

Epidemiological Aspects on Apical Periodontitis

Studies based on the Prospective Population Study of Women in
Göteborg and the Population Study on Oral Health in Jönköping,
Sweden

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Abstract

The objectives of this thesis were to describe endodontic status in Swedish populations, to study clinical and socio-economic risk factors for apical periodontitis (AP) and to explore a possible association between AP and coronary heart disease (CHD).

In papers I, III and IV the Prospective Study of Women in Göteborg (PSWG) was used. In paper I dentate women examined in 1968-69 (N=1220), 1980-81 (N=1023) and 1992-93 (N=867) were included for cross-sectional and longitudinal (N=586) analysis of endodontic status over 24 years in individuals aged 38-84 years. In papers III and IV a cross-sectional sample (N=844 and N=867, respectively) from 1992-93 was used for exploring associations between AP, socio-economic risk factors and CHD in multivariate logistic regression models. In paper II random samples of dentate individuals aged 20-70 years from the Population Study on Oral Health in Jönköping (PSJ) were used. The first examination in 1973 (N=498) was followed by new examinations in 1983 (N=530), 1993 (N=547) and 2003 (N=491). Full mouth radiographic examinations were restudied, yielding 3981 root filled teeth for the analysis. AP was recorded according to the Periapical Index (PAI) and the root filling quality was assessed with respect to length and seal. The association between root filling quality and AP was studied on the tooth-level as well as on the individual level.

The results from multivariate logistic regression analysis did not reveal a significant association between AP and CHD and socio-economic risk factors and AP, respectively. The ratio of root filled teeth increased with age longitudinally and cross-sectionally, but decreased over time for comparable age groups. The ratio of AP increased with age cross-sectionally, but decreased with age longitudinally and for comparable age groups over time. Inadequate root filling quality was predictive of AP with an odds ratio of 4.5. The root filling quality was improved over time without a concomitant decrease in ratio of root filled teeth with AP.

Keywords: Apical periodontitis, Coronary heart disease, Cross-sectional, Endodontics, Epidemiology, Health, Longitudinal, Root filling, Socio-economic status, Treatment quality, Women.

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Contents

Preface	9
Introduction	11
Clinical features of apical periodontitis	
Health effects of apical periodontitis.....	13
Treatment.....	14
Epidemiology of apical periodontitis	
Cross-sectional studies.....	15
Repeated cross-sectional studies.....	16
Longitudinal studies.....	16
Presence of apical periodontitis.....	17
Presence of root filled teeth and treatment quality.....	17
Methodological considerations	
Apical periodontitis.....	19
Treatment quality.....	21
Socio-economic risk factors and health	23
Methodological considerations.....	24
Dental infection and cardiovascular disease	25
Methodological considerations.....	27
Aims	29
Material	
The Prospective Population Study of Women in Göteborg, Sweden	
Setting.....	31
Subjects.....	31
Non-participation.....	32
The Populations Study on Oral Health in Jönköping, Sweden	
Setting.....	34
Subjects.....	34

Method

The Prospective Population Study of Women in Göteborg, Sweden

Examinations.....37

Variables (papers I, III, IV).....37

The Populations Study on Oral Health in Jönköping, Sweden

Radiographic examination (paper II).....40

Statistical methods.....42

Results and Discussion

Epidemiology of apical periodontitis (papers I, II)

Cross-sectional findings

Number of teeth.....45

Prevalence of apical periodontitis.....45

Prevalence of root filled teeth.....47

Longitudinal findings

Number of teeth.....47

Prevalence of apical periodontitis.....48

Prevalence of root filled teeth.....48

Association of root filling quality with apical periodontitis (paper II).....48

Socio-economic factors and apical periodontitis (paper III).....52

General health and apical periodontitis (Paper IV).....54

Methodological considerations

PSWG (papers I, III, IV).....57

PSJ (paper II).....58

Conclusions.....59

References.....61

Abbreviations.....76

Acknowledgements.....77

Papers I-IV

Preface

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

- I. Frisk F, Hakeberg M. A 24-year follow-up of root filled teeth and periapical health amongst middle aged and elderly women in Göteborg, Sweden. *Int Endod J.* 2005 Apr;38(4):246-54
- II. Frisk F, Hugoson A, Hakeberg M. Technical quality of root fillings and periapical status in root filled teeth. Submitted.
- III. Frisk F, Hakeberg M. Socio-economic risk indicators for apical periodontitis. *Acta Odontol Scand.* 2006 Apr;64(2):123-8.
- IV. Frisk F, Hakeberg M, Ahlqwist M, Bengtsson C. Endodontic variables and coronary heart disease. *Acta Odontol Scand.* 2003 Oct;61(5):257-62.

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Introduction

Apical periodontitis (AP) is an inflammatory response directed mainly to a root canal infection in teeth (Örstavik & Pitt Ford 1998). The condition is commonly a result of caries and its related restorative treatments. As indicated by the term, the primary location is in the periapical area of the tooth where bone tissue may be lost to a varying extent. Overt clinical signs are sporadic. Radiography is, therefore, an important tool for detection of AP. There are several synonymous terms, essentially describing the same disease but may vary with regard to clinical and radiological expressions. Throughout this text, the term AP will be used for any periradicular lesion of endodontic origin.

Epidemiological surveys, mainly from Scandinavia but with a growing number of studies from other parts of the world, demonstrate that AP certainly is a common disease in the adult population (Table 1). However, data on the prevalence of AP vary between populations and countries and depend on differences in caries prevalence, access to dental care and methodological issues such as measurement and sampling variation. Thus, it is important to conduct epidemiological surveys on oral health in different settings using established scientific methods, in order to get results valid for different populations.

Root canal treatment (RCT), is aimed to prevent and eradicate root canal infections. Clinical follow-up studies demonstrate that RCT has the potential of being highly successful given that the treatment meets high demands on technical quality (Sjögren et al. 1990, Strindberg 1956, Grahnén et al. 1961, Kerekes et al. 1979, Kojima et al. 2004). Yet endodontic treatment is widely recognised as a delicate task and epidemiological studies report on high frequencies of root filled teeth with suboptimal technical quality. As a result, AP is most commonly found in root filled teeth and the healing rate after RCT in general practice may be estimated to 50-75% (Ödesjö et al. 1990, Kirkevang et al. 2000, Kabak & Abbott 2005, Dugas et al. 2003). There are reports indicating an improving technical quality of root fillings over time, however without a decreasing frequency of AP in root filled teeth (Skudutyte-Rysstad & Eriksen 2006, Petersson 1993b, Kirkevang et al 2001b). Explanations as to the reasons for these conflicting results are lacking.

Dentistry has a history of a complicated view on dental infections and general health. During the focal infection era, several serious conditions were thought to be

Table 1. Number of teeth and proportions of root filled teeth and apical periodontitis from cross-sectional studies.

	No teeth	R end (%)	R AP (%)	R endAP (%)	Samp end (%)	Samp AP (%)	Details	Country
Bergenholtz et al. 1973	22.8	12.7	6.1	30.5		57	N=240. Patients referred to radiologist. Mean age 45 years(20->70).	Sweden
Lavstedt 1978	22.6	2.5(teeth)	1.2 (roots)		72.2	45	N=1391. Random sample. Age 18-65 years	Sweden
Allard & Palmqvist 1986	14.2	18	10	27		72	N=188. Old subjects >65 years, non-institutionalized. Random sample. Mean age 73(65->75)	Sweden
Bergström et al. 1987	26.4	6.5	3.5	28.8%(roots)		46.8	N=250. Patients with regular dental care. Age 21-60år	Sweden
Eckerbom et al. 1987	24.4	13	5.2	26.4	83.5	63	N=200. Patients referred to radiologist Mean age 40(20->60)	Sweden
Eriksen et al. 1988	27.8	3.4	1.4	25.6		53	N=141. 35 year olds in Oslo 1973 and 1984. Random samples. Data from 1984 are presented here	Norway
Ödesjö et al. 1990	23.5	8.6	2.9	24.5		43.2	N=743. Random sample. Age 20->80	Sweden
Eriksen & Bjertness 1991	24.7	6	3.5	36.6		56	N=119. 50 year olds in Oslo. Random sample	Norway
Imfeld 1991	14.0	20.3	8.0	31	77.6		N=143. 66-year olds in Zurich. Random sample	Switzerland
DeCleen et al. 1993	22.8	2.3	6.0	39.2		44.6	N=184. Patients referred to oral surgeon. Age 20->59	Netherlands
Eriksen et al. 1995	27.8	1.3	0.6	38.1	24	14	N=118. 35 year olds in Oslo 1993. Random sample	Norway
Soikkonen 1995	13.9	21.5	7.1	16.8	78	41	N=169. Random sample of elderly subjects. Age 76-86 years	Finland
Saunders et al. 1997	24.6	5.6	4.9	58.1	54	67.7	N=340. Random sample of patients at a university clinic. Age 20->59	Scotland
Weiger et al. 1997	24.7	2.7	3.0	61			N=323. Patients in general practice, Stuttgart Mean age 35.2 (12-89)	Germany
Marques et al. 1998	24.8	1.5	2.0	22	22	26	N=179. Age 30-39. Random sample	Portugal
Sidaravicius et al. 1999	26.5	8.2	7.2	35	72	70	N=147. Age 35-44. Random sample	Lithuania
De Moor et al. 2000	22.4	6.8	6.6	40.4		63.1	N=206. Age 18->59. Patients at a university clinic.	Belgium
Kirkevang et al. 2001	26.0	4.8	3.4	52.2	52	42.3	N=614. Age 20->60. Random sample	Denmark
Boucher et al. 2002	25.8	19.1	7.4	29.7			N=208. Age 18->70. Patients seeking treatment	France
Lupi-Pegurier et al. 2002	22.8	18.9	7.3	31.5			N=344. Age >20. Patients at a university clinic	France
Dugas et al. 2003	26.5	2.5	3.1	45.4	34.3		N=610. Age 25-40. Random samples of patients seeking dental care at two university clinics	Canada
Loftus et al. 2005	24.6	2.0	2.0	25.0	31.8	33.1	N=302. Age 16->75. Patients seeking treatment	Ireland
Kabak & Abbott 2005	21.9	20	12	45		80	N=1423. Age 15->65. Patients seeking emergency dental treatment	Belarus
Tsuneishi et al. 2005	24.2	20.5	9.4	40	86.5	69.8	N=672. Age 20-89. Patients at a university clinic	Japan
Skudutyte-Rysstad & Eriksen 2006	27.2	1.5	1.1	43	23	16	N=146. 35-year olds in Oslo 2003. Random sample	Norway

No teeth=mean number of teeth

Rend=ratio of endodontically treated teeth

R AP=ratio of teeth with periapical destructions

RendAP=ratio of endodontically treated teeth with periapical destructions

Samp end=sample prevalence ratio of subjects with ≥ 1 endodontically treated tooth

Samp AP=sample prevalence ratio of subjects with ≥ 1 tooth with periapical destruction

N=number of subjects

caused by dental infections, and extraction therapy was advocated rather than conservative treatment (Pallasch & Wahl 2003). In recent decades, dental infections have been recognised as a risk factor for cardiovascular diseases, eg coronary heart disease (CHD), and statistically significant associations between marginal periodontitis and CHD have been reported (Beck et al. 1996, Khader et al.2004). Data on endodontic infections as a risk factor for CHD are scarce (Caplan et al 2006, Frisk et al 2003 (paperIV)).

