Thesis for doctoral degree (Ph.D.)
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# Prenatal, socio-demographic and oral hygiene-related risk factors on dental caries and periodontal conditions in adolescents

Clinical and register-based studies

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Annika Julihn

From the Division of Pediatric Dentistry,
Department of Dental Medicine
Karolinska Institutet, Sweden

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Annika Julihn
DDS


Karolinska Institutet

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**Opponent**

Professor Ivar Espelid, University of Oslo, Faculty of Dentistry, Department of Paediatric Dentistry and Behavioural Science, Norway, Tannhelsetjenestens kompetansesenter for Nord-Norge, Tromsø, Norge

**Examining committee**

Associate Professor Christina Stecksén-Blicks, Pediatric Dentistry, Department of Odontology, Faculty of Medicine, Umeå University, Sweden

Professor Anders Hjern, Nordic School of Public Health, Göteborg, Sweden, Centre for Epidemiology, National Board of Health and Welfare, Stockholm, Sweden

Associate Professor Anette Oliveby, Divisions of Cariology and Endodontology, Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden

**Supervisors**

Professor Thomas Modéer, Divisions of Pediatric Dentistry, Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden

Med Dr. Monica Barr Agholme, Divisions of Pediatric Dentistry, Department of Dental Medicine, Karolinska Institutet, Huddinge, Sweden

Professor Anders Ekbom, Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

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To Magnus, Charlotta, Alexander,
my father and in memory of my mother

# ABSTRACT


## Prenatal, socio-demographic and oral hygiene-related risk factors on dental caries and periodontal conditions in adolescents

### Clinical and register-based studies

Annika Julihn (2010). Thesis, Division of Pediatric Dentistry, Department of Dental Medicine, Karolinska Institutet, Box 4064, SE-141 04 Huddinge, Sweden. Department of Hospital Dental Care and Pediatric Dentistry, Mölndal, Specialist Dental Care, region Västra Götaland, Sweden.

The overall aim of these studies was to identify risk determinants for dental caries and periodontal conditions in adolescents using clinical and register-based data.

This thesis is based on two parts. Part 1 (Papers I and II) constitutes the clinical and radiographic cross-sectional studies of 800 19-year-olds living in seven suburbs of Stockholm with different socio-economic profiles. Part 2 (Papers III and IV), was designed as a longitudinal register-based cohort study and included all adolescents at 13 years of age who resided in the county of Stockholm, Sweden, in 2000, and followed them up to 19 years of age. Finally, 15538 subjects were examined. Socio-demographic and health related information was collected from local and national data sources.

The novel findings are that the prenatal factors maternal smoking and maternal overweight during the first trimester are identified as risk factors for caries increment in their offspring between 13 and 19 years of age. In addition, our results disclosed that parental immigrant background is a risk factor of caries development during adolescence, irrespective of whether the child was born in Sweden or abroad. These children developed 53% and 109% more approximal caries lesions, respectively, compared to their counterparts with Swedish-born parents. Further, children born in eastern Europe, or western Europe exhibited an increased risk for approximal caries increment, and developed 83% and 46% more approximal caries lesions, respectively, compared to Swedish-born adolescents.

We also found that variables significantly associated with high caries experience at 19 years of age were dental fear, gingival inflammation, irregular toothbrushing at night and a mother born abroad. In addition, an increased relative risk for incipient alveolar bone loss was found in subjects with the presence of subgingival calculus as well as one or more proximal restoration(s).

The main conclusions from this thesis are that: 1) maternal overweight and smoking are identified as new risk factors for caries development in offspring; 2) children with foreign-born parents, irrespective of whether the children were born in Sweden or not and children born in eastern Europe should be regarded as risk patients for dental caries; 3) dental fear, gingival inflammation, a foreign-born mother and irregular toothbrushing at night are variables strongly associated with high caries experience in 19-year-olds; and 4) adolescents with subgingival calculus and proximal restorations are at higher relative risk of exhibiting incipient alveolar bone loss compared with those without.



*Key words:* Adolescents, Caries development, Dental caries, Epidemiology, Ethnicity, Longitudinal, Oral hygiene, Obesity, Periodontal disease, Pregnancy, Register-based studies, Risk factors, Risk indicators, Smoking, Socio-economic determinants, Subgingival calculus.

## LIST OF ORIGINAL PAPERS

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

I. Julihn A, Barr Agholme M, Modéer T. Risk factors and risk indicators in relation to incipient alveolar bone loss in Swedish 19-year-olds. Acta Odontol Scand 2008; 66: 139–147.

II. Julihn A, Barr Agholme M, Grindefjord M, Modéer T. Risk factors and risk indicators associated with high caries experience in Swedish 19-year-olds. Acta Odontol Scand 2006; 64: 267–273.

III. Julihn A, Ekbom A, Modéer T. Migration background: a risk factor of caries development during adolescence. Eur J Oral Sci 2010, *submitted*

IV. Julihn A, Ekbom A, Modéer T. Maternal overweight and smoking: prenatal risk factors for caries development in offspring during the teenage period. Eur J Epidemiol 2009;24: 753–762.

## LIST OF ABBREVIATIONS

| | |
|---|---|
| AC | Alveolar Crest |
| BMI | Body Mass Index |
| CEJ | Cemento-Enamel Junction |
| CI | Confidence Interval |
| DMFS | Decayed, Missing, Filled Surfaces |
| DMFSa | Decayed, Missing, Filled Surfaces, approximal |
| DMFT/S | Decayed, Missing, Filled Teeth/Surfaces |
| EpC | Centre of Epidemiology |
| ETS | Environmental Tobacco Smoke |
| GBI | Gingival Bleeding Index |
| OR | Odds Ratio |
| MBR | Medical Birth Register |
| PIN | Personal Identity Number |
| SBU | The Swedish Council on Technology Assessment in Health Care |
| SCB | Central Bureau of Statistics |
| SD | Standard Deviation |
| SES | Socio-Economic Status |
| SIC | Significant Caries Index |
| SOS | The Swedish National Board of Health and Welfare (Socialstyrelsen) |
| VPI | Visible Plaque Index |
| WHO | World Health Organization |

## CONTENTS

# 1 INTRODUCTION

## *1.1 General background*

This thesis focuses on dental caries and periodontal conditions among adolescents in relation to different risk determinants. In spite of a substantial decline in the prevalence of caries in children and adolescents in Sweden, as in many other highly industrialized countries,[1,2] dental caries is still one of the most prevalent chronic human diseases.[3,4] However, the distribution is skewed and the major treatment need is concentrated to a small proportion of individuals.[5-7] Both dental caries and periodontal diseases are multifactorial diseases with a complex etiology over time, including a dynamic interplay between the microbial biofilm and host response.[8-12] In addition, the micro-organisms' ability to ferment carbohydrate to organic acids and the load of available substrate as well as inadequate salivary flow and composition are crucial factors for the development of dental caries.[11,12] However, the diseases are also influenced by hereditary and environmental factors, including social and cultural factors.[9,12] It is believed that the development of dental caries and periodontal diseases occurs in individuals where homeostasis between disease-promoting and disease-inhibiting factors is not successfully balanced by the host.[12,13]

Although there has been an increased interest in the risk determinants of oral diseases among children and adolescents during recent decades, information and knowledge about the risk determinants associated with dental caries and periodontal diseases in adolescents are limited. So far, most studies are cross-sectional studies and in contrast to medical research, register-based follow-up studies within dental research are relatively uncommon. Thus, it was of interest to perform both clinical and longitudinal register-based studies with the purpose of investigating risk determinants in relation to dental caries and the periodontal conditions of adolescents.

## *1.2 Dental caries*

### *1.2.1 Epidemiology of dental caries in adolescents*

Dental caries is still a major oral health problem in most industrialized countries, affecting 60–90% of schoolchildren,[14] and is also the most prevalent oral disease in several Asian and Latin American countries, whereas it seems to be less common and less severe in most African countries.[14] In 2004, the total estimated global caries burden (DMFT) among 12-year-olds was 1.61 (Table 1).[15] However, comparisons of the global frequency and distribution of dental caries are complicated due to different diagnostic criteria used among the studies.[16,17]

**Table 1.** The estimated global caries burden of disease in 2004, for the indicator age of 12-year-olds expressed using the DMFT index.

| Part of the world | DMFT |
|---|---|
| The Americas | 2.76 |
| Europe | 2.57 |
| Eastern Mediterranean | 1.58 |
| Western Pacific | 1.48 |
| Africa | 1.15 |
| South East Asia | 1.12 |
| **Global** | **1.61** |

In Europe, the prevalence of caries has decreased markedly since the 1970s[2,18,19] and most experts consider fluoride toothpaste to be the most important factor behind the caries decline in the western world.[20] As can be seen in Table 2, the prevalence of caries differs among European countries.[2,21] In central and eastern Europe, the prevalence of caries is still high and there are no signs of substantial improvements.[2] By contrast, several countries in western Europe, including the Nordic countries, report that DMFT averages among 12-year-olds have fallen to 1.0 and below (Table 2).[21] A consistent finding in all countries with a marked caries decline during recent decades is that the decrease in mean DMFT/S is followed by an increase in the skewness of the distribution according to DMFT/S.[22,23]

