 (1.20)	2.40 (4.20)
1	–	2.40 (3.00)	2.40 (2.40)	1.80 (3.00)	1.80 (1.80)	8.40(10.20)
Total	30.00 (60.00)	7.20 (9.60)	8.70 (11.70)	3.00 (5.70)	6.30 (8.10)	55.20 (95.10)

Altogether, the costs of sealant treatment and later restorative treatment during the follow-up time was EUR 131.70 per subject in all-sealed subjects and EUR 28.50 per subject in unsealed subjects in Kemi (Table 15). In Vantaa, the cost of the treatment of all-sealed subjects was EUR 139.20 per subject and for unsealed subjects EUR 95.10 per subject. The mean cumulative cost of treatment by sealing and restoring of all patients (including caries risk determination and caries prevention by xylitol in Kemi) was about EUR 184.20 per subject in Kemi and EUR 234.30 per subject in Vantaa at the age of 12 years (Table 15).

Table 15. The costs of caries risk determination, prevention by xylitol, sealing and restorative treatment of first permanent molars and incisors per one subject in euros in all-sealed and in unsealed subjects during the follow-up period.

Subjects	Risk determination and prevention by xylitol		Sealing treatment		Restorative treatment		Total	
	Kemi	Vantaa	Kemi	Vantaa	Kemi	Vantaa	Kemi	Vantaa
The cost of								
- all-sealed subjects	-	0.00	84.00	84.00	47.00	55.20	131.70	139.20
- unsealed subjects	-	0.00	0.00	0.00	28.50	95.10	28.50	95.10
The total cost of all-sealed and unsealed subjects	24.00	0.00	84.00	84.00	76.20	150.30	184.20	234.30

6 Discussion

6.1 General discussion

6.1.1 Main findings

This study suggested that differences exist between sealant treatment strategies and the outcomes of sealant treatments in different countries and health centres in everyday dental practice. However, some common features were found: conducted caries risk strategy, both, in different countries (Sweden and Greece) and in one health centre in Finland (Kemi), resulted in more favourable outcome in terms of dental health and reduced treatment cost. A new finding was the fact that sealant treatment is not sufficient in very high caries risk subjects.

Database compiling was observed to be a convenient way for analysing ordinary, electronic patient record files from the health centres' databases also for scientific purposes in a practice-based research fashion. This research line is a new one dedicated to translational research, as the Science Magazine´s new journal states (Zerhouni 2009). Its goal is to compare observations made in real-life conditions on findings of epidemiological studies made based on traditional evidence-based principles (Mjör *et al.* 2005, Niederman & Leithch 2006).

The effectiveness of fissure sealant treatment of first molars was higher in individuals and in teeth with caries risk, which is in line with previous studies (Ahovuo-Saloranta *et al.* 2004, 2008, Simonsen 2002, Weintraub 2001). Caries-resistant subjects do not necessarily benefit from sealant treatment (Oulis & Berdouses 2009).

The caries-preventive effect of sealants could be achieved the best if sealing treatment were targeted at the individual level so that all first molars of caries-risk children should be sealed before the eight years of age. Partly sealed individuals had the lowest survival times of their first molars which is in line with the study by Tickle *et al.* 2007.

As regards sealing the high caries-risk individuals, the risk strategy is more cost-effective than routine sealing of all children. This is concluded also in previous studies (Bhuridej *et al.* 2007, Quiñonez *et al.* 2005, Virtanen *et al.* 2003, Locker *et al.* 2003, Griffin *et al.* 2002, Weintraub *et al.* 1993).

6.1.2 Strengths and limitations of the study

This study provides a good overview on the situation in the real-life conditions, where non-calibrated dentists are treating thousands of patients each in their own way. The large number of subjects and monitoring the dental health of these individuals in real-life conditions provide a reliable picture, based on which the evidence-based dentistry study results can be applied to everyday dental practice. Thus, this study represents a new branch in science. It is not a scientific analysis of the effectiveness of fissure sealants since this is not a multifactorial retrospective analysis of two study groups in any country or community. For that reason, the design, analysis and interpretation of the study findings have a number of inherent limitations. The results of the present study are acceptable when taking account the limitations, such as difficulties to consider all confounding factors, the disadvantages or weaknesses of cohort studies, and other factors than caries prevention (fissure sealants), which have an effect on caries prevalence.