Concerning dental caries, behavioural factors such as dietary and dental care habits have been found to be significant risk factors (Sakki et al. 1994, Zero 2004). Also, low socio-economic status (SES) has been demonstrated to be associated with dental caries in children, with implications for adult oral health (Thomson et al. 2004). Since AP is a prevalent sequel to dental caries, caries and AP could share common risk factors, such as SES. There is little information on the association between SES and AP, and published results are inconclusive (Kirkevang & Wenzel 2003, Aleksejuniene et al. 2000).

This thesis addresses issues related to the prevalence of AP and endodontic treatment quality and associated local and general health implications. Secular changes in prevalence of AP and technical quality of root fillings will be investigated. Also non-clinical risk factors for AP will be explored as well as AP as a risk factor for CHD.

Clinical features of apical periodontitis

By far, the most common cause of AP is a root canal infection whether it is in a tooth with a necrotic pulp or a root filled tooth (Sundqvist 1976, Möller et al. 1981, Molander et al. 1998)). The infection is constituted by a mixed flora dominated by anaerobic bacteria, showing similarity with the marginal periodontal infection (Dahlén & Haapasalo 1998). Other causes of AP may be iatrogenic, following endodontic procedures, such as extrusion of medicaments and foreign-body reactions against root filling materials (Happonen & Bergenholtz 2003).

Health effects of apical periodontitis

As AP in general develops and perseveres without clinical signs most teeth with AP will be diagnosed by means of radiographic examination. To our knowledge there are no

conclusive data on how often local manifestations in terms of pain and swelling may occur. With data from Peterson's study (1993a) Eriksen (1998) has estimated the annual incidence of exacerbation of chronic AP to be 5%.

Untreated, endodontic infections may spread to the brain, cavernous sinus and the mediastinum. Also, left untreated, it may cause osteomyelitis (Skaug 2003). However, there are no data on the incidence of spontaneous bacteremia from teeth with AP (Pallasch & Wahl 2003). Thus, it is difficult to estimate the risk for severe conditions to occur if teeth with AP are left untreated.

During the era of the Focal Infection Theory it was argued that infections of dental origin caused systemic disease or damaged distant tissues (Murray & Saunders 2000). Radical treatment in terms of extraction of teeth was advocated. Endodontic treatment was abolished for several years. In 1940 and afterwards, the Focal Infection Theory was criticised and eventually abandoned (Pallasch & Wahl 2003). In recent years the potential systemic effects of dental infections has received renewed interest (Mattila et al 1989, Meurman 1997).

Treatment

Since the root canal infections for the most part are confined to the root canal system they cannot be eliminated by host defence mechanisms. Treatment is necessary to eliminate the infection. Although this object may be met by extraction of the tooth, root canal treatment (RCT) can render teeth with healthy periapical status. RCT is about treatment measures aimed at elimination of the root canal infection by mechanical instrumentation of the root canal, irrigating the root canal system with antibacterial chemical agents, placing inter-appointment medicaments and finally obturating the root canal space. Properly performed RCT is highly successful (Sjögren et al. 1990, Strindberg 1956, Grahnen et al. 1961, Kerekes et al. 1979, Kojima et al. 2004). However, endodontic treatment fails repeatedly at eliminating the infection, or prevent reinfection, probably due to poor asepsis and technical problems in conjunction with the chemomechanical treatment and root filling procedure (Ödesjö et al. 1990, Kirkevang et al. 2001a, Kabak & Abbott 2005, Dugas et al. 2003). In these cases extraction, retreatment or apical surgery are indicated with the same objective as RCT – elimination of the root canal infection. Retreatment and apical surgery are traditionally

considered less predictable than RCT since numerous clinical studies demonstrate a lower healing rate following these procedures (Hepworth & Friedman 1997). However, contemporary technique, accurate case selection and a better understanding of the post treatment flora may lead to a better prognosis for the treatment of teeth with failed RCT (Gorni & Gagliani 2004, Chong et al. 2003).

Although the prevalence of dental caries is declining in most age groups (Hugoson et al 2005), endodontic treatment is still a frequent procedure in dental practice. Björndal & Reit (2004) reported on an increase of the number of endodontically treated teeth in Denmark between 1977 to 2003.

Epidemiology of Apical Periodontitis

Cross-sectional studies

The literature contains a number of cross-sectional studies, mainly presenting data regarding the prevalence of AP and root-filled teeth (Table 1). Studies vary with regard to study population, radiographic method and classification of AP. Not uncommon, patients referred to an institution, such as a university or specialist dental clinic, have been selected to study the prevalence of AP and root filled teeth. This is a convenient and inexpensive way to gather a sample, and the radiographic examination may have to be performed for clinical reasons. The major shortcoming is that the patients are not necessarily representative for the whole population since they may be more affected of disease. Population based random samples render representative results if the attendance rate is sufficient. However, it may be questionable to subject healthy individuals to an extensive radiographic examination.

Since data in a cross-sectional study is sampled at a single point in time, there is no temporal dimension providing information on etiology. However, if the current exposure is likely to be similar to past exposure it may be considered etiological (Rothman & Greenland 1998a). In the case of technical quality of root fillings and its association with periapical status, cross-sectional studies do not provide information on how long the subject has been exposed to the root filling. Thus, the biological reaction cannot necessarily be determined as healing or developing disease, and secular changes in clinical technique cannot be accounted for.

The cross-sectional study design is however well suited for studying prevalence of AP and root filled teeth since both parameters are chronic (Fletcher et al. 1996). Moreover, it is a comparatively simple study to perform with good chances of high participation rate since recall is irrelevant. However, there are events that cannot be captured, because some conditions are short lasting or dynamic in nature. In an endodontic context, incidence of exacerbating AP and healing or developing of AP are entities that warrant other study designs.

Repeated cross-sectional studies

The major oral health concerns during past decades have been caries and its sequel (infected pulp necrosis and AP) and marginal periodontitis. Interventions designed to prevent or inhibit disease have been implemented by means of water fluoridation, information and profylaxis programs. To measure the effect of these interventions on a population level repeated cross-sectional studies may be necessary. They permit comparisons of similar age-groups at different time points and can reveal changes in disease prevalence and severity, thus providing information for evaluation on a population level. As is the case with the longitudinal study design, it is important that the time between studies is long enough for the event to take place, and short enough to reveal changes in direction of the event. Moreover, changes over time in disease and treatment outcome with respect to treatment methods among therapists in a specific area or community may be possible to reveal with repeated cross-sectional studies.

Longitudinal studies

To prospectively follow cohorts over time provides information on etiology and may capture the dynamics in disease patterns. The disease under study must be prevalent in order for the survey to provide a sufficient number of cases to be compared with non-cases (Fletcher et al 1996). AP is prevalent enough for a longitudinal study to provide enough cases and the dynamics of AP can be monitored, when the same individuals are followed over time permitting investigators to study changes in periapical status. There are two major pitfalls; the period between baseline and recall must be long enough for the event under study to take place, but short enough to be captured before the event is impossible to identify (Rothman & Greenland 1998b). Another problem is the

participation rate at recall. The individuals participating throughout the study may just be a small and selected fraction of the individuals once sampled from the population. The results from such studies may thus be problematic since the representativeness can be questioned. There are only a few studies in the literature reporting on AP using a prospective and longitudinal study design.

Presence of Apical Periodontitis

Quite a few, mainly cross-sectional, studies demonstrate prevalence data from different populations (Table 1). Scandinavian populations are well represented in this context. Data display a wide range, reflecting different compositions in study populations and different diagnostic methods and criteria between studies.

Frequently, studies report prevalence of apical periodontitis between 1-14% on a tooth level and 22-80% on an individual level. The prevalence tends to increase with age and AP seems to be more frequently found adjacent to root filled teeth. Looking at repeated cross-sectional studies, the prevalence of AP decreases over time for comparable age-groups, probably as a result of decreasing incidence of caries (Eriksen et al 1995, Petersson 1993b), although Skudutyte-Rysstad & Eriksen (2006) reported a slight increase of teeth with AP. The ratio of AP adjacent to root filled teeth has not decreased over time (Kirkevang et al 2001b, Petersson 1993b, Skudutyte-Rysstad & Eriksen 2006). Far less is known about the longitudinal perspective. Available data suggest small variations with increasing age (Eckerbom et al 1989, Petersson 1993a, Kirkevang et al. 2006). This observation may be a result of rather short follow-up and bias due to attrition.

Presence of root filled teeth and treatment quality

In cross-sectional studies both number and ratio of root filled teeth increase with age. The higher ratio may be explained by tooth loss alone. Older individuals in general show a higher number of missing teeth, where primarily periodontal disease and caries, but also related sequels to caries in terms of endodontic complications, are the main reasons for extraction (Eckerbom et al. 1992, Caplan et al. 1997). However, because the number of root filled teeth increases as well, the higher caries exposure experienced may be of importance. Longitudinally, increasing age is associated with an

increasing number of root filled teeth (Eckerbom et al. 1989, Kirkevang et al. 2006). Repeated cross-sectional studies demonstrate a decrease in the frequency of root filled teeth and individuals with root filled teeth over time (Pettersson 1993b, Eriksen et al 1995), even though Skudutyte-Rysstad & Eriksen (2006) report on a slight increase between 1993 and 2003.

In accordance with clinical studies, epidemiological studies repeatedly demonstrate an association between endodontic treatment quality and periapical status. Generally, teeth with root fillings which are judged as having an adequate seal and end short of the radiographic apex are more often found to have a healthy periapical status, whereas deviations from this technical standard more frequently result in AP (Bergenholtz et al. 1973, Bergström et al. 1987, Ödesjö et al. 1990). Cross-sectional studies report quite discouraging results on endodontic treatment quality when the technical standard of the root filling, as it appears on the radiograph, is considered. Although discouraging, these data must be analysed in the context of general dental practice which may have economic limitations and time constraints in comparison to specialist/university clinics where most of the clinical studies have been performed (Eriksen et al. 2002). In these institutions, clinicians are provided with optimal facilities and are highly motivated, knowing that their performance is monitored following a standardised treatment protocol. Thus, the clinical study is controlled in every relevant detail regarding asepsis and choice of medicaments and material. The epidemiological study lacks this information making it difficult to establish which factors that are important for the remedy and prevention of AP. However, such surveys can be considered to represent what is achieved in endodontics in every day practice, taking time constraints and varying techniques and clinical skills into consideration. Thus, a direct comparison between clinical and epidemiological studies is invalid even if the epidemiological results warrant measures to improve treatment quality in general practice. To some extent, such measures have been taken, for example in postgraduate training of dentists in general practice where new clinical techniques are taught and awareness of the problem is highlighted (Molander et al. 2007). Repeated cross-sectional studies verify that, over time, treatment quality has improved as a result (Pettersson 1993b, Kirkevang et al. 2001b, Skudutyte-Rysstad & Eriksen 2006). Inconsistent with this finding, they repeatedly fail to demonstrate a significant

improvement in periapical status in conjunction with root filled teeth (Pettersson 1993b, Skudutyte-Rysstad & Eriksen 2006).