**Table 2.** Caries experience (DMFT) among 12-year-olds in Europe.

| Country | Year | DMFT |
|---|---|---|
| Albania | 2005 | 3.1 |
| Austria | 2002 | 1.0 |
| Belarus | 2000 | 2.7 |
| Belgium | 2001 | 1.1 |
| Bosnia and Herzegovina | 2004 | 4.2 |
| Bulgaria | 2000 | 4.4 |
| Croatia | 1999 | 3.5 |
| Cyprus | 2005 | 1.1 |
| Czech Republic | 2002 | 2.5 |
| Denmark | 2007 | 0.7 |
| Estonia | 1998 | 2.7 |
| Finland | 2000 | 1.2 |
| France | 2006 | 1.2 |
| Germany | 2005 | 0.7 |
| Greece | 2000 | 2.2 |
| Hungary | 2001 | 3.3 |
| Iceland | 2005 | 1.4 |
| Italy | 2004 | 1.1 |
| Latvia | 2004 | 3.4 |
| Lithuania | 2001 | 3.6 |
| Macedonia | 1999 | 3.0 |
| Netherlands | 2002 | 0.8 |
| Norway | 2004 | 1.7 |
| Poland | 2003 | 3.2 |
| Portugal | 1999 | 1.5 |
| Romania | 2000 | 2.8 |
| Russian Federation | 1996-98 | 2.9 |
| Slovakia | 1998 | 4.3 |
| Slovenia | 1998 | 1.8 |
| Spain | 2000 | 1.2 |
| Sweden | 2005 | 1.0 |
| Switzerland | 2004 | 0.9 |
| United Kingdom | 2004-05 | 0.7 |

In Sweden, the prevalence and/or experience of caries for three-, six-, 12- and 19-year-olds has been reported by the National Board of Health and Welfare (SOS) since 1985. In 2005, the mean DMFT values of 12- and 19-year-olds were 1.0 and 3.1, respectively. The corresponding values in 1985 were 3.1 and 8.5 (SOS 2006). In Stockholm, however, the reported dental health among children and adolescents is somewhat poorer than Sweden as a whole.[24] At the beginning of the 21st century, the Significant Caries Index (SIC) was introduced,[25] describing that one-third of the population with the highest caries scores should be analyzed separately. In 2008, the reported SIC index of 13-year-olds residing in the county of Stockholm was 2.60 and 5.09 in areas with a high and low socio-economic profile, respectively.[24]

## *1.3 Periodontal conditions*

Various inflammatory reactions in periodontal tissue can occur in children and adolescents, ranging from those limited to gingival tissue to a loss of connective tissue attachment and supporting bone. The classification about periodontal diseases distinguishes between 1) dental plaque-induced gingival diseases, 2) aggressive periodontitis, 3) chronic periodontitis, 4) periodontitis as a manifestation of systemic diseases, and 5) necrotizing periodontal diseases.[26]

### *1.3.1 Epidemiology of chronic periodontitis in adolescents*

Although gingivitis is a common finding among young people,[27-32] its development into chronic periodontitis, as characterized by the minor loss of periodontal support and pathological periodontal pockets,[33] is infrequently.[27,34] Most epidemiologic studies in developed countries report a prevalence of chronic periodontitis in adolescents and young adults of less than 5%,[35,36] whereas in the United States a higher prevalence is reported in African Americans compared with Hispanics and Caucasians.[37,38]

In Scandinavia, several epidemiological studies have investigated the prevalence of radiographic alveolar bone loss as a surrogate variable for chronic periodontitis. In most studies, alveolar bone loss is recorded as present when the distance from the cemento-enamel junction (CEJ) to the alveolar crest (AC) on radiographs exceeds 2.0 mm, although there is lack of consensus as to what constitutes alveolar bone loss on radiographs in adolescents.[39,40] Nevertheless, the prevalence of radiographic alveolar bone loss among adolescents in Scandinavia is reported to be between 1% and 11.3%.[41-50]

## *1.4 Risk assessment*

Since both dental caries and periodontal diseases are multifactorial diseases that develop in individuals, identifying individuals who are susceptible and at risk is of the utmost importance to target the most precise and efficient preventive treatment procedures. It has been demonstrated that children who develop caries at an early age are more likely to have caries later into adolescence.[51-56] A Norwegian study investigated the increment of caries from 12 to 18 years of age and found that the best predictor for the increment of manifest caries on approximal surfaces were approximal caries in premolars and second molars at the age of 12.[57] In addition, if a child has more than three approximal caries lesions or restorations by the age of 11–13, the risk of developing new approximal caries lesions is reported to be 3–4 times higher than those who were radiographically caries free (including enamel lesions) in their approximal surfaces at these ages.[58]

### *1.4.1 Risk*

Risk is defined as the probability that a harmful or unwanted event will occur within a given period of time,[59] and is most often used to express the probability that a particular outcome will occur following a particular exposure.[60] Different types of risk terms are used in the literature:

*Risk factor* – an environmental, behavioral or biological factor confirmed by temporal sequence, usually in longitudinal studies, which if present directly increases the probability of a disease occurring, and if absent or removed reduces the probability. Risk factors are either part of the causal chain or expose the host to the causal chain. Once disease occurs, removal of a risk factor might not result in a cure.[61,62] Any definition of a risk factor must clearly establish that the exposure has occurred before the outcome.[60] Risk factors can also be divided into two groups: those that can be modified (e.g., levels of putative pathogens) and those that are non-modifiable (age, gender and race/ethnicity).[62]

*Demographic risk factors* – this term is used for non-modifiable risk factors and tends to comprise a number of other characteristics that might be more likely to expose the host to the causal chain than if they were part of the causal chain. Previous studies have referred to this type of risk factor as *background characteristics*.[62]

*Risk indicator* – this term is used for factors associated with the outcome, as established in cross-sectional studies, in which correlations between various factors and the disease are investigated.[59,63] A risk indicator might be a risk factor if validated in prospective trials.[62]

*Risk predictor (risk marker)* – a characteristic associated with the elevated risk of disease (i.e., it predicts well), but is not thought to be part of the causal chain (e.g., caries prevalence is a good predictor of future caries).[62] Risk predictors are useful in the identification of individuals who are at risk.

*Risk determinant* – an attribute or exposure that increases the probability of occurrence of disease or another specified outcome.[64]

### *1.4.2 Sensitivity/Specificity*

The chosen method for risk assessment should have a high precision and accuracy. This means that it should be sensitive enough to catch as many as possible of those with a true disease risk but also correctly identify those with a low risk.[65] To estimate the validity of a risk assessment method or diagnostic test the terms sensitivity, specificity and negative and positive prediction values are often used. Sensitivity is the proportion of diseased subjects with a positive risk factor, whereas specificity denotes the proportion of non-diseased subjects whose risk factor is negative. The predictive values express the probability of an individual with a positive or negative risk factor to developing the disease or remaining healthy.[65]

## *1.5 Determinants of dental caries and chronic periodontitis*

There are a complex interplay between several risk determinants involved in the initiation and progression of dental caries and chronic periodontitis, including biological (i.e., factors operating within the oral cavity), demographic, socio-economic and lifestyle factors. Since parental lifestyle factors have an impact on the establishment of oral health habits in children[66,67] and their important role persists during childhood[68-70] and adolescence,[71] it is important to identify risk determinants for dental caries as early as possible (i.e., during pregnancy). Furthermore, the interaction of parent and child immigrant background and its influence on caries development has not yet been addressed.

### *1.5.1 Pre- and perinatal factors on dental caries*

During pregnancy, a fetus is at risk of developing chronic disorders in later life,[72-76] including genetic endowment, nutrition and other biological influences such as maternal health conditions (e.g., obesity), and lifestyle factors. Obesity is a risk for a multitude of potential medical and obstetric problems during gestation, which might have adverse short- and long-term effects on a fetus.[75] Risk factors, such as poor maternal nutrition and smoking, increase the risk of a low birth weight or a preterm birth.[77,78] In addition, smoking during pregnancy is reported to increase the risk of various chronic disorders in offspring, including cardiovascular diseases,[79,80] respiratory infections,[81] asthma,[82] type 2 diabetes,[83] rheumatoid arthritis and other inflammatory polyarthropathies,[84] gastrointestinal dysregulation,[85] and cleft lip/palate.[86] Interestingly, prenatal maternal smoking also seems to increase the risk of obesity in later life,[87] indicating the complex interaction between biological and social determinants.

Although an enhanced relative risk of dental caries in children with a low birth weight and those of a preterm birth has been demonstrated in both primary dentition[88] and permanent dentition,[89] conflicting results are reported.[90-94] In addition, regarding the effect of maternal obesity and smoking during pregnancy, the relationship with caries development in offspring, has not yet been investigated.