The most important benefit of this kind of study is the fact that sealants (analysed in an EBD fashion) really work in everyday dental practice cost-effectively when targeted at subjects at risk, but not so effectively in subjects who have very high caries risk. The latter observation cannot be obtained if calibrated examiners are used.

In non-experimental studies (cohort study), the researcher is an observer rather than an agent who assigns interventions (Rothman & Greenland 2008). Comparisons of disease experience are made within the cohort across subgroups defined by one or more exposures. An attractive feature of cohort studies is the opportunity they provide to study a range of possible health effects stemming from a single exposure. However, cohort studies are usually large enterprises, and the expense of the studies often limits their feasibility. Most diseases affect only a small proportion of a population, even if the population is followed many years. Furthermore, the average risks and occurrence times cannot be measured directly from the experience of a cohort because the outcome of lost subjects during the study period is unknown. The average risk and occurrence time must be estimated using survival (life-table) methods (Rothman & Greenland 2008), which were used in this study.

In 1985, individual oral examination intervals for children and adolescents were suggested in Finland (Eerola *et al.* 1998). However, in 1994 about 74% of children under 18 years of age were still examined annually. According to the study by Wang & Holst (1995), prolonging of the re-call intervals did not interrupt the long-term trend towards better dental health in children.

Comparisons between age cohorts 1970 and 1980 in different countries were conducted in a manner that in the retrospective follow-up time, the subjects included in the study had to be examined annually (± 6 months). Due to this condition, many "irregular" visitors were excluded. Therefore, an important parameter, examination and dental health education interval, could not be analysed. In the more recent study cohort, born in 1990 in Finland, the effect of examination interval could be analysed, which is also a subject for a future research.

One can assume that children who attended to annual/individual dental examinations received more preventive care, including oral hygiene instructions and professionally made preventive care, fissure sealants included. This could have influenced the results of this study such that these children could have been included in the sealed group because their teeth were routinely sealed (I, II, III). However, according to a study by Luoma (1993), the 11–13-year-old children whose annual examinations were not individualized (control group) received approximately two times more fissure sealants "just in case" compared to the study group, which had individual re-call intervals. Despite of this, the filling increment was still higher in this control group.

The fluoridating of drinking water and the widened use of fluoride toothpaste have been considered to be the main reasons for the reduction in children caries prevalence in the 1970s–1990s. In addition, the living conditions and general well-being improved and the level of education, including the level of knowledge on health and hygiene issues, rose significantly in Finland. Children's primary teeth care was started, and different types of preventive programmes (including the use of xylitol) related to systematic dental care were launched.

As the municipal dental care was dependent on the State subsides, the National Board of Health was able to issue binding guidelines, which emphasized the role of preventive measures in the dental care strategy. Health centre dentists could take preventive measures and give dental education without suffering any income losses, because this was based on a monthly salary, not on fees.

The effect of the large variation of preventive treatments provided over the thirty years covered in this study in different health centres could not be studied exactly, because their duration was not scientifically recorded, and therefore the confounding factors could not be scientifically analysed.

With this reservation in mind, however, it is clear that the sealant treatment used had a clinically and statistically beneficial effect on the children's permanent first molars.

While the PBDr investigations do not have the same scientific strength as controlled trials in the classical scientific sense, the research setting, comprising community-based studies, offers important advantage for including individuals who do not enter the dental care system, thereby allowing investigation of a disease that is not altered by clinical treatment (Mjör *et al.* 2005).

Survival analysis for the exploration of longitudinal caries studies has an advantage over traditional statistical methods, as it takes into account censored observations and incorporates the concept of risk over time (Larmas 1995, Hannigan *et al.* 2001, Bogaerts *et al.* 2002, Hannigan 2004).

Most clinical trials on the caries-preventive effect of fissure sealants have used the split-mouth design, in which the caries-preventive effect can be assessed by comparing the teeth with sealants to the untreated control teeth of an individual. However, for evaluating the effect from a population perspective (effectiveness), the split-mouth design has certain serious disadvantages, i.e. not all children have the same chance to participate, since the inclusion criterion is that a child must have at least one pair of caries-free molars, and thus all caries-active children must be excluded (Hannigan 2004). This explains the observation of the present study that sealant treatment is not sufficient for preventing caries in very high-risk children. Furthermore, the longer the time after eruption is, the greater is the risk that the caries-active child will be excluded from the study (Hannigan 2004).