Methodological considerations

For whichever diagnostic test used in clinical dentistry or research, a common feature is that the measurement will never be completely accurate. When discussing the performance of tests, one usually divides the performance into validity and reliability.

Validity refers to the test's ability to measure what it is intended to measure. It may be estimated by comparing the test measurement with a golden standard, and calculating sensitivity and specificity. Sensitivity is defined as the proportion of cases with disease with a positive test result. Specificity is defined as the proportion of cases without disease with a negative test result. A test with a high sensitivity performs well in ruling out disease (low number of false negative results), and a test with high specificity performs well in ruling in disease (low number of false positive results) (Fletcher & Fletcher, 1996).

Reliability, or reproducibility, indicates whether a test is able to yield the same results after repeated measurements. In the context of observing radiographs, different observers may vary in their judgements, both within themselves over time (intra-observer variation) and between each other (inter-observer variation). The observer variation may be calculated in several ways. In studies concerning radiographic diagnosis of AP, kappa is often used to estimate intra- and inter-observer variation (Altman 1991, Brunette 1996). Since most studies to date have used dichotomised measurements of AP (periapical destruction present or not present) there is a possibility that some degree of agreement in observations is a result of chance which the kappa statistic adjusts for.

Apical periodontitis

There are methodological problems in the study of AP in an epidemiological context which has been addressed by some authors. The radiograph is usually the only diagnostic tool. The periapical radiolucency may represent other conditions than AP, because one will have no knowledge of the histological diagnosis (Ricucci et al. 2006). However, it is acknowledged, that AP is the most probable diagnosis when a periapical

radiolucency is registered why misdiagnosis seems to be of minor concern in an epidemiological context (Bhaskar 1966). More problematic then, is the intra- and inter-observer variation. When small, minute periapical destructions are encountered there may be difference of opinion whether or not the radiological condition represents actual pathology. Hence, observers tend to vary in their judgement whether the observed destruction is to be considered a pathologic condition or not (Reit & Hollender 1983). There are strategies suggested to cope with this problem. In calibration, observers use recognized criteria for AP and examine a series of radiographs and discuss in which cases the periapical status meets the criteria for AP. Authors argue that the benefit of calibration is limited (Reit 1986). Reit & Gröndahl (1983) found that the variation decreased when the number of false positive observations was small. In other words, one should only register a periapical radiolucency when absolutely certain. According to this strategy, the true prevalence of AP can not be established, but the relation between populations may be determined.

Another method to measure periapical status is the periapical index (PAI) suggested by Örstavik et al (1986). A five-graded scale is used to describe the periapical expression on the radiograph. Data from Brynolf's study on an autopsy material were used (Brynolf 1967). In her study, Brynolf demonstrated a correlation between histological and radiographic expression of periapical lesions in maxillary incisors. Using examples of different radiographic and histological expressions, reference radiographs with five different expressions are provided for the observer. The observer is instructed to designate a score of the tooth under study, which is decided by the most similar periapical image from the reference radiographs. When in doubt, the observer is instructed to designate a higher score. The rationale for this strategy, is that Brynolf found that the radiographic image underestimated the histologic expression. Moreover, the observer should follow a calibration course of 100 radiographs at which "true" periapical status has been established by consensus from 10 observers. The observer variation is then calculated according to Cohen's kappa. If Cohen's kappa is below 0.6, the calibration course should be taken again.

PAI, as forwarded by Örstavik et al (1986), has been proposed to be a valid system because it makes use of correlations to histological status. Moreover, using reference radiographs, observers from different institutions may compare their results

since they use visual definitions of different periapical expressions and have been calibrated against the same radiographic material. Also, using an ordinal scale, PAI is more sensitive to changes in periapical status than a system using a dichotomous scale. However, in most epidemiological studies using PAI, the five graded scale is dichotomised into “healthy” or “disease” categories by using a cut-off point between 2 and 3.

Which ever method used, the problem of observer variation cannot be totally eliminated, making it necessary to account for it in the analysis of data. Inter-observer variation may be analysed by examination of randomly selected radiographs which are examined by each observer and the variation between observers is calculated. By re-examination of the radiographs and comparison with the first registration the intra-observer variation may be calculated.

A problem encountered when performing a cross-sectional study, is if the periapical radiolucency represents a healing lesion or chronic lesion, and if the lack of a periapical radiolucency represents a sound periapical status or a developing lesion. The latter may be the case since the periapical destruction must have a sufficient size and involve the cortical bone to be detectible on the radiograph (Bender & Seltzer 1961). Findings from a follow-up study suggest that this problem is of minor concern from an epidemiological point of view since the number of developing lesions and healing lesions was found similar in endodontically treated teeth (Petersson et al 1991).

Treatment quality

As is the case with AP, assessment of endodontic treatment quality is problematic and is limited to the radiographic appearance of the root filling. Inter- and intra-observer variation must be taken into account when results are analyzed as well as the validity of the radiographic image to assess treatment quality.

Strategies to deal with observer variation when assessing root filling quality are not as thoroughly discussed in the literature as for AP. Treatment quality consists of at least two factors; length of the root filling in relation to radiographic apex and density and seal to the root canal walls. Determination of the length is a lesser problem from an observer variation point of view than is the seal of the root canal system which is more difficult to judge with high reliability (Kirkevang & Hörsted-Bindslev 2002).

The measurement and categorisation of root filling quality differs among studies. Some studies use only length for determining technical quality (deCleen et al 1993, Saunders et al 1997, de Moor et al 2000). The desirable length of the root filling has been under debate for years, but there are conclusive results indicating that outcome is distinctly better if a root filling ends within the root canal (Bergenholtz et al 1973, Ödesjö et al 1990). Other studies have used both length and adequate seal, reporting results for both entities (Kirkevang et al. 2000) or have combined length and adequate seal (Ödesjö et al. 1990, Bergström et al. 1987). Petersson et al. (1986) reported only on complete/incomplete obturation and if teeth were overfilled.

When determining length and seal of a root filling in a radiographic image, one will have only a two dimensional view and no information about the termination of the root canal. The seal is of course a three dimensional entity and the location of the apical foramen is known to differ in relation to the radiographic apex. One in-vitro study demonstrated the agreement between bucco-lingual and mesio-distal projections to be low when the seal of the root filling was considered, while a fairly good agreement was found considering length of the root filling (Eckerbom & Magnusson 1997). Nonetheless, studies repeatedly demonstrate an association between adequate seal and a sound periapical status (Kirkevang & Hörsted-Bindslev 2002).

Recent cross-sectional studies have failed to show an improvement in periapical status as a result of improved treatment quality (Petersson 1993b, Skudutyte-Rysstad & Eriksen 2006). This may be due to a shift in attitude among dentists and patients regarding tooth extraction. It may also be a result of a more pronounced restorative need in the past, providing other reasons for extraction than endodontic. Petersson (1993b) speculated that a growing reluctance to extract teeth may result in conservative treatment of teeth with doubtful prognosis. Thus, in the past, dentists may have been more prone to extract teeth. Some of those teeth may have had AP, but periapically healthy teeth with varying treatment quality may have been left, resulting in a highly selected sample of endodontically treated teeth provided for the cross-sectional study. Hence, there are factors that the cross-sectional studies do not provide information about; a possible shift in attitude and treatment strategy, as well as endodontic treatment quality and periapical status prior to extraction.

Most epidemiological studies on AP use bivariate statistical models to investigate the association between root filling quality and AP. As pointed out by Strindberg (1956) and Caplan (2004) this is not optimal since one individual may contribute with more than one observation. Thus, since observations in one individual may be correlated, the variation decreases and the confidence interval becomes smaller than the true variation. One way to deal with this problem is to make just one observation per individual. However, information would be lost why a multilevel approach on both the tooth-level and on the individual-level seems more feasible, taking all observations into consideration.

Socio-economic risk factors and health

The literature shows that there has been an increasing interest in the association between socio-economic status (SES) and health (Adler & Ostrove 1999, Oakes & Rossi 2003). A growing body of researchers seems to agree that the understanding of the etiology of disease demands other information than that limited to biological mechanisms in the individual. Several diseases have been demonstrated to have a socio-economic gradient. Generally, this means that low socio-economic status increases the risk for developing disease. In egalitarian societies the gradient is less pronounced, and the slope of the gradient may also vary between diseases (Adler & Ostrove 1999). The pathways between socio-economy and health are debated, but psychosocial stress and behavioural factors may be important (Adler & Ostrove 1999, McEwan & Seeman 1999).

Oral health has been found to be affected by SES. This association may to some extent be explained by behavioural factors such as dental visiting habits and dietary habits. Halling & Bengtsson (1984) studied women from a prospective population study, sampled in 1968-69 aged 38-60 years. They found a statistically significant correlation between low education, low social class and number of lost teeth. However they failed to demonstrate the same association between SES-variables and marginal bone height. Gilbert et al (1997) reported that low-SES persons and african-americans had more negative attitude toward dental care and worse dental health. In another study Gilbert et al (2002) found low-SES subjects and african-americans to seek dental care in response to a specific problem rather than for preventive care. However, Sanders et al (2006) found that poor oral health in poor people was not explained by differences in

self-care. Sakki et al (1994) reported that a negative lifestyle with respect to dietary habits, smoking, alcohol consumption and physical activity had an association with dental caries in every social class, but more pronounced so among low-SES individuals.

Hobdell et al. (2003) reported that the greatest gradient was demonstrated between SES and periodontitis, while weaker for SES and caries. Burt et al. (1990) reported on an association between low SES and total tooth loss over 28 years, while the association with partial tooth loss was less clear and Treasure et al (2001) reported that low educational level was predictive of total tooth loss. Studying a cohort of 18-year old New Zealanders with follow up at 26 years of age, Thomson et al (2000) showed that low SES subjects had lost more teeth than their medium- and high-SES counterparts. Among children, caries has been demonstrated to have a socio-economic gradient that becomes less pronounced in adulthood (Marthaler 2004, Bjertness & Eriksen 1992, Treasure et al 2001). The cumulative nature of caries may have an impact on oral health and endodontic treatment needs later in life. Little is known about the possible association between endodontic and socio-economic status, and available data are inconsistent. Kirkevang & Wenzel (2003) studied 613 individuals in Denmark with respect to risk factors for AP. Using a multivariate logistic regression model, they could demonstrate that age, smoking and dental visiting habits were explanatory for AP, while other information on SES was not. Aleksejuniene et al (2000) studied 147 individuals from Lithuania, aged 35-44 years. They found high education and regular dental visiting habits to be predictive of AP. They also found that perceived general health was associated with AP. However, from both studies cited, it is apparent that clinical variables such as root filled teeth and caries are stronger indicators for AP than SES and behavioural factors.

Methodological considerations

There appears to be no consensus as to which socio-economic variables capture the socio-economic status in an individual (Oakes & Rossi 2003). The literature demonstrates a multitude of variables where perhaps convenience has been more important than validity. The most widely used measures to date have been occupational status/position, education and income. Authors argue that these parameters are not sufficient since it is doubtful if they capture the social context of the individual (Adler

& Epel 2000, Oakes & Rossi 2003). When applying these variables into statistical models, results must therefore be interpreted with caution and with respect to the variance that remains unexplained by the statistical model.