### *1.5.2 Socio-demographic factors on dental caries and chronic periodontitis*

It is well known that social determinants play an important role in the risk assessment of many chronic disorders, including dental caries[95-98] and periodontal diseases[95,99-101]. Already during a child's first year, social factors such as number of siblings and housing are reported to be associated with high caries experience at 13 years.[89] Socio-economic status (SES) or social class is often measured in terms of occupation, income or education level. Although only a few longitudinal studies about SES and dental caries have been published in western Europe, a higher risk of caries increment has been reported in adolescents from working class homes.[102]

The link between socio-economic difficulties and ethnicity is strong.[103] Over the past three decades, Sweden, like many other European countries, has become a more multicultural society. Of the approximately two million children in Sweden, 25% have an immigrant background (i.e., they were either born abroad or born in Sweden to a foreign-born parent).[104] In Stockholm, the proportion of children with an immigrant background is well over 30%, which is in agreement with other big cities in Sweden such as Göteborg and Malmö.[105]

The average health of individuals with an immigrant background in Sweden is poorer than the rest of the population.[106] Many Scandinavian studies have reported a considerably higher caries prevalence in migrant children compared with non-migrant children, especially for preschool children.[107-118] However, the results for school children are contradictory.[48,102,109,115,116,119-123]

Migrants are not a homogeneous group and large differences are reported on the prevalence and/or experience of caries between ethnic minorities,[109,115,116,124] indicating that the culture of the country of origin is a risk determinant for the development of caries. Although dental caries is among the most prevalent health problems in children from migrant families, a literature search showed a lack of longitudinal studies about the influence and interaction of child and parental migration background on caries development.

Ethnicity is also associated with a higher risk of developing chronic periodontitis in adolescents.[38] It has been reported in the United States that 14–17-year-old African Americans and Hispanics were 5.5 and 1.6 times more likely to suffer chronic periodontitis than Caucasians.[37] The increased risk of periodontal disease in African Americans might be partly because of a biological predisposition.[99] In addition, it has been suggested that different ethnic groups might harbor various types of bacteria as well.[125-127]

### *1.5.3 Oral hygiene-related factors on dental caries and chronic periodontitis*

Daily toothbrushing with fluoridated toothpaste is the most important caries-inhibiting factor and is well-documented in the young permanent dentition.[128,129] Parents in Sweden are recommended to introduce toothbrushing with the eruption of the first tooth, and start brushing the child's teeth with a small amount of fluoride toothpaste with the eruption of the first primary molar, around 1.5-2 years of age.[130]

Most studies about toothbrushing habits and dental caries have focused on the frequency, i.e., if subjects brushed their teeth more or less than twice a day. Recently, a higher caries increment during adolescence was demonstrated in subjects who brushed their teeth less frequently than twice a day.[131] In a cross-sectional study by Macgregor et al. (1996),[132] the authors found that of those who reported only toothbrushing once a day, 75% did so in the morning and only 23% before going to bed. Since knowledge about irregular toothbrushing habits, either in the morning or at night, in relation to dental caries as outcome is limited,[133] it was of interest to study this risk determinant in relation to high caries experience.

Regular toothbrushing is also of particular importance for the maintenance of a healthy periodontium. In a Chilean study, individuals who brushed once a day or less often were, respectively, 1.3 and twice as likely to have attachment loss as those brushing twice or more times a day.[134] The accumulation of bacterial plaque on the teeth opens onto calculus, which is formed by the mineralization of the dental plaque. Longitudinal studies have shown that subgingival calculus is associated with a higher rate of periodontal disease progression in adolescents.[135-140] The presence of active caries lesions and dental restorations might also increase the accumulation of dental plaque and might predispose a subject to a significant loss of periodontal attachment.[141, 142]

### *1.5.4 Diet and dental caries*

Dietary habits develop early in life and the family bears the responsibility for establishing healthy dietary habits from birth. It has been demonstrated that once a high sucrose intake is adopted in early childhood, changes later in life are unlikely[143] and mostly persist until adulthood.[144] The association between diet and dental caries are reported in numerous studies.[113,145-149] However, in the modern age of frequent fluoride exposure, the relationship between sugar consumption and caries experience is inconsistent.[128,150]

The choice of food and traditions of dietary habits differ between ethnic minorities.[151-153] For instance, a part of Bosnian food tradition is that breastfeeding is recommended for as long as possible.[152] In addition, homemade breast milk made from semolina, rice and "petit biscuits" is often used that can lead to Bosnian children soon became accustomed to sweet tastes.[152] Breakfast traditions also differ between migrants and non-migrants.[154,155] It has been demonstrated that irregular breakfast eating among teenagers is strongly connected with having a non-Nordic origin.[156] Children who skip breakfast can be at an increased risk of developing dental caries because previous studies have shown that skipping breakfast is associated with snacking later in the day.[157]

### *1.5.5 Obesity and dental caries*

Dental caries and obesity are both multifactorial diseases with a complex etiology and both are associated with dietary habits.[158,159] Previous studies have demonstrated a relationship between maternal obesity during pregnancy and the risk of childhood and adolescent obesity in offspring.[75,160] Children born to obese mothers (based on their body mass index (BMI) in the first trimester) are twice as likely to be obese at two years of age.[160] Although the relationship between maternal obesity and dental caries in offspring has not yet been addressed, a link between dental caries and obesity in adolescents has been suggested,[161-163] although a systematic review from 2006 revealed contradictory results.[159]

### *1.5.6 Smoking in relation to chronic periodontitis and dental caries*

Smoking is well documented as an important risk factor contributing to a higher prevalence and severity of periodontitis.[9,164-168] Among the potential mechanisms of smoking in the pathogenesis of chronic periodontitis, several studies have disclosed the effects on the local vasculature and host immune systems.[9] It has been demonstrated that there are differences in the oxygen saturation of hemoglobin in the gingiva of smokers and non-smokers, suggesting that smokers have functional impairments in the gingival microcirculation.[169] Furthermore, it has been shown that smoking has significant adverse effects on the immune system, including the modification of the humoral and cellular immune systems, such as cytokines and adhesion molecule network.[170-173] However, only a few studies on the effect of smoking on chronic periodontitis in young cohorts have been performed, with contradictory results.[134,174,175]

In recent years, there has been a growing interest in the negative effect of environmental tobacco smoke (ETS) on dental caries in children.[176-181] Preschool children who are raised in families and subsequently exposed to parental ETS, are reported to have an increased relative risk of dental caries,[176-180] but conflicting results have been reported for schoolchildren.[177,181,182] It seems that the negative effect of maternal smoking is of greater importance than paternal smoking.[176,179] However, whether these mothers smoked during pregnancy has not yet been investigated. In the light of this, it was of great interest to investigate if maternal smoking in early pregnancy influences caries development in offspring during the teenage period.

# 2 AIMS

The overall aim of this thesis was to determine risk determinants for dental caries and periodontal conditions in adolescents using clinical data and register-based data from Swedish national registers.

The specific aims were:

- To investigate risk factors and risk indicators in relation to incipient alveolar bone loss in Swedish 19-year-olds;
- To investigate risk factors and risk indicators associated with a high caries experience in Swedish 19-year-olds;
- To investigate the influence and interaction of child and parental immigrant background on approximal caries development in offspring during teenage years; and
- To investigate the influence of pre- and perinatal determinants on approximal caries development in offspring during teenage years.

# 3 MATERIALS AND METHODS

The material in this thesis is based on two parts. Part 1 (Papers I and II), has a cross-sectional design and was approved by the local ethics committee at Karolinska Institutet, Huddinge University Hospital, Sweden. Part 2 (Papers III and IV), is designed as a retrospective, longitudinal cohort study and was approved by the regional ethical board in Stockholm, Sweden.

## *3.1 Study population (Papers I and II)*

The study population comprised 800 19-year-olds living in seven suburbs of Stockholm, representing different socio-economic profiles (Alby, Hallunda, Huddinge C, Västra Flemingsberg, Sollentuna C, Bromma and Viggbyholm). A letter of information about the purpose of the investigation was enclosed with the annual recall notices sent to the subjects by seven public dental clinics. The recall examinations were conducted between 1 March and 30 November 2001. Of the 800 consecutively randomly selected subjects, 696 (87%) subjects attended the examination appointment (364 males and 332 females). For 10 subjects, data on periodontal variables were missing and they were excluded. Of the participants (n = 696), 557 were born in Sweden, 28 in other European countries and 111 outside Europe. In addition, 207 subjects were living in suburbs with a high socio-economic profile, 189 subjects were living in suburbs with a medium socio-economic profile and 300 subjects were living in suburbs with a low socio-economic profile. Of the dropouts (n = 104), 56% failed to keep their appointment, 33% had technical reasons and 11% refused to participate.

## *3.2 Questionnaire*

The subjects answered a structured questionnaire and an interpreter assisted those who did not understand the Swedish language. The questionnaire contained questions about their parents' SES and country of birth, and their own general health, smoking habits, dietary habits, oral hygiene habits and attitudes to dental care.

### 3.2.1 Papers I and II

In Paper I, questions about their SES, country of birth, general health, smoking habits, oral hygiene habits and self-perceived gingival bleeding were analyzed.

*Socioeconomic status* was described in terms of their parents' educational levels and occupational statuses. Educational level was stratified according to years of schooling: low (≤ 9 years), medium (10–12 years) and high (> 12 years), and occupational status was stratified according to Swedish socio-economic classifications: unemployed, manual workers or non-manual employees.[183] Their parents' *country of birth* was coded on a geographic basis: born in Sweden, born in Europe and born elsewhere. In the final statistical analyses, born in Europe and born elsewhere were combined into one group termed born abroad. An individual was defined as having parents born abroad if at least one of their parents was born outside Sweden. Regarding *general health*, subjects were asked if they had a chronic disease and/or used regular medication. *Smoking habits* were described and analyzed in terms of cigarette smoking and snuff use. Regarding *oral hygiene habits*, subjects were asked about their frequency of morning and evening toothbrushing and use of dental floss. In addition, *self- perceived gingival bleeding* was studied.