From the statistical point of view, most methodologies demand independent data, which is not possible inside the same mouth. In other words, teeth are “dependent” from each other inside an individual’s mouth, and for that reason, the comparison would be possible only, for example, between the same tooth groups (molars, premolars, etc.) of different persons.

We used a more modern survival analysis method, which is suitable in the sense that it does not need the determination of dental health as the mean of the study cohorts, but the individuals are followed as long as their information is available, even decades. In electronic patient records, the date of the birth of each subject, the date of examination, and the dates of individual treatment procedures are normally recorded with an accuracy of one day. It is also possible to use the birth date of the subject (chronological age) or the date of eruption of a tooth (tooth age) as the origin of analysis. Each parameter is followed as long as the subject is monitored.

The survival analysis is usually time consuming, and the most modern frailty-based approach supplemented with empirical estimates demands plenty of computer capacity, and is thus suitable for scientific analyses of longitudinal clinical trials in EBD. Therefore, a simplified empirical approach for the determination of lifetime of sound teeth and tooth surfaces should be developed for the clinical practice (PBD). For that purpose, either the subject-specific or the tooth-specific approach seems appropriate from the statistical point of view.

The survival analysis needs independent data, and therefore the study was constructed around comparing sealed molars to non-sealed molars retrospectively in different individuals (I, III) and comparing sealed subjects (= all their first molars sealed) to unsealed subjects (= none of their first molars sealed) (I, II), which should guarantee the independency between the individuals analysed.

While a PBR study gives a good overview in a situation of everyday dental practice, as regards this kind of a study method, there are some methodological problems in analysing study results.

First, as in most retrospective studies, the reliability and validity of the registered data of patient treatments largely depends on the completeness of the documentation. In this work, however, the dentists gathered the registered data from patient paper records for this analysis. Despite of the assumption that what is documented in patient records has also been performed clinically, previous studies have identified oral health records that were maintained insufficiently (Rasmusson *et al.* 1994, Helminen *et al.* 1998). There is always the possibility that some clinicians have not documented all the procedures, which disturbs the situation, especially when the dentist change rate is high. The change rate has been relatively high. For example, in Kemi in total approximately 40 different dentists were treating patients during the follow-up time of ten years covered this study. Estimating all the changes that could affect the study results was not possible, since no calibration was performed between dentists.

On the other hand, since public oral health service pays additional salaries to dentists based on the numbers of units of service, such as dental fillings and sealants, we assumed that sealant and restorations were used to be marked in general quite correctly (even overestimating is possible). Thus the results of this study could be valid in practical sense, although the use of non-calibrated examiners does not fulfil the scientific demands.

Second, the collected data can be considered reliable because they were collected from the original patient records and recordings had been made at actual clinical examinations where the dentists treated children as a part of their daily routine. In addition, the number of oral health records/subjects was high, guaranteeing that the data were highly representative of the real-life recordkeeping practice.

Third, during the collecting of data from the dental records, some matching errors that were made during and between the examinations conducted for the present study were found in the patient records, such as wrong numbering of teeth or lack of markings. In these cases, however, those mistakes had been usually corrected in the next annual examination, which decreased their effect on the results.

6.2 Results of the study

6.2.1 Caries experience and the effectiveness of sealant treatment in Finland, Sweden and Greece in the 1970s–1980s (I)

It was suggested that the decreasing caries incidence in the Western world in the 1970s–1990s was attributable not only to less caries in the child population, but also to changing treatment philosophies (von der Fehr 1994) resulting in fewer filled surfaces. One major obstacle in comparing conditions in different countries was that the available epidemiological data had been collected at different times using varying criteria, e.g. sometimes the examiners had been calibrated, sometimes not. Again, there are few available comparable international data from different but comparable times, and interpretation of the findings is thus difficult. One way to solve the problem is to compare the amount of survived teeth in sealed and unsealed children from the available dental records, using the PBD research approach.

A marked decline in caries experience in terms of the dmf index in primary and the DMFT index in permanent dentition during the last three decades has been reported in the Nordic countries (von der Fehr 1994, Widström *et al.* 1997). Percentage of caries-free (dmfs=0) 5-year-old children in Athens, Greece was 54.5%, in Stockholm, Sweden 74.0% (Bolin 1997), and in Finland 65% in 1994 (Nordblad *et al.* 2004). This means that prevalence of caries was 45.5%, 26.0%, and 35.0% respectively. The DMFT index in 12-year-olds was 2.4 in Athens, Greece, 1.9 in Stockholm, Sweden (Bolin 1997), and 1.2 in Finland in 1994 (Widström *et al.* 1997, Nordblad *et al.* 2004).