Information on SES in an individual can be collected from public archives or questionnaires. It seems advantageous that data which can be measured objectively are collected from public sources if available, to avoid errors, e.g regarding income. However, are objective data valid when studying an association between SES and health? Perhaps the perceived financial or social situation rather than data on income or social class are more valid predictors on health, or satisfaction with family situation or educational level, rather than objective information on marital status or education. Since psychosocial stress may be a pathway between socio-economy and health, a subjective estimation of satisfaction with life situation may be an important part of the analysis. Adler & Epel (2000) presented data suggesting that subjective information on social status had higher association with health related outcomes than several objective SES indicators.

Dental infection and cardiovascular disease

Cardiovascular disease (CVD) is a consequence of atherosclerotic formations in the vessels, causing ischemia (Camm 1994). Important clinical manifestations may be angina pectoris, myocardial infarction and stroke. Several potential risk factors have been discussed in the literature, but well established risk factors for CVD are age, hypertension, low socio-economic status, smoking and other life style factors (Camm 1994). In Sweden, 45% of all deaths among men, and 44% among women, were related to CVD in 2002. Both morbidity and mortality related to CVD have decreased during recent decades, probably as a consequence of a decrease in number of smokers and changes in diet (The National Board of Health and Welfare, 2005).

Besides well known etiological factors, infections have become recognized as a possible risk factor for vascular events specific for the development of atherosclerosis (Valtonen 1999). Chlamydia pneumoniae have gained some attention and has been found to be predictive of coronary heart disease (CHD) (Pesonen et al 2007). Dental infections, especially marginal periodontitis, have also been associated with CVD. Numerous studies have been published, of which some report an elevated risk for CVD

(Beck et al. 1996) and CHD (DeStefano et al. 1993) in patients with marginal periodontitis. Other studies fail to establish a statistically significant association (Joshipura et al. 1996, Hujoel et al. 2000). For those demonstrating an elevated risk, the odds ratios reported are generally below 2.0 (Beck & Offenbacher 2005). In a meta-analysis of seven cohort studies and four studies of other designs Khader et al. (2004) reported an increased risk with an odds ratio of 1.15 (1.06-1.25 95% CI) for subjects with periodontitis.

Besides using CVD as an outcome measure, studies have demonstrated associations between periodontal disease and intermediate variables such as elevated levels of CRP and fibrinogen, which are regarded as well-established biomarkers indicating elevated risk for CVD (for review, see Meurman et al. 2004). Recent intervention studies have shown that dental extractions in patients diagnosed with severe periodontitis may decrease CRP levels (Taylor et al. 2006, Ellis et al 2007).

The biological mechanism explaining the association between chronic infections and CVD is not fully understood, but one possible pathway may be both through direct bacterial impact and systemically elevated levels of inflammatory cells and mediators causing damage to the vascular endothelium, thus promoting the development of atherosclerosis. Once damaged, the endothelial cells express adhesion molecules that allows for leukocytes to bind to the endothelium. Lipids accumulate in the atheroma and released growth factors recruit monocytes, macrophages and smooth muscle cells. A fibrous cap is formed, which, if it ruptures, may lead to stroke or myocardial infarction (Ross 1999).

AP shares common features with marginal periodontitis. The flora is dominated by anaerobic microorganisms which elicit an inflammatory response involving the periodontium (Dahlén & Haappasalo 1998). It is only during recent years a few authors have studied the relationship between AP and CHD and pulpal inflammation and CHD. Caplan et al. (2006) studied the incidence of AP among 708 male subjects with a medium follow up time of 24 years. The cumulative burden of AP was estimated as “lesions-years”, and it was found that for those under 40 years of age, “lesion-years” was statistically significantly associated with time to CHD diagnosis. Joshipura et al. (2006) studied a sample of 34 683 health professionals with the hypothesis that pulpal inflammation, as assessed by number of root filled teeth, is predictive of CHD. Data

regarding root filled teeth was collected by questionnaires in which the participants were supposed to estimate number of root filled teeth as well as the time point for endodontic treatment. Also CHD was reported in the questionnaire, but in cases reporting CHD, medical journals were reviewed. The study reported on an overall statistically significant association between root filled teeth and CHD with a risk ratio of 1.21 (1.05-1.40 95% CI).

Methodological considerations

To date, no study has been able to establish a causal association between periodontal or endodontic infection and CVD. Moreover, several studies have failed to demonstrate an association at all, and in studies indicating periodontitis to be predictive of CVD, the association is generally weak. Some authors argue that periodontitis share common risk factors with CHD and thus the two diseases may be regarded as coexisting (Hujoel et al 2000). Danesh (1999) argues that future studies should be performed in socially homogenous populations to reduce bias, and Hujoel et al. (2002) claim that studies on periodontitis as risk for systemic disease should be limited to non-smokers, since smoking is believed to bias the association. Others acknowledge that the mechanisms involved in the association between periodontitis and CVD are not fully understood. Thus, studies may over-adjust for factors that may be influenced by periodontal disease (Genco et al. 2002). Perhaps the same concerns should be addressed when studying the association between AP and CVD, even though the associations between smoking, SES and AP, respectively, are not as established as those for periodontitis.

Concerns have been raised regarding differences in measurement and classification of both periodontitis and CVD between studies (Genco et al. 2002, Beck & Offenbacher 2005). Regarding AP, the diagnosis is straight forward by comparison which should be more favourable from a methodological point of view. However, compared to the measurement of attachment level, which estimates the historical burden of periodontal disease and thus risk for CVD, there are difficulties in assessing the historical burden of AP, since successful RCT eradicates the endodontic infection (Caplan 2004). In the longitudinal study by Caplan et al. (2006) the exposure “lesion-years” was used, and since all participants were followed up every three years, it was

possible to regularly evaluate all teeth with regard to changes in periapical status, and thus evaluate the burden of AP over time.

To establish causality, the exposure under study must precede the outcome. This cannot be determined in a cross-sectional study regarding CVD, but even in cohort studies where the association of periodontitis or AP have been found to be predictive of CVD, the association cannot be regarded as proven to be causal (Beck & Offenbacher 2005). Causality may be established in a randomized controlled trial, where subjects diagnosed with periodontitis/AP would be randomly allocated to treatment or no treatment. Differences in outcome in terms of CVD would be measured. Obviously, such a study design is replete with ethical problems making it impossible to conduct. However, if the outcome would be known biomarkers for elevated risk for CVD, the study design would be acceptable. D'Aiuto et al. (2006) compared standard periodontal therapy with intensive periodontal therapy (standard therapy with support of a locally delivered antibiotic). In the latter group, compared with the former, there were significant reductions in biomarkers indicating risk for CVD, and it was concluded that the intensive periodontal treatment reduced cardiovascular risk as compared to standard treatment. No such study has been performed in the context of AP as risk factor for CVD.

Aims

The overall aims of this thesis were to

1. describe the changes in the prevalence of apical periodontitis and root filled teeth over time in Swedish populations
2. explore clinical risk factors and socio-demographic factors associated to apical periodontitis
3. investigate the association between apical periodontitis and coronary heart disease

Material

The Prospective Population Study of Women in Göteborg, Sweden

Setting

The city of Göteborg had during the period 1968-1992 around 450 000 inhabitants. It is the second largest city in Sweden and a regional centre for commerce, culture and education on the Swedish west coast. Dental care is provided by both public dental services and by dentists in private practices.

Subjects

In 1968, 1462 randomly selected women living in the city of Göteborg were sampled for a medical, psychiatric and dental survey. The sample represented a participation rate of 90%, and was obtained from the Revenue Office Register. The participants were aged 38, 46, 50, 54 and 60 years and selected according to birth day divisible by six (Bengtsson et al. 1973).

The survey was repeated in 1974-75, 1980-81 and 1992-93 when the same individuals examined in 1968-69 were invited. No dental examination was conducted in 1974-75. In 1980-81 the participation rate of those participating in 1968-69 was 78.9%. Along with these individuals, a new group of 38-year old, 109 out of 145 invited, and additional individuals to the cohort of 50-year olds were invited to ensure representativeness and provide information regarding secular trends. The new participants aged 50 years, 42 out of 60 invited, had all moved to Göteborg after the initiation of the study in 1968. Compared to the original sample of 50-year olds in 1980-81, they had fewer remaining and restored teeth.

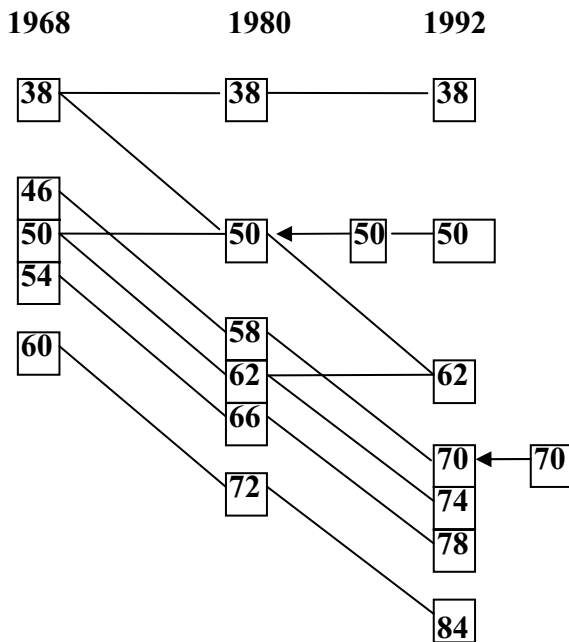
In 1992-93 a new group of 38-year old women participated (N=61) and with the same incentive as in 1980-81, individuals aged 70 years (N=58), who had moved to Göteborg after the initial study, were sampled. The participation rate in 1992-93 was 57.2% of those participating in 1968-69.

In the dental study, 1417 women participated in 1968-69, and 1031 of those were re-examined in 1980-81. In 1992-93, 49.5% of those participating in both previous studies (N=702) were re-examined.

In the dental part of the longitudinal study, 702 women participated at all examinations. Of those 595 had ≥ 1 tooth in 1992-93. In the longitudinal study in paper I, women born in 1908 were excluded due to a large drop-out, leaving 586 participants for the analysis.

In the context of this thesis, only dentate subjects were included (Table 2). The study design is illustrated in Figure 1.

Fig 1. Study design PSWG. Examination years and age cohorts examined (Papers I, III, IV).



Non-participation

Of those invited in 1968, eight women had died between sampling and invitation to the study, 20 had moved from the city, 128 refused to participate and four were not accessible. Of those not participating, there was an over-representation of single women compared to participants. Women examined in 1968-69 who refused participation in

Table 2. Number of subjects in the dental substudy (PSWG; Papers I, III, IV) with regard to age group at the different examinations, and number and mean age of edentulous and dentate subjects compared to the total sample.

Year of birth	1968-69			1980-81			1992-93		
	AgeTotal	Dentate	Edentulous	AgeTotal	Dentate	Edentulous	AgeTotal	Dentate	Edentulous
1954	-	-	-	-	-	-	38	66	0
1942	-	-	-	38	108	106	50	98	97
1930	38	356	342	50	323	310	62	268	254
1922	46	421	378	58	305	261	70	275	233
1918	50	390	319	62	295	225	74	200	153
1914	54	172	133	66	125	97	78	70	52
1908	60	78	48	72	41	24	84	16	12
Sum	1417	1220	197	1197	1023	174	993	867	126
Mean age	46.8	46.2	50.6	56.3	55.5	61.4	65.3	64.4	72.0

1980-81 were found to have fewer teeth and fewer restored teeth in the initial study than women participating in both studies. In the 1992-93 dental study, non-participants were more often edentulous and had fewer teeth as compared to 1980-81. Of those participating in 1968-69, 265 had died, 89 had moved from Göteborg, two were inaccessible and 270 refused further participation in the 1992-93 study (Bengtsson et al. 1997).