In Paper II, questions about their SES, country of birth, general health, dietary habits, oral hygiene habits and attitudes to dental care were analyzed. Their parents' SES and country of birth and their own general health were analyzed according to the descriptions in Paper I. The subjects' *dietary habits* were described in terms of the frequency of their consumption of fast food, starch-based snacks, sweet beverages and sweets. *Oral hygiene habits* were described in terms of their frequency of morning and evening toothbrushing, use of dental floss and use of fluoride toothpaste and fluoride supplements. In addition, *attitudes to dental care* were described in terms of dental fear and missed dental appointments.

### *3.3 Clinical and radiographic examination*

Two or three dentists at each of the public dental clinics (n = 7) conducted a clinical and radiographic (two bitewing) examination of the subjects. Before the study, all examiners (n = 17) were invited to attend a day-long course of training on the registration of dental caries, plaque and periodontal conditions according to specific diagnostic criteria and the interpretation of responses to the questionnaire. Moreover, the examiners were calibrated with respect to the registration of dental caries, visible plaque index (VPI)[184] and gingival inflammation (using the gingival bleeding index; GBI).[184] All measurements of radiographic alveolar bone loss were carried out by two of the authors (A.J and M.B.A). Incipient alveolar bone loss was recorded when the distance between CEJ and AC was 2.0 mm or more at one or more sites. An inter-examiner test was also conducted. Full agreement in the classification of sites with a CEJ–AC (≥ 2.0 mm) or a CEJ–AC (< 2.0 mm) was 89% with a mean kappa of 0.63.

#### *3.3.1 Papers I and II*

In Paper I, the following variables were analyzed:

*Plaque and gingival inflammation*: The presence of dental plaque was recorded when clearly visible and expressed using the VPI. Gingival inflammation was based on bleeding on probing in the gingival sulcus and expressed using the GBI. The proportion of surfaces (%) with dental plaque and gingival inflammation was estimated for each individual.

*Dental caries:* The number of decayed, missing and filled teeth/surfaces was registered and expressed using the DMFT/S indices.

*Calculus*: Supragingival calculus was recorded as present when clearly visible in the upper and lower jaw. Clinically detected subgingival calculus was recorded as present after probing the gingival sulcus of the first molars and central incisors with a dental explorer. Radiographically detected subgingival calculus was recorded as present on the proximal surfaces of premolars and molars. In the statistical analysis, both clinically and radiographically detected subgingival calculus were combined to form the variable “subgingival calculus”.

*Incipient alveolar bone loss*: The mesial and distal surfaces of all first permanent molars on radiographs were analyzed (n = 5488 sites). The readable sites were 93% and of these 2408 sites were read from digital radiographs and 2696 sites from conventional radiographs. The distance between the CEJ and AC was determined on conventional radiographs using a Peak scale loupe (Carton Optic, Tokyo, Japan; sevenfold magnification). The loupe is provided with a scale that permits measurements to the nearest 0.1 mm. The distance from the CEJ to AC on digital radiographs was determined using the software program Dimaxis (Planmeca Oy, Helsinki, Finland).

In Paper II, the following variables were analyzed:

*Plaque* and *gingival inflammation:* As described in Paper I.

*Dental caries*: At the clinical examination only manifest caries lesions were registered and expressed using the DMFT/S indices. Approximal caries on the radiographs was registered as initial or manifest caries. Initial caries – a lesion in the enamel that has not reached the dentinoenamel junction or that has reached or penetrated the dentinoenamel junction but not extended into the dentin. Manifest caries – a lesion that clearly extends into the dentin.

### *3.4 Study population (Papers III and IV)*

All children born in 1987 and residing in the county of Stockholm, Sweden in 2000 were included in the study. At baseline, 18,142 subjects were examined at 13-year-olds. The cohort was followed until individuals were 19-years-old. During this period, the subjects received regular dental check-ups at either the Public Dental Health Service, with private practitioners, or at the Division of Pediatric Dentistry at the Karolinska Institutet. A total of 15,538 adolescents had clinical and radiographic dental examinations at both 13 and 19 years of age and this constituted the final study cohort. The dropout rate was 14% and the most common reason for dropping out was that the child had moved out of the area.

### *3.5 Data sources*

Papers III and IV are based on information collected from data sources at the Public Health Care Administration in Stockholm, and from Swedish National Registers at the Central Bureau of Statistics (SCB) and from the Centre for Epidemiology (EpC) at the SOS.

*The Medical Birth Register (MBR)*: The MBR was established in 1973 and is administered by the SOS, Stockholm. Its purpose is to compile information on ante- and perinatal factors, and their importance for the health of the infant. The first antenatal care visit usually takes part between weeks 10 and 12. One advantage of the MBR is its large database content, harboring maternal and neonatal data of nearly all infants born in Sweden (coverage 97-99%).[185] In addition, exposure data are obtained prospectively (before the birth of the child), which eliminates the problem with recall and interviewer bias. The register has been evaluated three times, in 1976, 1998 and 2001,[186,187] with the conclusion that it is a valuable source of information for reproduction epidemiology. However, to make full use of it, an understanding of its deficiencies is necessary.

*The Register of the Total Population (RTB)*: Since 1968, Statistics Sweden has kept the RTB. This register includes variables on country of birth, date of immigration and emigration, citizenship, civil status and family structure (number of family members living in the same residence). The information in the RTB is often used as background information in medical research.

*The Swedish Population and Housing Census*: Sweden has a long census history, the first being performed as early as 1749. Between 1860 and 1930, population censuses took place every 10th year, and from 1930 until 1990 every fifth year with the exception of 1955. No census has been carried out since 1990. When a census was performed, every household in Sweden had an obligation to respond to and return the census questionnaire. Among other items, each census gathered information about age, gender,

occupation, employment and education. One member of the household had to answer questions about the nature of the household dwelling, and also enumerate every person the household, their relationship and their personal identity number (PIN). Hence, it was possible to link individuals in any one household on the basis of census information. The census of 1990 was evaluated and the results indicated that about 92% of the households had been correctly classified.[188]

*The Multigeneration Register*: The multigeneration register was founded in 2000 and is administered by Statistics Sweden. The register is a database in which persons born after 1931 and living in Sweden after 1961 can be linked to their parents, siblings and children and, to a lesser extent, grandparents and cousins.

*The Total Enumeration Income Register*: Data on individuals` annual income tax, founded on income tax returns and tax authority decisions, are collected by the National Swedish Tax Board. The board then sends summary statistics to Statistics Sweden. The information is processed further to create variables, such as income from employment and disposable income, which can then be assembled on the basis of information on certain relationships and presented on a family and an individual basis. Information is also available about the receipt of both social welfare allowance and unemployment benefit.

*The Education Register*: This register was established by Statistics Sweden in 1985 and is annually updated with information about the highest formal education attained by each individual, from elementary to post-graduate level.

*Database at the Public Health Care Administration*: Dental health in children and adolescents in Sweden is monitored on a national basis by the SOS, but is not linked to PINs. In Stockholm, however, data on dental caries, according to the DMFT/S indices in children and adolescents, are sent from the Public Dental Health Service, private practitioners and the Division of Pediatric Dentistry, Department of Dental Medicine, at Karolinska Institutet, to the Public Health Care Administration and is analyzed at three, seven, 13, and 19 years of age. Since 2000, all these data are linked to PINs.

### 3.5.1 Register linkage

Every resident in Sweden receives a PIN at birth or on arrival into the country. The PIN was first introduced in Sweden in 1947 and has three parts: date of birth, a three-digit birth number, and a check digit (introduced in 1967). The three-digit birth number is sex-specific and the check digit verifies that data of birth and three-digit number are correct.[189] The combination of specific date of birth and a specific birth number will allow all Swedish individuals to have a unique PIN and permits the linkage of each individual between different registers and allows the follow-up of non-patient populations over time.

In this thesis, the file about the dental caries of the study cohort was sent from the Public Health Care Administration to the SCB. Each subject received a file number, which made it possible to link them and their registered dental health to the different registers at the SCB and EpC. The key to relating names and codes was kept within the SCB and was not disclosed to the investigators.

### 3.5.2 Papers III and IV

In Paper III, data about the subjects' and their parents' country of birth and their date of immigration was collected from the RTB. To perform adjustments for potential confounders socio-demographic determinants were also collected. Marital status was collected from RTB. Information about family income and receipt of social welfare allowance was collected from the Total Enumeration Income Register and data on education were obtained from the Education Register. Information on the maternal number of children was collected from the Multigeneration Register.

In Paper IV, data were collected on pre- and perinatal factors and socio-demographic determinants. The following variables were collected from the MBR: weeks of pregnancy, method of delivery, weight at birth, congenital malformation, parity and maternal age. In addition, maternal smoking habits and the mother's height and weight at the first visit to the public maternity health care clinic were collected. On the basis of the mother's height and weight, the BMI was calculated (BMI = weight/height$^2$).

To control for potential socio-demographic confounders, the following variables were collected from the RTB: parents' countries of birth, family structure and marital status. From the Population and Housing census of 1985, information about occupation and employment was collected, and regarding the mothers' receipt of social welfare allowance information was collected from the Total Enumeration Income Register. Data on education were obtained from the Education Register.