In the 1970 age cohort in Finland, the cumulative incidence of fissure caries in first molars was markedly higher than in the 1980 cohort. This would suggest that the benefit of sealing fissures is more pronounced when caries prevalence is higher. This is supported also by the findings of our study on the 1980 cohort in Greece, where caries prevalence was about at same level as in Finland in the 1970 cohort, and the sealant treatment had about the same effectiveness (I). The subject-level analysis resulted in disappearance of significant sealant effect on the first molars in Sweden in the 1980 cohort, whereas sealant application was effective in Finland in the 1970 and 1980 cohort and in Greece in the 1980 cohort (I).

The socioeconomic status has an impact on the caries prevalence level within a population, but that difference in the economical sense should be eliminated as regards Finland and Sweden, since the public dental health centres serve the entire population in these age cohorts free of charge. Our inclusion criteria also eliminated the non-attendees or infrequently examined subjects, normally having lower socioeconomic status. Economical analyses indicate that most of the differences of the geographical variations in the caries prevalence are explained by broad socioeconomic factors (Nadanovsky & Sheiham 1995). In Greece, patients visiting the private office for dental care came from the medium- and upper-level socioeconomic groups. In contrast, patients visiting the health centre belonged mainly in the lower-level socioeconomic group. This can explain the difference between the survival curves of Greece and the Nordic countries (I).

The criteria for restoration and decision to seal or not to seal should be nearly the same in the countries, but this could not be analysed in scientifically standardized ways between the countries. There are significant differences in the diagnostic criteria and caries-preventive methods between the different decades and countries. Overall, the caries prevalence level decreased during the follow-up time of over ten years in Finland, where the survival time of non-sealed first molars/unsealed subjects increased nearly 30%. A study conducted in the Nordic countries has revealed considerable inter-country differences in the caries-preventive methods used by the dental professionals, while the caries prevalence and severity was similar (Kallestål *et al.* 1999). For this reason, we concentrated the efforts to describe the differences between the survival of sealed and non-sealed first molars primarily within the countries.

6.2.2 The effectiveness of sealant treatment in Finland, Kemi and Vantaa in 1995–2003 (II, III)

The majority of studies concerning pit and fissure sealants in Finland conducted on the EBD basis are from the 1970s, when caries prevalence in general was much higher than it is today. Some "over-treatment" of occlusal and smooth-surface caries may have occurred in the 1970s because caries was "overdiagnosed" and filling scores were seemingly dependent only on dentists' indications for filling placement. It can therefore be questioned to what extent the populations studied are representative of today's child populations.

In the 1980s, the use of fissure sealants was favoured in Finland, and the preference of this measure resulted in a fast increase in the amount of fissure sealants. The number of sealed teeth was at the highest level in the survey of 1988, when a good half million sealants were applied to teeth of persons aged from 6 to 18 years. In the 1990s, the treatment practices were changed, and the use of fissure sealants reduced (Nordblad *et al.* 2004).

In this study, a difference in the survival curves of first molars of unsealed subjects was found between the two studied towns in Finland. In Kemi, caries had affected first molars in around 20% less cases in unsealed subjects than in Vantaa at the end of the follow-up period (II). One reason for this result was thought to be the successful selection of non-risk subjects who were left unsealed. Vantaa followed its strategy more routinely and sealed all first molars after their emergence. The difference between the sealant strategies resulted in practices that 40% of the subjects in Kemi and only 17% in Vantaa were left unsealed (II). The finding that sealant treatment helps to decrease caries in individual teeth and thereby the caries prevalence levels in the population is in line with general opinion but conflicts with the findings of our study on a subject level (II). The unsealed subjects in Kemi had less caries than the control group in this retrospective analysis. Our hypothesis that caries-resistant subjects do not benefit from sealant treatment, thus holds true (II).