The Population Study on Oral Health in Jönköping, Sweden

Setting

The city of Jönköping had approximately 110 000 inhabitants in 1973 and 120 000 inhabitants in 2003, thus being the tenth largest city in Sweden. It is the seat of the county government in the county of Jönköping. Dental care is provided by public dental services and dentists in private practices.

Subjects

In 1973 a random sample of subjects (N=1000) aged 3, 5, 10, 15, 20, 30, 40, 50, 60 and 70 years from four parishes in the city of Jönköping were examined clinically and radiologically. Selection was based on date of birth, between March and May, and all subjects in each age group were listed in chronological order, resulting in lists of 140-170 subjects per each age group. The first 100 individuals from each list were invited to a clinical and radiographic examination. In the event of non-attendance, the next individual on the list was invited, until the study sample consisted of 100 respondents in each age group. No information was available regarding differences between respondents and non-respondents or reason for non-attendance (Hugoson & Koch 1979).

In 1983, 1993 and 2003 the study was repeated in the same geographical area with the same age groups as in 1973, with the addition of a cohort of 80-year olds. In each age group, 130 randomly selected individuals were invited for a clinical and radiographic examination. The participation rate was 77.2% in 1983, 75.4% in 1993 and 69% in 2003. For details regarding attendance rate and reasons for non-attendance, see Table 3 (Hugoson et al 1986a, Hugoson et al. 1995a, Hugoson et al 2005a).

Information regarding differences in socio-demographic and oral health parameters between respondents and non-respondents was not available.

In paper II, only dentate subjects aged 20-70 years were studied. Because of loss of radiographs the present sample was smaller than the original one (Table 4). The participation rate for those aged 20-70 years varied between 65-80%.

Table 4. Number of dentate participants according to time of examination, age and gender. Original sample of dentate participants in parenthesis. Differences are due to loss of radiographic material (Paper II).

	1973		1983		1993		2003	
	men	women	men	women	men	women	men	women
20	36 (40)	56 (60)	44 (45)	53 (55)	50 (50)	50 (50)	46 (46)	37 (38)
30	41 (51)	41 (49)	48 (50)	45 (48)	62 (63)	38 (39)	41 (42)	46 (50)
40	46 (48)	43 (51)	46 (47)	51 (52)	54 (54)	39 (39)	43 (47)	32 (36)
50	38 (40)	58 (60)	39 (42)	53 (57)	45 (45)	52 (52)	35 (41)	50 (50)
60	33 (34)	44 (50)	44 (46)	38 (38)	45 (45)	37 (38)	40 (44)	40 (42)
70	31 (32)	31 (31)	38 (38)	31 (32)	26 (26)	49 (51)	37 (40)	44 (47)
Total	225 (245)	273 (301)	259 (268)	271 (282)	282 (283)	265 (269)	242 (260)	249 (263)

Table 3. Reasons for non-attendance in 1983, 1993 and 2003 (Hugoson et al. 1986, Hugoson et al. 1995, Hugoson et al. 2005) (paper II)

Age	20			30			40		
	1983	1993	2003	1983	1993	2003	1983	1993	2003
Year of examination									
Could not be reached by letter or telephone.									
Ex-directory telephone number		5	18	6	8	6	12	5	5
The time was inconvenient			1		1	2	1	4	4
Moved	12	9	11	7	5	5	2	4	4
Could not leave work	1			2	1	1	1		6
Military service	6	3	2						
Afraid of dentists	2			2	1	1	1		1
Had recently visited his/her dentist	2	2		2	1		1	2	
Have no own teeth-therefore nothing to examine									
Seriously ill, handicapped, senile				1			1	1	1
Does not speak Swedish					2	2		1	1
Deceased									
No special reason. Not interested	7	21	10	10	9	20	12	20	22
Pregnant. No time, many siblings/children				2					

Age	50			60			70			Total
	1983	1993	2003	1983	1993	2003	1983	1993	2003	
Year of examination										
Could not be reached by letter or telephone.										
Ex-directory telephone number	8	7	7	4	6	6	5	6	6	120
The time was inconvenient		2	1		2	2				20
Moved		1	1	1	2	1	1		2	68
Could not leave work		3	3	1						19
Military service										11
Afraid of dentists	1	1	1		2	2		2	2	19
Had recently visited his/her dentist	2	1		3	2			5		23
Have no own teeth-therefore nothing to examine	2			1			8		1	12
Seriously ill, handicapped, senile	5	2	1	4	3	2	8	5	4	38
Does not speak Swedish					1	1			1	9
Deceased	1			1	2					4
No special reason. Not interested	8	16	20	17	18	22	9	12	19	272
Pregnant. No time, many siblings/children										2

Method

The Prospective Population Study of Women in Gothenburg

Examinations

All women were invited for a full day multidisciplinary examination of medical, psychiatric and dental status including blood sampling, questionnaires answered verbally and in writing and a dental examination. At all examinations the latter comprised a radiographic examination by means of OPG taken by a trained dentist or dental assistant. In 1992-93 a clinical examination, including screening of the oral mucosa and periodontal condition was added and performed by three calibrated dentists who also conducted an interview. The OPG was examined by one specialist in oral radiology.

Variables used in papers I, III, IV

Age (I, III, IV); age was used as a continuous variable in papers III and IV, and as a categorical variable in paper I

Periapical status (I, III, IV); AP was considered present when the periapical ligament space was widened equal to or more than double the normal width or when an overt radiolucency was present (Ahlqwist et al. 1986, personal communication).

Number of teeth (I, III, IV); Number of teeth, number of restored teeth (III) and number of teeth with carious lesions (III) were registered from the radiograph (OPG) with the 32-teeth dentition used as reference.

Root-filled teeth (I, III, IV); registered from the radiograph and presented in absolute numbers as well as ratio. No assessment of technical quality of root fillings was made.

Masticatory function and dental aesthetics (III); data were collected from a questionnaire on a scale 1-5, dichotomized to acceptable (4-5) or poor (1-3) and used as crude measures of perceived oral health.

- CHD (IV); Subjects with CHD were those with angina pectoris and/or a history of myocardial infarction. Angina pectoris was diagnosed using the questionnaire by Rose (1962), and myocardial infarction was diagnosed if two or more of the criteria 1) central chest pain, 2) transient rise of transaminase activities, and 3) typical ECG changes of recent onset, were present
- Diabetes (IV); yes/no
- Hypertension (IV); present if the systolic blood pressure was ≥ 160 and/or diastolic blood pressure ≥ 95 and/or if the subject was treated pharmacologically against hypertension.
- Cholesterol (IV); concentration measured as mmol/l from blood samples
- Triglycerides (IV); concentration measured as mmol/l from blood samples
- Body mass index (BMI) (IV); weight/height^2
- Waist-hip ratio (WHR) (IV); Ratio of circumference of waist and hip
- Smoking (III, IV); never, former or current (IV), smoker or non-smoker (III)
- Alcohol habits (III, IV); wine consumption never, weekly or daily. The intake of spirits and beer was excluded because of negligible consumption of spirits and confusing data regarding intake of type of beer (Bengtsson et al. 1998).
- Marital status (III, IV); married, widow or unmarried/divorced (IV), married, unmarried (III)
- Dental visiting habits (III); time elapsed since previous dental visit dichotomized to <1 year vs ≥ 1 year and regular dental visiting habits dichotomized to ≥ 1 time/year vs <1 time/year.
- Dental fear (III); The dental anxiety scale (DAS) consists of four questions regarding situations during dental treatment to assess dental fear. Each question has five alternatives of responses on a scale from 1 to 5 (from calm to terrified). The sum of scores, 4-20, is calculated. Scores between 8-9 are regarded as normal, whereas scores of 15 or higher suggest severe

dental fear. In the present study, a cut-off was set at DAS ≥ 13 (dental fear) or < 13 (no dental fear).

Life situation (III, IV); all subjects were asked to assess their life situation on a scale 1-7 after being asked “are you satisfied with your life situation?” Data was dichotomized into acceptable (1-4) and poor (5-7).

Socio-economic variables (III); all subjects were asked to assess their economic situation, life situation and health answering the question “are you satisfied with your --- situation?”, on a scale 1-7. Data were dichotomized into acceptable (1-4) and poor (5-7).

Paper I (PSWG)

Data were collected from the examinations in 1968-69, 1980-81 and 1992-93. Number of teeth, number of root filled teeth and number of teeth with AP were presented and used to calculate the ratio of root filled teeth (root filled teeth/number of teeth) and ratio of teeth with AP (number of teeth with AP/number of teeth). Also, the sample prevalence of AP, defined as the fraction of subjects with ≥ 1 tooth with AP, was calculated.

Paper III (PSWG)

This study used participants from the 1992-93 examination, omitting edentulous subjects and subjects born in 1908. AP was used as the dependent variable. The independent variables related to dental, demographic and socio-economic conditions were those stated previously.

Paper IV (PSWG)

Only subjects from the 1992-93 study were used. There were 1056 subjects with data on CHD status, where 106 subjects were diagnosed with CHD. In the analysis of tooth loss and CHD both dentate and edentate subjects were included (N=993), whereas in the analysis of endodontic variables and CHD, edentulous subjects were excluded (N=867). CHD was used as the dependent variable. The dental related independent variables were

tooth loss, dichotomized to loss of ≤ 16 teeth or > 16 teeth, number of root-filled teeth and number of teeth with AP were categorized to 0, 1, 2 and > 2 .

The Population Study on Oral Health in Jönköping, Sweden

Paper II

At all examinations, a radiographic and a thorough clinical examination were performed along with a questionnaire regarding socio-demographic factors, dental habits and perceived dental health. In paper II, information was used from the radiographic examination only, where all radiographs were restudied.

Radiographic examination

1973

For those aged 10-70 years a full mouth radiological examination (FMR) was performed, consisting of 16 periapical and 4 bitewing radiographs, using an Eggen film holder.

1983

Subjects aged 20-80 years were examined with both FMR and an orthopantomogram (OPG). In cases where an individual recently had had a radiographic examination, radiographs were obtained from the subject's dentist and if necessary supplemented with additional apical radiographs. All apical radiographs were taken with an Eggen film holder.

1993

In subjects aged 15-30 years 6 bite-wing radiographs and an OPG were taken. In cases with deep carious lesions and root filled teeth, the examination was supplemented with apical radiographs. Subjects aged 40 years and older were examined with FMR and OPG. Apical radiographs were taken with an Eggen film holder.

2003

In subjects aged 10-40 years, an OPG and 6 bitewing radiographs were taken. In cases with deep caries lesions and root filled teeth, additional periapical radiographs were taken. Subjects aged 50-80 years, were examined by means of FMR, consisting of 16 periapical and 4 bitewing radiographs, as well as OPG.