### *3.6 Statistical methods*

In Papers I and II, a power analysis was performed before the start of the study to detect differences in the prevalence of dental caries and radiographic alveolar bone loss between subjects with or without foreign-born parents. The following assumptions were made about dental caries: 2.5% significance level, 90% power and one-sided hypothesis (required a sample size of 800 subjects). However, regarding radiographic alveolar bone loss, only a sample size of 191 subjects was required based on following assumptions: 5% significance level and 80% power.

The final outcome in Paper I was incipient alveolar bone loss (CEJ–AC ≥ 2.0 mm) and subgingival calculus and in Paper II high caries experience (DMFS of ≥ 10). Statistical analyses included the chi-squared test and logistic regression. Bi- and multivariate logistic regression were used to calculate odds ratios (ORs) and 95% confidence intervals (95% CI). Inter-correlations between independent variables, significant in the bivariate logistic regression analyses, were studied to detect possible multi-colinearity between factors. Factors significant in the bivariate analyses were competed in the multivariate analysis, which was carried out in a stepwise logistic regression. Variables significant in the multivariate analysis were further analyzed in an "interaction model". None of the pairwise interaction terms were significant in the interaction model. Logistic regression analyses were also used to calculate the cumulative probability (%) of incipient alveolar bone loss and high caries experience.

In Papers III and IV, approximal caries increment (DMFSa > 0) between 13 and 19 years (i.e., the difference between DMFSa values at 13 and 19 years of age,

respectively) was used as the outcome in the statistical analyses. In Paper IV, the outcome variable, approximal caries increment, was categorized according to the magnitude of approximal caries increment: DMFSa > 0, DMFSa > 4, DMFSa > 6, DMFSa > 8 and DMFSa > 10, respectively.

For analyzing the data, frequency tables, chi-squared tests and logistic regression were used. In addition, the one-way ANOVA test was used in Paper III to assess the significance of differences in means. The ORs with 95% CI were used as estimates of the effects. To analyze whether immigrant background in children and in parents and pre- and perinatal factors were risk factors for caries increment during teenage years, covariates were adjusted for socio-demographic confounders. All the socio-demographic variables were categorized and classified, and possible confounders were entered into the logistic regression model in different groups and adjusted multiple logistic regression analyses were performed for each group of determinants to select variables associated with the outcome.

# 4 RESULTS

## *4.1 Periodontal conditions at 19 years of age (Paper I)*

Of the 686 subjects examined, 5.1% (n = 35) exhibited incipient alveolar bone loss (CEJ–AC ≥ 2.0 mm) at one or more sites. The mesial and distal surfaces of the upper first molars were the most affected surfaces. Of the 35 individuals with incipient alveolar bone loss, 86% exhibited one affected site, 9% had two affected sites and 5% three affected sites. Gingival inflammation (GBI > 25%) were presented in 12% of the subjects and 14% showed an occurrence of subgingival calculus. Questions on oral hygiene habits, revealed that 75% of all individuals brushed their teeth every morning and 71% every night. The males brushed significantly less than the females. However, no significant differences between males and females were observed regarding gingival inflammation and incipient alveolar bone loss.

## *4.2 Factors related to incipient alveolar bone loss (Paper I)*

On subject-based level, the factors most strongly associated with the presence of incipient alveolar bone loss in 19-year-olds were subgingival calculus ($P < 0.001$) and proximal restorations ≥ 1 ($P = 0.05$). Subjects with the presence of subgingival calculus or proximal restorations had a fourfold (OR = 4.2) and twofold (OR = 2.1) increased risk, respectively, of exhibiting incipient alveolar bone loss compared with whose without. The logistic regression analysis was used to estimate the probability of incipient alveolar bone loss for the given profile of independent variables. In the absence of all the significant variables, the estimated probability of incipient alveolar bone loss in adolescents was 2.6%. When subgingival calculus was present, the probability increased to 10.3%. When both subgingival calculus and proximal restorations were present, the cumulative probability increased to 19.6%.

### *4.3 Dental caries at 19 years of age (Paper II)*

Of all examined adolescents (n = 696), 81% exhibited decayed, missing and filled teeth and 43% decayed, missing and filled approximal surfaces (Table 3).

The mean DMFT and DMFS values were 3.9 and 5.1, respectively. There was no significant difference between males and females. About 15% (n = 105) of the subjects had 10 or more decayed, missing and filled surfaces (DMFS ≥ 10), representing the group with highest caries experience in this study.

Caries indices and the socio-demographic background of the subjects in relation to participating clinics are shown in Table 3. The poorest dental health was found in subjects belonging to the clinics 2 and 3, representing suburbs with a low socio-demographic profile.

**Table 3.** Caries indices and the socio-demographic background of 19-year-olds (n = 696) in relation to participating clinics in the county of Stockholm.

| **Clinics** | **Percentage of adolescents with:** | | | **Mean value** | | | **Percentage of families with:** | |
|---|---|---|---|---|---|---|---|---|
| | DMFT > 0 | DMFSa > 0 | DMFSa >0 | DMFT | DMFS | DMFSa | Migration background | Low social profile |
| Clinic 1 n = 109 | 80 | 80 | 47 | 3.6 | 5.4 | 1.6 | 77 | 68 |
| Clinic 2 n = 98 | 90 | 89 | 64 | 4.7 | 7.0 | 2.6 | 86 | 75 |
| Clinic 3 n = 93 | 87 | 86 | 49 | 4.8 | 5.1 | 2.3 | 66 | 67 |
| Clinic 4 n = 104 | 80 | 87 | 39 | 3.0 | 6.5 | 1.2 | 20 | 39 |
| Clinic 5 n = 91 | 85 | 79 | 36 | 4.0 | 4.5 | 1.2 | 33 | 38 |
| Clinic 6 n = 115 | 77 | 77 | 36 | 3.3 | 3.5 | 1.3 | 13 | 22 |
| Clinic 7 n = 86 | 71 | 71 | 30 | 3.0 | 3.6 | 1.0 | 20 | 29 |
| **Total (n = 696)** | **81** | **81** | **43** | **3.9** | **5.1** | **1.5** | **44** | **48** |

D=decayed, M=missing, F=filled, T=teeth, S=surfaces, a=approximal, CI=caries initial,

### *4.4 Factors related to high caries experience (Paper II)*

The factors most strongly associated with high caries experience in 19-year-olds were dental fear ($P < 0.001$), GBI ≥ 15% ($P = 0.003$), mother born abroad ($P = 0.007$) and irregular toothbrushing at night ($P = 0.008$). The ORs of the variables associated with high caries experience was 2.8 for dental fear, 2.1 for GBI ≥ 15%, 2.0 for mother born abroad and 1.9 for irregular toothbrushing at night. The logistic regression analysis was also used to estimate the probability of DMFS ≥ 10 for the given profile of risk determinants. In the absence of all the significant risk determinants, the estimated probability of high caries experience in 19-year-olds was 4.7%. The cumulative probability of high caries experience increased to 9% when the variable mother born abroad was added. Furthermore, this increased to 16% when both mother born abroad and irregular toothbrushing at night were added, and increased further to 32% when dental fear was also added. When all significant risk determinants were present, the cumulative probability was 52%.

### *4.5 Caries development between 13 and 19 years of age (Papers III and IV)*

In Papers III and IV, we performed a longitudinal register-based cohort study. Of the 18,142 examined subjects at baseline, 15,538 adolescents were examined at both 13 and 19 years of age. Caries development in terms of approximal caries increment (DMFSa) between 13 and 19 years was studied. Of the subjects, 39% developed approximal caries lesions during the follow-up period, and approximately 10% exhibited an approximal caries increment of more than four lesions. The approximal caries increment was 1.34 as an average with a skewed distribution (Fig 1).

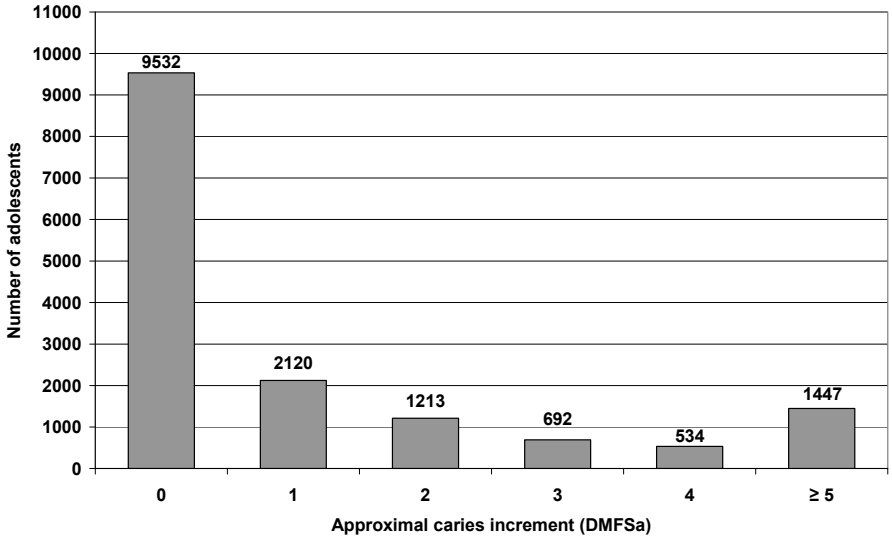


**Fig 1.** Distribution of approximal caries increment (DMFSa) between 13 to 19 years of age in a cohort of Swedish adolescents (n=15,538).