Based on the findings of our study, the partly-sealed subjects had the shortest survival times of their first molars in both Kemi and Vantaa, which indicates that the caries-preventive effect of sealants on an individual tooth level is not always seen in the oral cavity as a whole when some teeth are sealed and some are not (II, III). This also explains the differences between the subject-specific (II) and tooth-specific (III) analyses. The tooth-specific approach is not always an appropriate way to study/test sealant effectiveness, and therefore subject-specific analyses are also needed (II). The other explanation may be hidden in the fact that the partly-sealed subjects were those whose one permanent molar was restored before the age of eight years, and therefore classified here as belonging to the very high risk group.

The clinical judgements and treatment lines were to some extent different in Kemi and Vantaa. This may have affected the study results: First, in Vantaa, a non-targeted sealant policy was employed and 80% of the first molars were sealed. The remaining non-sealed teeth (20%) may belong to a high caries risk group, being carious already at the first examination at seven years of age, or they might be the teeth of subjects who neglected dental care in the health centre. Owing to the individualized check-up intervals, the entire age cohort is not examined every year. For example in 1995 about 68% of those under 19 years of age were clinically examined in public dental clinics in Vantaa (Helminen *et al.* 1999). In Kemi, the strategy was to focus sealant treatment selectively and primarily on high caries-risk subjects, which is expressed by a lower cumulative sealant incidence (about 62%) compared to Vantaa (80%) (III). The result was that teeth determined to belong to high caries-risk subjects were "transformed" into low-risk teeth simply by using the sealing treatment applied in Kemi (III). Only very low-risk teeth could have been left unsealed in Kemi, and these non-risk teeth did not necessarily need sealant treatment: the non-sealed teeth had the highest survival rate (75–80%) (III).

There has been no evidence that there are diagnostic tests today that, with sufficient predictive power, can identify groups or individuals at high risk (Fejereskov 1995, Hausen 1997). There is one exception, however: those who early in life exhibit a relatively high caries experience are much more likely to have more severe symptoms later on than the remaining individuals (Fejereskov 1995). Furthermore, in recent studies (Ollila & Larmas 2007 and 2008), it has been shown that the early colonization of *lactobacilli* and *candida* as well as consumption of candies and inadequate oral hygiene at two years of age made children more caries prone even several years later.

In Kemi, the caries-preventive programmes additionally included the supervised use of xylitol in the form of chewing gum in day care centres and elementary school. Previously, the application of sealants or supervised use of xylitol for 2–3 years from the age 12 onwards has been demonstrated to be effective in preventing fissure caries after five years of follow-up (Virtanen *et al.*1996). Furthermore, there were no statistically significant differences between sealant and xylitol groups in caries increment figures either (Alanen *et al.* 2000). It has also been reported in a re-analysis of a trial, applying survival method instead of classical comparisons of mean increments, that the caries-preventive effect of xylitol is beneficial especially for teeth that have erupted during the use of xylitol and also for teeth that have erupted after stopping the regular, supervised use of xylitol (Hujoel *et al.* 1999).

The use of xylitol to prevent caries saves dental resources (Mäkinen *et al.* 1995, Kovari 2002) but needs motivated patients or supervised use in groups.

6.2.3 Cost-effectiveness of sealant treatment (IV)

The financial costs of sealing teeth as part of community- or school-based programmes (Crowley *et al.* 2000, Werner *et al.* 2000) are often lower than those found in clinical settings are. Unfortunately, these economic assessments do not aid general oral health-care practitioners in determining whether pit and fissure sealants are worth the true cost of placement. As a result, real-word pragmatic studies are required that fully account for all resource uses and the opportunity costs of the clinicians' time.

It must be kept in mind that the cost analyses of fissure sealants in preventing tooth decay were conducted on different population groups, in different years, in different countries with different population sizes, and even with different diagnostic criteria. The cost analyses should be assessed on an individual country basis to determine which preventive modality may be the most cost-effective for that country. The task is easily stated but will be difficult to accomplish, as cost-effective initiatives in one locale may not be the same for another.

With the increasing pressure on the health sector in general to become more efficient and to base its activity on scientific evidence, it is time for the dental profession to reconsider how to develop the most appropriate and cost-effective ways for controlling dental caries. The benefits and cost-effectiveness of any caries-preventive programme must be examined in detail on national, local and individual levels.

The risk assessment is important to minimize the efforts and cost of treatment. The negligible difference between the high-risk children and low-risk children groups implies that intensifying prevention produced practically no additional benefit (Hausen *et al.* 2000). By offering all children only basic prevention, virtually the same preventive effect could have been obtained with substantially less effort and lower costs (Hausen *et al.* 2000).