All periapical radiographs were restudied using observer binoculars according to Mattson, and for length measurement of root fillings a magnifying device was used (Eschenbach x7). The length between the root filling and the radiographic apex was measured to the nearest 0.1 mm and then categorised according to Fig 2. In cases where periapical radiographs were lacking or unreadable, observations regarding periapical status and presence of root filled teeth were made from OPG from the examinations in 1983, 1993 and 2003. Periapical status was assessed according to the periapical index (PAI) from periapical radiographs as well as length and seal of root fillings (Table 5). Third molars were excluded.

Fig 2. Frequency of apical periodontitis according to length of root filling (Paper II).

Frequency of AP	54.8%	33.3%	14.6%		21%		
Length category	Overfilling	flush	0.5-2mm		>2mm		
	Overfilling	<0.5	0.5-1mm	>1-2.mm	>2.-3mm	>3-4mm	>4mm
Frequency of AP	54.8%	33.3%	14.5%	14.7%	20.1%	20.4	21.8%

Table 5. Variables recorded on apical radiographs regarding root filling quality and periapical status (Paper II).

Adequate seal; No voids laterally or apically to the root filling. The root filling should appear homogenous.

Length; Distance between the root filling and radiographic apex measured on a scale to the nearest 0.1 mm.

PAI-score; 1. Normal periapical structure
 (Örstavik et al 1986) 2. Small changes in bone structure
 3. Changes in bone structure with some mineral loss
 4. Periodontitis with well-defined radiolucent area
 5. Severe periodontitis with exacerbating features

All recordings were made on tooth-level. In cases with multiple rooted teeth, the root with the most severe PAI score was recorded, both with regard to periapical status and quality of the root filling. If all roots were assessed as having the same PAI score the root with the worst root filling quality was recorded.

One observer (the author of this thesis, FF) was calibrated against a set of 100 reference radiographs with different periapical expressions according to PAI (Örstavik et al 1986). For assessment of lateral and apical seal a calibration was made between two examiners (FF+MH), but all registrations were made by FF. Intra-observer agreement was calculated according to Cohen's kappa. Observer agreement to PAI scores from a set of reference radiographs was kappa=0.70. Intra-observer agreement over seven months after a re-recording 67 cases for length of root filling, seal and periapical status according to PAI was 0.80, 0.73 and 0.73 respectively. PAI-scores (1-5) were dichotomized to 1-2 (healthy) and 3-5 (disease).

When recordings were made from OPG, the quality of a root filling was not assessed and AP was recorded when the periapical membrane was widened equal to or more than twice the normal width or an overt periapical lesion was present. Thus, when periapical status was studied on OPG, the PAI-score was not used. This reduced the underlying material for analysis of root filling quality and periapical status. Also a number of radiographs were of poor quality, making assessment of root filling quality and/or periapical status precarious. Teeth that had been treated with pulp amputation or apical surgery were omitted, leaving 3981 root filled teeth for the analysis of the association between root filling quality and periapical status (Table 6).

Statistical methods

The χ^2 -test was used to make inferences about the association between root filling quality and AP. Cohen's kappa was used to analyse observer variation. The general linear model was used for analysing longitudinal data and cross-sectional data was analysed by means of analysis of variance. Independent t-test was used for continuous variables and χ^2 -test for categorical variables to compare group characteristics. Multivariate logistic regression analysis was used to assess odds ratio for risk indicators of CHD and AP, respectively. Binary logistic regression models were applied to estimate odds ratios for root filling quality categories as independent variables and AP as dependent variable. Since several participants contributed with more than one observation, a multilevel logistic analysis was performed.

Table 6. Number of teeth eligible for analysis of periapical status according to PAI and assessment of treatment quality (Paper IV).

	1973		1983		1993		2003	
	No teeth	No RF	No teeth	No RF	No teeth	No RF	No teeth	No RF
Total no	10941	1291	12343	1209	13464	1007	12433	682
OPG	-	-	119	2	5455	1	6643	57
NR	296	27	39	3	11	3	3	2
Amp		13		11		6		1
Surg		32		24		13		7
Sum	10645	1217	12185	1169	8009	984	5787	611

No teeth=Number of teeth

No RF=Number of root filled teeth

Total no=Number of teeth/root filled teeth in the study sample

OPG=Number of teeth/root filled teeth recorded on OPG

NR=Number of teeth/root filled teeth not recordable on radiographs

Amp=Number of teeth treated with pulp amputation

Surg=Number of teeth treated with apical surgery

Sum=Number of teeth/root filled teeth eligible for analysis according to PAI and assessment of treatment quality

Results and discussion

Epidemiology of apical periodontitis (Papers I, II)

These studies reported on changes in endodontic status from the PSWG- and PSJ-samples over 24 and 30 years, respectively. It was concluded that the number of teeth decreased with age cross-sectionally and longitudinally, but the number of retained teeth increased over time for comparable age groups. The ratio but not the number of root filled teeth increased with age cross-sectionally and longitudinally and the number of teeth with AP decreased with age longitudinally in the PSWG-sample. Accordingly the number of root filled teeth increased with age in the PSJ-sample. The ratio of root filled teeth and teeth with AP decreased over time for comparable age groups in the PSWG-sample, as did the number of root filled teeth and teeth with AP in the PSJ-sample. The sample prevalence of AP decreased over time in both samples.

Cross-sectional findings

Number of teeth

As expected, the number of teeth decreased with ageing in the PSWG- and PSJ-samples. Over time, the number of teeth increased for comparable age groups. These findings have been repeatedly demonstrated in other population surveys cross-sectionally (Lavstedt 1978, Bergström et al. 1987, Ödesjö et al 1990, Kirkevang et al 2001). Repeated cross-sectionally, Skudutyte-Rysstad & Eriksen (2006) found only small changes in number of teeth in a study on 35 year-olds between 1973 and 2003. This finding could be attributed to the rather young population studied, where small changes over time may be expected. However, in the corresponding age groups in our studies, 38-year olds (PSWG) and 30-and 40 year olds (PSJ), the increase in retained teeth was statistically significant over 24 years and 30 years, respectively.

Prevalence of apical periodontitis

In paper I (PSWG) the frequency of teeth with apical periodontitis showed a trend of increasing with age in the youngest age group compared with the older age groups. The number of teeth with AP generally differed non-significantly between all age groups at all examinations. The sample prevalence decreased from 41.9% in 1968 to 31.1% in

1992. In the repeated cross-sectional analysis there was a statistically significant decrease in both number and ratio of teeth with AP over 24 years in 38-year olds but not in 50-year olds between 1968 and 1980. In paper II the number of teeth with AP increased significantly with age comparing the younger and the older age groups. Repeated cross-sectional analysis showed a statistically significant decrease in number of teeth with AP over 30 years in 30-, 40- and 50-year olds. The sample prevalence decreased from 51.2% in 1973 to 31.8% in 2003 in the age groups 20-70 years. Lupi-Pegurier et al (2002) found a trend towards increasing ratio of teeth with AP with ageing, but this increase was almost only between the youngest age groups, with small variations among the oldest age groups. Lavstedt (1978) demonstrated an increasing ratio of AP with ageing, but there was no data on number of teeth with AP presented. Ödesjö et al (1990) reported on an increasing ratio of AP with ageing as well as Kirkevang et al (2001) and Bergström et al. (1987). The ratio of AP was relatively small in the PSWG-sample compared with other studies, especially among the older age groups (Kirkevang et al. 2001, Ödesjö et al. 1990, Allard & Palmqvist 1986). Comparing similar age-groups between PSWG and PSJ with regard to number of teeth with AP, the results were almost identical. Repeated cross-sectional studies show only small variations with regard to ratio of teeth with AP (Skudutyte-Rysstad & Eriksen 2006), but Petersson (1993b) found that the number of individuals with a premolar or molar with AP decreased over time. The sample prevalences of AP were similar between the PSWG-sample and PSJ-sample. In the literature, the sample prevalence varies between studies, 22-80% (table 1). The variation may to some extent be a result of some studies using patients who seek dental care, but it is remarkable that the sample prevalence from two recent studies using random samples were 42.3% (Kirkevang et al. 2001) in Denmark and 70% (Sidaravicius et al. 1999) in Lithuania.

In the context of measuring prevalence of AP, an interesting methodological problem emerged. Is it better to calculate the mean number of teeth with AP rather than the ratio of AP? Using percentages of teeth with AP is more sensitive in identifying differences, but the ratio of teeth with AP is not only a product of the number of teeth with AP, but also the total number of remaining teeth. Thus, an increased ratio of AP with age, does not necessarily indicate that older individuals are more affected by periapical disease, as this observation may only be an effect of tooth loss. Consequently,

if one wants to assess the burden of periapical disease in an individual as the number of periapical lesions, it would be more sensible to present the mean number of teeth with AP.

Prevalence of root filled teeth

The ratio and number of root filled teeth had a trend of increasing with age at all three examinations in the PSWG-sample. However, in 1992 there were only small differences among the oldest age groups. Parallel to the results for AP, the ratio measure displayed larger differences than absolute numbers. In the repeated cross-sectional study, 38-year olds in 1992 showed a statistically significant decrease in both number and ratio of root filled teeth. Among 50-year olds there were no significant differences between 1968 and 1980. In the PSJ-sample, number of root filled teeth increased significantly with age at all examinations, without significant differences among the older age groups. Repeated cross-sectional analysis showed a significant decrease in number of root filled teeth for all age groups over time, except for 60- and 70-year olds. Lavstedt (1978) reported on an increasing number of root filled teeth with age, and Loftus et al. (2005), Ödesjö et al. (1990) and Kirkevang et al. (2001) demonstrated an increasing ratio of root filled teeth with age. Skudutyte-Rysstad & Eriksen (2006) demonstrated a decreasing ratio of root filled teeth among 35-year olds between 1973 and 1993, with a slight increase in 2003. Petersson (1993b) reported on fewer individuals with an endodontically treated molar or premolar between 1974 and 1985. These findings are probably best explained by a reduced incidence in dental caries over time (Hugoson et al. 2005). However, Björndal & Reit (2004) reported on an increasing number of endodontic treatments in Denmark between 1977 and 2003 which was explained by a reduced tooth extraction rate and increased number of multi-rooted teeth treated with RCT.

Longitudinal findings (PSWG)

Number of teeth

The number of teeth decreased by age in all cohorts. Eckerbom et al (1989) found only a slight non significant decrease in number of teeth in a longitudinal study over 5-7 years. The small changes in that study may be explained by the short period of follow-up. Kirkevang et al. (2006) reported only on median number of teeth in 473 individuals

in a follow-up over six years where no changes in number of teeth were observed. However, they did not present age stratified data on number of teeth.

Prevalence of apical periodontitis

The number of teeth with AP decreased for all age groups except for women born in 1930, and the only statistically significant decrease was noted among women born in 1918 and 1922.

Longitudinal studies do not reveal an increase in number of teeth with AP with ageing (Eckerbom et al. 1989) or report only on a small increase (Kirkevang et al. 2006). Neither of these studies included a stratification by age. Petersson (1993a) found an increase in the ratio of teeth with AP in the youngest age group in a follow-up study over eleven years.

Prevalence of root filled teeth

The number of root filled teeth increased significantly with age in women born 1922 and 1930. Kirkevang et al. (2006) found a slight increase in the ratio of root filled teeth and Eckerbom et al (1989) reported on similar findings with a significant increase in the number of root filled teeth over 5-7 years. Petersson (1993a) found an increase in the proportion of individuals with an endodontically treated molar or premolar, and the change over 11 years was entirely attributed to the youngest age-group, 20-29 year olds at baseline.