### *4.6 Caries development in relation to immigrant background (Paper III)*

Of the 15,538 adolescents included in the final cohort, 1378 subjects (9%) were born abroad and 5134 (33%) of the subjects had an immigrant background in terms at least one foreign-born parents. The highest mean values of approximal caries increment (DMFSa) between 13 and 19 years of age was found in children born in eastern Europe, Africa and Asia, with mean values of 2.33, 2.27 and 2.25, respectively. Furthermore, children born in eastern Europe developed 83% more approximal caries lesions compared with their Swedish-born counterparts during the follow-up period.

Regarding adolescents with or without foreign-born parents, there were significant differences in the mean values of approximal caries increment (DMFSa) during the follow-up period between the three groups: Swedish-born adolescents with native parents, Swedish-born adolescents with foreign-born parents and foreign-born adolescents with foreign-born parents. The highest mean value of approximal caries increment was found in adolescents born abroad with foreign-born parents compared with Swedish-born subjects with native parents (2.43 and 1.16, respectively).

Furthermore, adolescents with foreign-born parents (i.e., Swedish-born and foreign-born subjects) developed 53% and 109% more approximal caries lesions, respectively, compared with their counterparts with native parents during the follow-up period.

### *4.7 Child and parental immigrant background and caries development (Paper III)*

The interaction of child and parental immigrant background in relation to approximal caries increment during teenage years was studied by logistic regression. Potential socio-demographic confounders were adjusted for by using different models. After the final adjustments, only adolescents born in Sweden with both parents born abroad (OR = 1.48; 95% CI = 1.24–1.77), and adolescents born abroad with a father born in Sweden and a mother born abroad (OR = 1.90; 95% CI = 1.29–2.82) or both parents born abroad (OR = 1.65; 95% CI = 1.22–2.25) exhibited an increased risk for approximal caries increment during teenage years.

### *4.8 The child's birth region and its influence on caries development (Paper III)*

To study the child's birth region in relation to approximal caries increment during teenage years, adjustments for potential socio-demographic confounders were also performed in a logistic regression analysis. Both the unadjusted and first adjusted models showed that the birth regions Africa, eastern Europe and Asia were significantly associated with an increased risk of approximal caries increment. In the final model, several potential confounders were entered (sex, age at migration, maternal birth region, maternal educational level, number of children, marital status, paternal birth region, paternal educational level, family income, social welfare allowance and the interaction term "maternal low education and mother receiving social welfare allowance"). After adjustments, the birth regions Asia and Africa were no longer significant, whereas adolescents born in western Europe (OR = 1.53; 95% CI=1.04–2.25) and eastern Europe (OR = 1.60; 95% CI = 1.15–2.23) exhibited a significantly increased risk for approximal caries increment.

### *4.9 Pre- and perinatal factors in relation to caries development (Paper IV)*

In this study, we also used logistic regression and performed adjustments for possible parental socio-demographic confounders in different models. After adjustments in the final model there several potential confounders were included (smoking, gender, parity, child's country of birth, maternal age, marital status, parental country of birth, maternal educational level, mother received social welfare allowance and the interaction term "unmarried mothers and maternal social welfare allowance"), the results showed that the prenatal factors maternal smoking and maternal overweight exhibited an increased risk of approximal caries increment (DMFSa > 0) in offspring during teenage years, (OR = 1.33; 95% CI = 1.22–1.44) and (OR = 1.21; 95% CI = 1.07–1.37), respectively.

In an additional statistical analysis, we investigated pre- and perinatal factors in relation to the magnitude of approximal caries increment. All cut-off levels for approximal caries increment (i.e., DMFSa > 0, DMFSa > 4, DMFSa > 6, DMFSa > 8 and DMFSa > 10) were analyzed according to the final model. Both maternal BMI ≥ 25 and maternal smoking were significantly associated and independent of the magnitude of approximal caries increment. The excess risk of maternal overweight was enhanced in relation to the magnitude of the caries increment.

# 5 DISCUSSION

The novel findings are that the prenatal factors maternal smoking and maternal overweight during the first trimester are identified as risk factors for caries increment in offspring between 13 and 19 years of age. In addition, our results disclosed that parental immigrant background is a risk factor of caries development during adolescence, irrespective of whether the child was born in Sweden or not.

## *5.1 Methodological considerations*

### *5.1.1 Study population*

This thesis is based on two parts. In Part 1 (Papers I and II) we used a cross-sectional design based on clinical and radiographic studies, and Part 2 (Papers III and IV), was designed as a longitudinal register-based cohort study.

Longitudinal studies are preferable since the same group of subjects is followed over time and they involve repeated observations of the same items over the study period, and consequently have stronger scientific evidence compared with cross-sectional studies. However, in Papers III and IV we took advantage of the opportunity to link information between Swedish national registers and the dental database at the Public Health Care Administration in the county of Stockholm, and this made it possible to study a large cohort over time, with a high statistical power. The 18,142 individuals examined at baseline represented approximately 87% of the total child population (13 years of age at the year of examination, (n = 20, 939)), and the dropout rate during the follow-up period was 14%, which must be considered as relatively low. Since the dropouts exhibited a lower socio-economic level (i.e., younger mothers, unmarried mothers, mothers with low education) and more often had parents born abroad compared with the final cohort, it is reasonable to assume that our results are not overestimated.

In Papers I and II, the study sample was chosen from different suburbs of Stockholm representing low, medium and high socio-economic levels and in this respect the study population was representative for the county of Stockholm as a whole. However, one has to consider that the study sample in Part 1 was not representative of Sweden as a whole since the proportion of adolescents with an immigrant background is higher in metropolises than the rest of the country.[190]

### *5.1.2 Register-based data*

The use of population-based registers has several advantages when identifying various risk factors since large numbers of exposed individuals are involved, leading to a reduction in the bias of diagnosis and selection of subjects. In Paper IV, we used the Swedish MBR to study the influence of pre- and perinatal factors on the caries increment in offspring during the teenage period. The main advantage of the MBR is the relatively large numbers of exposed women and their offspring (it covers between 97-99% of deliveries in Sweden).[185] In addition, information on several prenatal factors was collected before birth and in view of this the information was collected prospectively (i.e., before the outcome). All information about the family was collected independent of the study outcomes, which reduced problem with recall and interviewer bias, but did make it possible to adjust for potential confounding factors. Since the information was collected prospectively, the misclassification of risk determinants in the performed register-based studies is most likely *non-differential (random error)*. Non-differential misclassification of confounding factors will lead to less efficient adjustments, and thereby to some residual confounding. However, when performing dental register-based studies, there are also limitations regarding the available registers. At present, there is no national dentistry register in Sweden, although a register is now under construction.[191] Therefore, several important risk/confounding factors for dental caries (i.e., dietary habits, oral hygiene habits, obesity) were unable to be analyzed since the available registers did not store this information.

### 5.1.3 Questionnaire

Recall bias might have arisen in Papers I and II, for example, when the subjects answered the questionnaire about dietary habits (i.e., consumption of fast food, starch-based snacks, sweet beverages and sweets). In the questionnaire, the alternatives for the frequency of consumption were never, seldom, sometimes or often. It is possible that subjects with high caries experience were aware of the relationship between high sugar consumption and dental caries and answered sometimes instead of often. In the statistical analysis, all questions about dietary habits were then categorized into two groups where the alternatives never, seldom and sometimes were combined under the heading seldom and compared with the alternative often. Consequently, these subjects might have been wrongly regarded as controls. This example of recall bias is also called *differential misclassification (systematic error)* because it is related to the disease and can lead to some underestimation of associations between exposures and the outcome.[59]

### 5.1.4 Outcome

To minimize the *non-differential misclassification* in Papers I and II, all the examiners (n = 17) were invited to attend a day-long training course in caries diagnostic criteria. In addition, an inter-examiner test was performed to check the validity among the examiners participating in the study. The reproducibility values represented good agreement[192] and showed that the estimates of caries were reliable even when several examiners were used. In the register-based studies (Papers III and IV) there is a risk of random errors because the diagnosis of manifest caries can sometimes be under- or over-reported. However, random errors are affected by increasing the size of the study, and will be reduced to zero if a study becomes infinitely large.[59] When looking at the *differential misclassification* of manifest caries, there is a risk of under-reporting since the treatment philosophy in recent decades has moved towards stricter criteria for operative treatment in favor on non-operative procedures. This philosophy might lead to dentists waiting to restore a manifest caries lesion to see if it progresses. Differential misclassification in this case might have led to an underestimation of the caries experience and caries increment.

Clinical attachment loss (CAL) or radiographic alveolar bone loss are two common surrogate outcome variables used separately to evaluate periodontal disease.[193] In Paper I, we used radiographic alveolar bone loss since it has been shown that the radiographic assessment of proximal alveolar bone loss correlates well with the clinical assessment of attachment loss.[194,195] In most studies, alveolar bone loss is recorded as present when the distance from the CEJ to AC on radiographs exceeds 2.0 mm. This definition is strictly a surrogate variable for chronic periodontitis and is often used in all patients independent of age. In the literature, there is also a lack of consensus as to what constitutes alveolar bone loss in adolescents.[39,40] Therefore, because of the low age of the subjects, the cut-off level for the distance from the CEJ to AC on radiographs was set at ≥ 2.0 mm, and the outcome was classified as incipient alveolar bone loss.