In Kemi, the sealant treatment was targeted selectively to high caries-risk (= all sealed) children, who formed about one third of the age cohort there. The total treatment costs rose to be over four times more expensive per child compared to the total restorative treatment of low-risk (= unsealed) subjects, who did not receive any sealant treatment (IV). In Kemi, the need for sealant treatment was estimated by dentists, taking into account the caries susceptibility of each child. The restoration costs of the unsealed (= non-risk) subjects were over three times less in Kemi than in Vantaa. This emphasises the need for targeted sealing decisions.

In Vantaa, the high- and low-risk children were not estimated beforehand by any means, and this resulted in two consequences: first, healthy children were (unnecessarily) sealed, and second, the sealing treatment did not achieve those high-risk children who did not keep their appointments and thus did not receive the free preventive dental care services. This may explain the over three times higher costs of restorative treatment of unsealed subjects in Vantaa compared to Kemi (EUR 95.10 and EUR 28.50 per child respectively) (IV). The all-sealed group in Vantaa contained also low–risk children, and the treatment costs were formed mainly from the sealant treatment costs (IV).

It has been recognized earlier that the cost-effectiveness of sealant treatment was dependent upon a number of factors that were related to its use, such as the different tooth types (premolars, molars) sealed, whether all teeth and fissure sites were routinely sealed or based on specific indications, the retention of the fissure sealants, to what extent other caries preventive methods were used, and caries prevalence in the population (Raadal *et al.* 2001). Children of a high baseline caries risk status showed lower sealant retention and higher occlusal caries prevalence following sealant loss compared with those of moderate and low-risk status (Oulis & Berdouses 2009). Sealants improved the overall utility of first permanent molars after four years. Sealing first permanent molars in lower dental utilizers is the most cost-effective approach for prioritizing limited resources (Bhuridej *et al.* 2007).

Our findings indicated that leaving the non-risk subjects unsealed kept the health teeth sound in these subjects in Kemi. Sealing of teeth of high-risk children compared to sealing teeth of all children routinely resulted in equal but higher costs than leaving the non-risk subjects unsealed (IV). The risk assessment should be done in the early childhood, as it was done in Kemi, where the targeting of sealant treatment was successful (IV).

7 Conclusions and recommendations

Using the sophisticated survival analysis system for estimating the effectiveness of sealant treatment, the following clinical conclusions can be drawn:

Sealant application is indeed an effective preventive measure against caries in first permanent molars. The strategy of sealing all molar fissures (Finland *vs* Sweden, Vantaa *vs* Kemi) proved not to be more effective than sealing clinically evaluated high-risk molars of subjects or high-risk subjects (in Kemi, Finland; in Sweden, and in Greece). The effectiveness of sealant treatment was dependent mainly on the caries prevalence in each country such that the higher the caries prevalence was, the higher the effect was. Early sealing did not result in a better outcome than a late sealing (I).

Sealing treatment should be targeted at the individual level in a manner that all four permanent first molars, especially in the medium-risk subjects, should be sealed, taking account the difficulties in estimating high caries risk individuals.

Leaving the first molars unsealed in highly caries-resistant subjects helps to decrease unnecessary preventive work and thereby the efficacy of the method. On the other side, sealing seems not to be effective enough in long-term caries prevention in very high caries risk children, i.e. subjects having caries already on any of their first molars in the first post-eruptive examination of the permanent dentition before eight years of age (II).

The results support and confirm the findings of previous studies based on controlled clinical trials. In addition, the results suggest that routine fissure sealant treatment without personal caries risk determination is not the best choice of treatment in preventing dental restorations, but it effectively reduces caries rates in individual teeth in practice. It is therefore definitely beneficial to use an accurate targeting policy for sealant treatments to selected teeth with a high caries risk in order to avoid unnecessary work and costs (III).

Financial savings can be achieved by leaving caries-resistant population unsealed and by targeting sealant treatment selectively to high-risk subjects. In very high-risk subjects, the treatment of choice instead of sealant treatment could be preventive resin restoration. Defining locally the high-risk individuals seemed to be beneficial (in Kemi). The risk strategy would be more cost-effective the routine prevention, considering that only a small fraction of the population are at high risk (IV).

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ISBN 978-951-42-6341-5 (Paperback)
ISBN 978-951-42-6342-2 (PDF)
ISSN 0355-3221 (Print)
ISSN 1796-2234 (Online)

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