The literature show diverse results concerning the prevalence longitudinally and cross-sectionally of number of teeth, root filled teeth and teeth with AP. There may be several reasons for these differences such as selected samples with regard to gender, age and culture/country. However, expected differences in oral health are obvious due to dental care behaviours, eg dental visiting habits and preventive dental care in a public dental health perspective.

Association of root filling quality with apical periodontitis (Paper II)

Major findings from this study were improved endodontic status over time, in terms of a decreased number of root filled teeth and teeth with AP. At each examination root fillings of adequate quality were associated with healthy periapical conditions.

However, although the technical quality of root fillings improved over 30 years, the ratio of AP in root filled teeth did not decrease over time.

Adequate length was defined as a root filling ending within 0.5-2mm from the radiographic apex. Several authors propose adequate length to be within 2mm from the radiographic apex (Bergström et al. 1987, Bergenholtz et al 1973, Hommez et al. 2002, Skudutyte-Rysstad & Eriksen 2006) In accordance with other findings, it was demonstrated that root fillings with adequate length was significantly associated with healthy periapical status, as compared to teeth with root fillings ending flush with the apex or were overfilled (Bergström et al. 1987, Bergenholtz et al. 1973, Ödesjö et al. 1990). However, when controlling for adequate seal by stratification, it was found that there was no difference in ratio of AP between root fillings ending 0.5-2mm and more than 2mm from the radiographic apex. The higher ratio of AP in conjunction with root fillings flush with the apex or overfilling was not explained by adequate or inadequate seal. This is in reasonable accordance with findings by Ödesjö et al. (1990). Moreover, Bergström et al. (1987), without performing statistical analysis, found that inhomogeneous root fillings had an increased ratio of AP irrespective of length, and that homogeneous root fillings ending more than 2 mm from the radiographic apex had a lower ratio of AP than teeth with root fillings ending within 2 mm. Bergenholtz et al. (1973) demonstrated that root fillings flush with the apex and overfilled canals with improper seal had statistically significant higher ratio of AP than properly sealed canals with root fillings ending <2 mm from apex. They used 99% confidence intervals, which may explain why statistically significant differences between other root filling categories were not identified.

From this study and other epidemiological surveys, it seems that the length of the root filling is not as critical as proposed by clinical studies, as long as the root filling ends within the confines of the root canal and provides an adequate seal (Strindberg 1956, Sjögren et al. 1990, Farzaneh et al 2004, Örstavik et al. 2004). One explanation for this may be that the preoperative diagnosis is not known in epidemiological studies. In clinical studies the preoperative diagnosis has been shown to be predictive of treatment outcome (Sjögren et al 1990, Farzaneh et al 2004, Örstavik et al. 2004). A study from Denmark (Bjørndal et al. 2006) found that most teeth treated had vital pulps, thus generally periapically sound, prior to endodontic treatment. Teeth without AP

undergoing endodontic treatment may be less sensitive to deviations from an optimal root filling length than teeth with AP, as long as the root filling ends short of the apex (Åkerblom & Hasselgren 1988, Bergenholtz et al. 1979). Kirkevang et al (2007) found that the incidence of AP over six years in root filled teeth was not statistically significantly associated with the root filling quality. In root filled teeth with AP at base line, the odds ratio for inadequate root filling quality in relation to AP increased. The authors argued that inadequate root filling quality was associated with a poorer prognosis for healing.

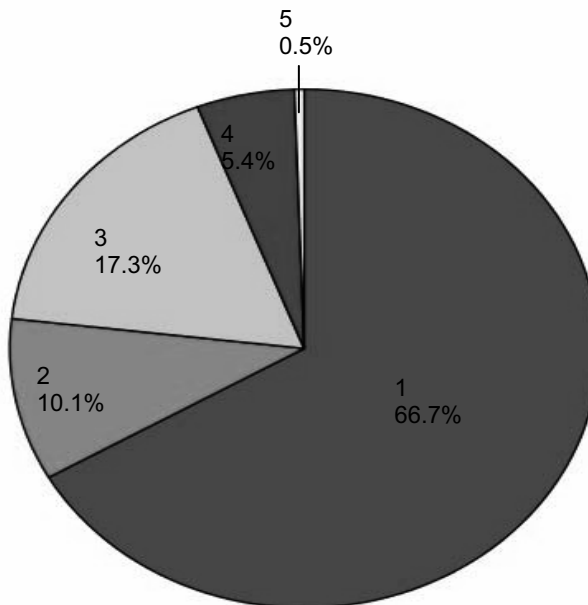
Although the technical quality of root fillings was associated with the periapical status, the overall improvement in technical quality over time did not yield an improved periapical status. This finding is in accordance with other repeated cross-sectional studies yet it seems difficult to find a rational explanation (Pettersson 1993b, Skudutyte-Rysstad 2006). Molar teeth are technically the most difficult teeth to treat endodontically and in our study root filled molars had a higher ratio of AP compared to premolars and incisors both in 1973 and 2003. The root filling quality in molars may be more complicated to assess than in incisors/premolars, since untreated root canals may be difficult to identify on the radiograph and untreated root canals may be an important reason for persistent AP. Compared to 1973, molars constituted a larger fraction of all root filled teeth in 2003. Thus, an expected improvement in treatment outcome being the result from a better quality of root fillings, may be distorted by the larger proportion of endodontically treated molars in 2003.

Another problem in the context of cross-sectional studies that may account for the result, is that teeth with root fillings of varying technical quality and with AP may have been extracted prior to the study, leaving a selected set of root filled teeth without AP. This suggests that the problem of AP in conjunction with root filled teeth may be underestimated in epidemiological studies.

In paper II, the Periapical Index (PAI) was used for measuring the periapical status. The rationale for using PAI has been discussed previously in this thesis. The distribution between PAI-scores in root filled teeth is shown in Fig 3. The distribution among “disease” categories, *ie* scores 3-5, is differently distributed compared to Skudutyte-Rysstad & Eriksen (2006). Excluding all teeth with scores 1-2, teeth determined as having AP was given the score 3 in 75% of the cases and score 4 and 5 in

23% and 2% respectively. There was no significant variation between examinations. In the Norwegian study, score 3 was found in 35% of cases with AP, score 4 in 35% and score 5 in 30% of the cases in 2003. Corresponding data from a Canadian study report score 3 in 79% of the cases, score 4 in 14% and score 5 in 7% of cases with PAI 3-5 (Dugas et al. 2003). The differences can be explained by misclassification, but may also be attributed to differences in the samples studied. Score 5 is supposed to be assigned to teeth with “severe apical periodontitis with exacerbating features” (Örstavik et al. 1986). Given that most subjects studied in our sample attended regular dental care, the proportion of individuals with exacerbating AP should be expected to be low. Most studies using PAI, do not present the distribution of scores, probably due to dichotomization between scores 2 and 3 representing categories “healthy” and “diseased”, respectively.

Fig 3. Distribution of PAI-scores assigned to root filled teeth



Strindberg (1956) identified the problem of interdependence in conjunction with a study on treatment outcome in endodontics. Since many individuals contribute with more than one tooth in both clinical and epidemiological studies, a correlation between the outcomes in different teeth in the same individual cannot be ruled out, *ie* the observations may not be considered independent from each other. Studies on outcome from endodontic therapy generally analyse the results on the tooth-level, thus erroneously neglecting potentially important variation between and within individuals. In a multilevel analysis on both the tooth-level and individual-level, it was concluded that inadequately root filled teeth were at four times greater risk of having AP than adequately root filled teeth (a root filling providing an adequate seal, ending within the root canal). The difference in OR was small between the tooth-level analysis and multilevel (tooth+individual) analysis, probably because of the large sample size and a large fraction of individuals only contributing with one tooth in the analysis. As expected however, the confidence interval was wider in the multilevel analysis. Furthermore, due to the results of the multilevel analysis showing small to moderate influence of interdependence between teeth/subjects analysis on the tooth-level was added.

Socio-economic factors and apical periodontitis (Paper III)

This study explored the association between SES, behavioural factors and AP. It was demonstrated that radiological evidence of carious lesions and root filled teeth were predictive of AP, while the only variable of socio-economic relevance statistically significantly associated with AP was perceived acceptable health. It was concluded that SES did not have an obvious impact on AP.

As found in other studies there were significant associations between caries, root filled teeth and AP (Kirkevang & Wenzel, 2003, Aleksejuniene et al. 2000). Information on other factors affecting the individual which may have implications for periapical status is scarce, but the results from our study are in some agreement with others. However, perceived acceptable health was surprisingly found to be predictive of AP. Aleksejuniene et al (2000) found perceived general health to be associated with the prevalence of AP. In a sub-analysis we found that women reporting acceptable health had more retained and restored teeth and visited the dentist more often than women

reporting poor health. Thus, women reporting acceptable health may be considered as more concerned about their oral health and thus more inclined to choose conservative dental treatment, including endodontic treatment, rather than extraction. As extractions result in resolution of AP at a higher rate than RCT it may be questioned whether AP can be considered a valid indicator of oral health; attitudes and economic restraints of the individual may affect the choice of treatment, *ie* endodontic treatment or extraction.

Dental visiting habits did not influence the presence of AP in our study. Aleksejuniene et al. (2000) found regular visiting habits to be predictive of AP, while Kirkevang & Wenzel (2003) found no usage of service of dental care to be associated with AP. The inconsistency in findings may be explained by differences in populations, where both the socio-economic context and prevalence of AP vary. Also, differences in measuring SES and AP may be contributory. For other diseases, the slope of the gradient between SES and disease has been found to differ between populations (Adler & Ostrove 1999). In the context of our own study, the same reasoning as for women reporting poor health probably applies, *ie* individuals with irregular dental visiting habits have fewer teeth and may choose extraction instead of conservative treatment. Dental care attendance has been found to be associated with dental status (Sakki et al 1994).

Regarding variables accounted for as socio-economic measures, the present study cannot be claimed to capture the complete socio-economic context of the subjects, because of the lack of objective information on education, income and occupational status. However, those variables used are self-reported and authors argue that self-reported information on social standing may be as predictive on health outcomes as objective information (Adler & Epel 2000). Scales used for self reported SES variables ranged from 1-7. A cut-off point between 4 and 5 was arbitrarily determined. These variables are not tested with regard to validity, neither is the chosen cut-off point. However, it seemed reasonable to dichotomize in order to get sufficiently large subgroups. In a sub-analysis we compared subjects reporting extreme values (1-2 and 6-7, respectively) which rendered non-significant odds ratios for all three SES-variables.

Contributing to the rationale for this thesis is the observation that caries has a socio-economic gradient in childhood, which is less pronounced among adults (Marthaler 2004, Bjertness & Eriksen 1992, Treasure et al 2001). Given the sequel to

dental caries in terms of restorative and endodontic treatment it seems reasonable that SES could have implications for the presence of AP. In a sub-analysis we studied risk factors for dental caries in a similar multivariate logistic regression model as presented in paper III, substituting AP as the dependent variable for ≥ 1 vs 0 teeth with dental caries. Factors predictive of dental caries were root filled teeth (OR=1.07(1.0-1.14) CI 95%), smoking (OR=1.90(1.12-3.24) CI 95%), unmarried women (OR=1.72(1.15-2.56) CI 95%), and irregular dental visiting habits (OR=4.76(2.08-10.89) CI 95%). The SES variables used in this model, the same used in paper III, did not turn out to be predictive of dental caries.