## *5.2 Findings*

### *5.2.1 Prenatal maternal overweight and smoking on caries development in offspring*

In Paper IV, maternal overweight (based on BMI in the first trimester) was identified as a risk factor for approximal caries increment in a mother's offspring during teenage years. In addition, we also found that the excess risk of maternal overweight for approximal caries increment was positively correlated to the magnitude of approximal caries increment during the six-year period. Possible explanations for the relationship between maternal overweight in the first trimester and dental caries in offspring include biological mechanism(s) and social factors. Regarding potential biological mechanism(s) the fetuses of obese mothers might be affected by hyperglycemic and hyperinsulinemic episodes,[196] which might negatively influence the metabolism and predispose towards a higher risk of obesity development in later life,[197,198] as well as an enhanced risk of chronic inflammatory diseases. Whether the host-microbe interaction in the oral cavity, important in initiation of caries, is also negatively influenced by prenatal overweight is so far unclear. Another biological explanation behind the link between maternal overweight and caries in offspring would be over-nutrition during pre- and perinatal development, which has previously been reported to result in long-term consequences of the appetite-regulating neural network. This imbalance, in which an individual regulates energy balance throughout later life,[199] might also be of importance for caries development.

Among the social factors individuals with lower socio-demographic backgrounds are more likely to eat low cost foods containing more sugar, which increases the risk of dental caries and overweight/obesity.[200] Noticeably, even after adjustments for country of birth and different socio-economic determinants, the OR of maternal overweight was still significantly associated with approximal caries increment. However, the link between maternal overweight and caries development in offspring might also be mediated by unhealthy dietary habits transferred from the mothers to their children. This assumption is based on the fact that unhealthy dietary habits are often transferred from parents to children[144,201,202] and on the importance of dietary habits in the development of dental caries.[159,203] However, since dietary habits are excluded from the register, which is a weakness, we were unable to evaluate them among teenagers or their mothers, and nor could we evaluate the potential role of consumption patterns as a mediator for the enhanced risk for dental caries among their offspring.

In Paper IV, we also demonstrated that maternal smoking in the first trimester was a risk factor for approximal caries increment in offspring between 13 and 19 years of age. In addition, we found that the variable smoking was robust across the various DMFSa outcome cut-off levels. The observed link between maternal smoking and caries development in offspring during the follow-up period might also be explained by biological and social factors. One possible biological mechanism is that prenatal maternal smoking might affect mediators of the immune system, since cigarette smoke exposure during pregnancy has been reported to exhibit adverse effects on the immune system by modifying fetal T-helper, Th-1 and Th-2 cell function,[204-207] through the effects on Toll-like receptors.[208] This might result in an enhanced susceptibility to infections at the post-delivery stage.[208] Whether the disturbance of the immune response of the fetus can influence the early microbial colonization of tooth surfaces in the oral cavity, a predisposition for caries, is an interesting hypothesis, that needs experimental research.

Another explanation could be unhealthy dental attitudes since it is reported that children raised by parents who smoke brush less frequently, receive less help with brushing and consume more between meals and nightly beverages.[180] The higher caries increment during teenage years might be a result of poor dental behavior established in early

childhood. Noticeably, lifestyle factors established in early life are often difficult to change.[143,209] Unfortunately, we have no information about toothbrushing or smoking habits in teenage offspring, but a strong association has previously been reported between parental smoking and the beginning of smoking among teenagers.[210,211] In addition, although only a few studies have reported an association between smoking and dental caries,[212-215] teenage smoking as a habit and an increased number of cigarettes smoked per day are reported to be positively correlated with increased caries prevalence.[213] Therefore, the reduction of prenatal and postnatal passive and current smoking in teenagers is important, not only for the prevention of various medical diseases, but also for the promotion of teenagers' oral health, including periodontal disease.

This is the first time these risk determinants have been studied in relation to dental caries in offspring. Consequently, our results are interesting and open the door for further investigation. However, before we can conclude that maternal smoking and overweight are risk factors for caries development in offspring during teenage years our results must be validated in an additional longitudinal study. Until then, these identified risk factors cannot be used in the risk assessment of dental caries in adolescents. However, an important drawback for the interpretation of data on maternal smoking use in relation to caries development in offspring is that interview data will probably understate estimated smoking use. It is unlikely that all smoking use is reported by pregnant women or recorded by midwives. The reporting rate for smoking might be lower because of the unwillingness to report these drugs, and this means that some infants exposed to smoking during embryonic life will wrongly be regarded as controls, and will bias the risk estimates towards 1.0. However, the effect will be slight because these misclassified cases will make up a small part of the reference population.

### *5.2.2 Immigrant background: a risk factor of caries development during adolescence*

In Paper III, we investigated the influence of an immigrant background on both the child and parents in relation to approximal caries increment during teenage years. This is the first longitudinal study, to our knowledge, that has investigated the interaction of child and parental immigrant background and its influence on caries development in children. Our findings revealed that children with foreign-born parents exhibited an

increased risk of approximal caries increment during adolescence, irrespective of whether the child was born in Sweden or not compared with those with Swedish-born parents. A search in the literature has only disclosed a few cross-sectional studies that have focused on both child and parental immigrant background and its relationship with dental caries.[109,123,216] Our results that even Swedish-born children with foreign-born parents exhibited an elevated risk for caries development was somewhat surprising because these children have been enrolled in the Swedish national dental health program since birth. Our finding is not in agreement with Jacobsson et al. (2007),[123] who reported that caries prevalence between Swedish-born adolescents of foreign-born parents and those of native-born parents was similar. However, our results are in line with those reported from a cohort of children in Germany.[216] In their cross-sectional study, the authors reported a poorer dental health in 11- to 14-year-old migrant children, either born in Germany or born abroad with foreign-born parents, compared with the indigenous population.

The impact of the child's birth region in relation to approximal caries increment between 13 and 19 years was also investigated. Our results showed that children born in eastern or western Europe exhibited a significantly higher risk of developing approximal caries lesions during teenage years compared with Swedish-born adolescents. Noticeably, the significant association between adolescents born in western Europe and approximal caries increment during teenage years emerged first when all socio-demographic confounders were included in the final model, with a *P* value of 0.031 (i.e., close to 0.05). In light of this, the higher risk of western European adolescents developing approximal caries during teenage years must be regarded as rather weak. However, the highest risk of approximal caries increment was found in adolescents born in eastern Europe. Our finding is in line with Källestål & Fjelddahl (2007),[102] who reported a higher risk of caries increment in adolescents from outside western Europe, with the highest ORs in adolescents from eastern Europe compared with native children.

Possible explanations for the result that immigrant background is a risk factor for caries development during adolescence is unhealthy oral behavior, such as poor dietary and oral hygiene habits. This assumption is based on the fact that food tradition and toothbrushing habits differ between migrant and non-migrant children. For instance,

eating breakfast regularly is a tradition that differs between ethnic minorities.[154,155] Children who skip breakfast could be at an increased risk of developing dental caries since it has been reported that they also have a large intake of sugar-containing foods later in the day.[154-157,217]

Another factor of importance is toothbrushing habits which differ in different parts of the world[218] as well as in different countries in Europe.[219,220] These differences in toothbrushing habits are already demonstrated during the child's first year. Recently, it was reported by Skaret et al. (2008)[218] that approximately 80% of mothers of western origin started to brush their child's teeth before they were one-year-old compared with 33% of mothers of non-western origin. In addition, foreign-born parents stop helping their children to clean their teeth at a younger age. Later, they seldom control and remind their children of toothbrushing. As a result, the children brush their teeth irregularly and less effectively.[116,221-223] In the light of this, our results in Paper II are in line since this study found that the determinants foreign-born mother and irregular toothbrushing at night were associated with high caries experience in 19-year-olds.

### *5.2.3 Toothbrushing habits and high caries experience*

Although the relationship between inadequate toothbrushing habits and dental caries is reported frequently, there is lack of studies regarding the relationship between toothbrushing at night or in the morning in relation to dental caries. Clinical studies so far have mostly focused on toothbrushing frequency per day. For instance, a higher caries increment during adolescence is reported in subjects who brushed their teeth less frequently than twice a day.[102,121,209] Our results that irregular toothbrushing at night, but not in the morning, was significantly associated with high caries experience was interesting although a previous study by Bruno-Ambrosius et al. (2005)[133] reported no correlation between irregular toothbrushing habits, night or morning, in relation to caries increment. Since toothbrushing with fluoride toothpaste twice a day is acknowledged as an effective caries prevention measure,[128] the results of the present study highlight the particular importance of regular nightly toothbrushing. Especially since salivary flow rate, which is caries inhibiting, is reduced at night.[224] This finding is interesting but needs further investigation.

### 5.2.4 Dental fear and high caries experience

We also found a significant association between self-reported dental fear and high caries experience among 19-year-olds (Paper II), indicating experiences of pain during previous dental treatments, since the number of surfaces with restorations was higher compared with the number of decayed surfaces in our outcome (DMFS ≥ 10]. The relationship between dental fear and high caries prevalence/experience has previously been reported.[109,225-227] Therefore, it is of utmost importance that dentists treating child patients must have a substantial knowledge of how to perform painless treatment to avoid behavior management problems and dental fear/anxiety in the future.