In cross-sectional studies, smoking has been demonstrated to be associated with AP (Bergström et al 2004, Kirkevang & Wenzel 2003, Aleksejuniene et al. 2000). We failed to confirm these findings, which may be due to the small fraction of individuals reporting smoking in our sample (22%).

General health and apical periodontitis (Paper IV)

The results of this study did not support the hypothesis that AP may be predictive of CHD. However, tooth loss and high age were demonstrated to be significantly associated with CHD after adjusting for traditional risk factors.

Comparing CHD-cases with non-cases showed significant differences between groups. Cases had fewer teeth, were older, reported more often hypertension, had higher levels of serum cholesterol and triglyceride, had higher BMI and WHR and more seldom reported former smoking and more often a poor life situation. Apart from smoking, these were expected results.

In the bivariate logistic regression analysis, two root filled teeth were significantly associated with CHD, but the significance did not prevail when adjusting for several known risk factors. Joshipura et al (2006) found root filled teeth to be predictive of CHD in a large scale survey, concluding that pulpal inflammation preceding the endodontic treatment may be a risk factor. It may be argued that the internal validity in that study was compromised by the data collection. Number of root filled teeth was assessed by interview of the subjects, introducing information bias in comparison to radiographic examination.

Root filled teeth, apart from being a surrogate variable for pulpal inflammation, could also be a proxy for AP. It has been demonstrated that root filled teeth often is affected by a periapical inflammation, not detectable on the radiograph (Brynolf 1967).

In a review on the possible association between AP and CHD, Caplan (2004) argued that the similarities between AP and marginal periodontitis is not straightforward from a microbiological point of view. The flora in the root filled tooth has been shown to be altered in comparison to the necrotic pulp, where the latter is subjected to an infection not unlike the periodontal infection (Molander et al. 1998, Dahlén & Haapasalo 1998). Since a majority of AP are found in root filled teeth, this may be a reason for the failure in establishing a relationship between AP and CHD. In a subanalysis, we studied non-endodontically treated teeth with AP separately, and found no significant association with CHD in neither bivariate nor multivariate logistic regression analysis. The multivariate analysis yielded an OR of 1.15(0.43-3.06 (CI 95%) in cases with one tooth with AP and 1.69(0.16-17.57 (CI 95%) in cases with two teeth or more with AP as compared to the reference category (AP=0). Apart from the composition of the microbiological flora, the magnitude of the microbiologic and inflammatory burden could be considered different in generalized marginal periodontitis and AP, since the area of affected tissue is larger in marginal periodontitis.

Compared to other population studies on AP, the frequency of teeth with AP was low in our sample (Bergström et al. 1987, Eriksen & Bjertness 1991, Eckerbom et al. 1987, DeCleen et al 1993). This could be due the radiographic method used, which may be considered less sensitive in comparison to full mouth radiographic examination. It may also be a result of the population studied; women in an urban area with great access to dental care. The low prevalence of AP may have contributed to the non-significant relationship between AP and CHD.

It has been debated whether smoking confounds the observed relationship of marginal periodontitis and CVD or not since smoking is a risk factor for both CVD and marginal periodontitis (Hujoel 2002). In some studies, smokers have been demonstrated to have a higher prevalence of AP, but there is no conclusive evidence that smoking impedes the healing of AP (Aleksejuniene et al. 2000, Kirkevang & Wenzel 2003).

Age is predictive of CVD, and in studies demonstrating significant associations between dental infections and CVD men under the age of 50 are usually the ones for

whom the relationship is established (DeStefano et al 1993, Mattila et al. 2000). In the study on the association between AP and CHD, AP was predictive for CHD among men under the age of 40 (Caplan et al. 2006). In our study, only women were examined, and no subject 50 years or younger, were diagnosed with CHD. Women are generally diagnosed with CHD later in life than men (The National Board on Health and Welfare). Due to the large drop-out in the oldest age groups, the remaining subjects may have been the healthiest with a low, non-representative prevalence of CHD, indicating an increased chance of a type II error in the analysis.

In paper IV, we did not adjust for marginal periodontitis in the regression model. Data on marginal periodontitis became available after completion of the analysis. Using a probing depth ≥ 6 mm as a marker for periodontal disease, subjects were divided into three categories depending on the number of gingival pockets ≥ 6 mm (Table 7). The multivariate logistic regression analysis did not yield any support for a statistically significant association between AP and CHD nor between marginal periodontitis and CHD.

Table 7. Distribution of subjects according to CHD-cases and non-cases and marginal periodontal status.

	<u>CHD (n=74)</u>	<u>non-CHD (n=793)</u>
<u>Probing depth (≥ 6mm)</u>		
No pathological pockets	41.9%	42.4%
1-5 pockets	12.2%	18.0%
>5 pockets	45.9%	39.6%

Several studies report on a statistically significant association between tooth loss and CHD (Paunio et al. 1993, Joshipura et al. 1998, Loesche et al. 1998). The association has been attributed to dental disease preceding tooth loss, as well as dietary

habits associated with poor masticatory function (Joshiyura et al 1998). In our study, tooth loss was found to be predictive of CHD after adjusting for established risk factors. In a 24-year follow up of data from the same survey as we studied, Cabrera et al. (2005) found that the association between tooth loss and CHD was not explained by SES. The interpretation of the results showing tooth loss as a risk factor may be that this variable acts as a surrogate measuring several important risk factors which are not tapped in different studies. Tooth loss may thus capture life style factors such as physical activity, dietary habits and health beliefs.

Methodological considerations

PSWG (I, III, IV)

With its random sampling and high participation rate, PSWG provides a representative sample of a middle-aged and elderly urban female population over a 24 year period of time.

The cross-sectional samples in 1980-81 and 1992-93 included subjects from the original random sample of women from 1968. Hence, it could be questioned if these samples were representative in 1980-81 and 1992-93, respectively. However, the cohorts of 38-year olds were new at both follow ups, and in 1980-81 a random selection of 50-year olds were added to the original cohort, as was the cohort of 70-year olds in 1992-93 to ensure representativity due to secular changes in the population. Thus, in the repeated cross-sectional study (paper I), we only used 38- and 50-year olds in the analysis.

The longitudinal sample had a participation rate of 49,5% among dentate subjects over 24-years. Compared to other longitudinal studies, the recall rate in this study was rather low (Kirkevang et al. 2006, Eckerbom et al. 1989, Petersson 1993a). However, with its long follow-up of 24 years, and age distribution towards a high mean age resulting in a large fraction of diseased subjects among drop-outs, significant attrition should be expected (Bengtsson et al. 1997). Differences in characteristics between participants and non-participants have been presented previously in this thesis.

The registration of root filled teeth, teeth with carious lesions and teeth with AP were collected from OPG. OPG may be considered as a less sensitive diagnostic tool compared to intra oral radiographs, but Ahlqwist et al (1986) argues that OPG provides

sufficient information on periapical status in an epidemiological context according to analysis of agreement. All registrations were made by one expert in oral radiology. Root filling quality was not assessed because of the radiographic examination chosen. Other studies have used OPG for assessment of root filling quality (Marques et al. 1998, DeCleen et al. 1993, De Moor et al. 2000, Kabak & Abbott 2005). Of these studies, all except Marques et al. (1998) were limited to determination of root filling length only.

Important medical variables used in the present study were diagnosed according to contemporary clinical and scientific standards by medical doctors. A discussion regarding methodological problems in conjunction with these variables is outside the scope of this thesis.

PSJ (IV)

In 1983, 1993 and 2003, the random sampling and substantial participation rate provided samples representative for an urban population. In 1973, however, non-participants were replaced which may jeopardize the representativity. Moreover, loss of radiographs in some cohorts contributed to the loss of the material.

The overall quality of the radiographic material was excellent. A majority of individuals were examined by means of FMR, but in the younger age cohorts in 1993 and 2003, the radiographic examination was restricted to OPG with supplementary intra-oral radiographs in teeth with deep carious lesions and root filled teeth. This method, in order to reduce the radiation dose, has been used previously (Eriksen & Bjertness 1991, Sidaravicius et al. 1999, Skudutyte-Rysstad & Eriksen 2006).

The periapical status was assessed according to PAI. The observer agreement with the reference radiographs provided, as well as the intra-observer agreement over seven months was acceptable according to Kappa analysis.

All registrations were made by one observer (FF). This introduces a risk for systematic error, and the relatively small prevalence of AP in the samples may in part be attributed to systematic error. However, it may be argued that this problem should be of minor concern since the observer agreement with reference radiographs and intra-observer variation was acceptable.

Conclusions

The findings from this thesis showed that ageing is associated with a cumulative need for restorative treatment, from our studies indicated by an increasing number of root filled teeth and loss of teeth. The number of teeth with AP did not change significantly with age intra-individually which may be a result of tooth extraction and endodontic treatment.

Over time comparable age groups showed an improving oral health with respect to an increased number of remaining teeth and a decreased number of root filled teeth and teeth with AP. This finding may have been a result of a decreasing incidence of dental caries, owing to preventive care and better access to dental care.

The results illustrate the dynamics of oral health. Thus, it is imperative that epidemiological surveys continue to monitor changes in oral health in order to evaluate the effect of interventions.

The root filling quality remained poor in a considerably high frequency of root filled teeth and although improvements were observed, the frequency of AP in root filled teeth did not decrease. This finding warrants educational efforts in general dental care. Other factors in endodontic treatment than root filling quality need to be addressed and the results need to be monitored in prospective follow-up studies.

In contrast to other aspects of oral health, low SES and sporadic attendance to dental care did not seem to have obvious implications on the risk for having AP. This was probably a result of factors such as attitudes towards dental treatment and economical restraints, resulting in a higher extraction rate instead of conservative treatment. However, according to the results from other studies, results may vary between populations. Thus, it is important that studies on this issue are conducted in different settings, since the SES-profile and access to dental care may vary between different populations.

Results from this thesis suggested that tooth loss is predictive of CHD. Conclusive explanations for this association are yet to be found, but previous dental disease and change in dietary habits as a result of poor masticatory function may be contributory. AP was not found to be significantly associated with CHD. However, findings from longitudinal studies have suggested an association between root filled teeth, AP and

CHD respectively. Prospective follow-up studies as well as clinical intervention studies with outcomes intermediary to CHD should be conducted in order to further elucidate the association.

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Abbreviations

AP: apical periodontitis

CHD: coronary heart disease

CI: Confidence interval

CVD: Cardiovascular disease

FMR: full mouth radiographic examination

OPG: orthopantomogram

OR: Odds ratio

PSWG: the Prospective Population Study of Women in Göteborg, Sweden

PSJ: the Population Study on Oral Health in Jönköping, Sweden

Ratio of root filled teeth: number of root filled teeth/total number of teeth

Ratio of AP: number of teeth with AP/total number of teeth

Ratio of root filled teeth with AP: number of root filled teeth with AP/total number of root filled teeth

RCT: Root canal treatment

SES: Socio-economic status

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