### 5.2.5 Determinants associated with incipient alveolar bone loss

In Paper I, the multivariate analysis disclosed only subgingival calculus and proximal restoration as significant variables associated with the occurrence of incipient alveolar bone loss. Adolescents with subgingival calculus and proximal dental restorations exhibited a fourfold and twofold, respectively, higher risk of exhibiting incipient alveolar bone loss. The association between subgingival calculus and periodontal disease in adolescents has previously been reported in longitudinal studies,[135-140] although previous studies have analyzed site-based level. Since our results are analyzed at a subject-based level and previous studies differ in the study design and outcome used, comparisons are difficult to perform. Altogether our finding support the concept that subgingival calculus is a risk factor of periodontal disease. The results about the link between proximal restoration and incipient alveolar bone loss is in line with previous reports,[141,142] indicating that proximal restoration is a risk factor for periodontal breakdown.

The lack of association between immigrant background and incipient alveolar bone loss in Paper I might to some extent be because of the limited number of subjects classified with incipient alveolar bone loss, despite the performed power analysis. Ethnicity, however, has been reported to be an important risk factor for chronic periodontitis.[37,38] In this study, we also investigated the risk of daily smoking in relation to incipient alveolar bone loss but the results showed no significant association. This lack of an association is probably because there were few daily smokers. This assumption was also confirmed by a performed post-hoc power analysis exhibiting a power of the variable daily smoking habit of only 40%.

### *5.3 Clinical considerations*

Maternal overweight and smoking are identified as new risk factors for caries development in offspring. Based on our findings one has to consider to address dental preventive strategies, regarding risk factors of dental caries in the offspring, to parents-to-be already at the maternity clinics.

We also demonstrated that adolescents with foreign-born parents, irrespective of whether the child was born in Sweden or abroad, exhibited an increased risk of caries increment (DMFSa), and developed 53% and 109% more approximal caries lesions, respectively. Thus children with foreign-born parents and children born in eastern Europe should be regarded as risk patients for dental caries. The findings also indicate that current preventive programs within the organized pediatric dental care in Sweden are insufficient for children with foreign-born parents, and it seems essential that new preventive strategies must be tailored to meet their particular needs.

The study also demonstrated that the current oral hygiene habits among adolescents are insufficient and has to be improved in order to minimize the future development of caries and periodontal diseases. Based on this, the dental profession needs to stress the importance of proper oral hygiene procedures even more in the preventive treatment of adolescents.

# 6 CONCLUSIONS

The main conclusions from this thesis are as follows:

- Maternal overweight and maternal smoking, as evaluated in the first trimester, are identified as risk factors for approximal caries development in offspring during the teenage period (Paper IV);

- Parental immigrant background is a risk factor for caries development in offspring during adolescence, irrespective of whether the child was born in Sweden or not (Paper III);

- Dental fear, gingival inflammation, irregular toothbrushing at night and a mother born abroad are associated with high caries experience in 19-year olds (Paper II); and

- Adolescents with subgingival calculus and proximal restorations are at a higher relative risk of exhibiting incipient alveolar bone loss (Paper I).

# 7 SVENSK SAMMANFATTNING (SWEDISH SUMMARY)

## *7.1 Bakgrund*

Denna avhandling fokuserar på olika riskdeterminanter i relation till karies och parodontala förhållanden hos ungdomar. Trots att kariesförekomsten bland barn och ungdomar minskat avsevärt sedan 1960-talet är karies fortfarande en av våra vanligaste kroniska sjukdomar i Sverige såväl som i den övriga industrialiserade världen. I Sverige är fördelningen av karies är dock skev och det är endast ett litet antal individer som har ett stort behandlingsbehov. Både karies och parodontala sjukdomar är multifaktoriella sjukdomar som utvecklas över tid. Etiologin är komplex och innefattar ett dynamiskt samspel mellan orsaksfaktorer och försvarsfaktorer där sjukdom utvecklas hos individer med otillräckligt balanserad jämvikt.

Dagens kunskaper avseende riskdeterminanter för karies och parodontala sjukdomar hos ungdomar är begränsade. De flesta tidigare studier är tvärsnittsstudier och det finns endast ett fåtal longitudinella studier. Odontologiska registerbaserade studier är dessutom sällsynta. Sålunda fanns det ett intresse att utföra både kliniska och registerbaserade studier med syftet att identifiera riskdeterminanter för karies och parodontala förhållanden hos ungdomar.

## *7.2 Material och metod*

Avhandlingen är baserad på två delar. Del 1 (delarbete I och II) utgörs av kliniska och röntgenologiska studier av 800 ungdomar boende i Stockholm, tillhörande sju olika folktandvårdskliniker belägna i områden med olika sociodemografiska profiler.
Ungdomarna fick i samband med sin ordinarie revisionsundersökning vid 19 års ålder fylla i en enkät med frågor avseende medicinering, kronisk sjukdom, rökvanor, kostvanor, munhygienvanor samt beteende vid tandvård. Dessutom fanns det frågor om föräldrarnas ursprung, utbildningsnivå och yrkesstatus.
Den kliniska och röntgenologiska undersökningen bestod av registrering av plack, tandköttsinflammation, supra- och subgingival tandsten, karies och alveolär fästeförlust.

Del 2 (delarbete III och IV) är registerbaserade studier av samtliga ungdomar boende i Stockholms läns landsting, födda 1987, och där ungdomarnas tandvård utförts antingen på folktandvården, hos privattandläkare eller vid tandläkarhögskolan i Huddinge. Ungdomarna undersöktes när de var 13 år gamla (n = 18142) och följdes till 19 års ålder. Den slutliga kohorten bestod av 15538 ungdomar undersökta både vid 13 och 19 års ålder. Information avseende kariesdata (DMFT/S) inhämtades från beställarenheten för tandvård, Stockholms läns landsting och information avseende möjliga pre- och perinatala så väl som sociodemografiska riskdeterminanter inhämtades från nationella register vid Epidemiologiskt Centrum (EpC), (Socialstyrelsen) och vid Statistiska Centralbyrån (SCB).

## *7.3 Resultat*

### *7.3.1 Delarbete I*

Av de 800 inbjudna var det slutligen 686 19-åringar som undersöktes parodontalt, 5.1% uppvisade begynnande alveolär fästeförlust (CEJ-AC ≥ 2.0 mm) vid en eller flera tandytor. Tandköttsinflammation (GBI > 25%) registrerades hos 12% och subgingival tandsten hos 14% av ungdomarna. Multivariat logistisk regressionsanalys avslöjade att riskdeterminanter signifikant associerade med en begynnande alveolär fästeförlust var subgingival tandsten samt förekomst av en eller flera approximala fyllningar.

### *7.3.2 Delarbete II*

Av 800 inbjudna 19-åringar undersöktes 696 ungdomar avseende karies. Totalt uppvisade 81% karierade, saknade och fyllda tänder (DMFT) och 43% karierade, saknade och fyllda approximala tandytor (DMFSa). Hög kariesförekomst (DMFS ≥10) sågs hos cirka 15% av ungdomarna. Resultaten visade att signifikanta riskdeterminanter till hög kariesförekomst var: tandvårdsrädsla, tandköttsinflammation, oregelbunden tandborstning kvällstid samt om modern var född utomlands.

### *7.3.3 Delarbete III*

I denna registerbaserade delstudie studerades riskdeterminanten "utländsk bakgrund" hos ungdomar såväl som hos deras föräldrar i förhållande till ungdomarnas approximala kariesutveckling (DMFSa) mellan 13 till 19 års ålder. Information om barn och föräldrars födelseland samt tid de vistats i Sverige inhämtades från registret över

totalbefolkningen (RTB). Ytterligare information om familjens socioekonomiska bakgrund erhölls från olika nationella register vid SCB.

Resultaten visade att föräldrar med utländsk bakgrund är en signifikant riskfaktor för approximal kariesutveckling under tonåren, oavsett om barnet är född i Sverige eller utomlands. Svenskfödda ungdomar med utlandsfödda föräldrar samt utlandsfödda ungdomar med utlandsfödda föräldrar utvecklade 53% respektive 109% fler approximala kariesangrepp jämfört med ungdomar med svenskfödda föräldrar. Vidare sågs en ökad risk för approximal kariesutveckling hos ungdomar födda i Östeuropa samt i Västeuropa, vilka utvecklade 83% respektive 46% fler approximala kariesangrepp jämfört med ungdomar födda i Sverige.

### *7.3.4 Delarbete IV*

Syftet med denna delstudie var att studera faktorer under graviditet och förlossning i relation till det blivande barnets approximala kariesutveckling mellan 13 till 19 års ålder. Information avseende barn och moder inhämtades från det medicinska födelseregistret vid EpC. Vidare inhämtades information om familjens socioekonomiska bakgrund från olika register vid SCB.

Resultaten visade att rökning samt övervikt hos modern vid det första besöket på mödravården (vecka 10-12) var signifikanta riskfaktorer för approximal kariesutveckling hos det blivande barnet under tonårsperioden. Avseende variabeln ”övervikt hos modern”, ökade risken i relation till omfattningen av den approximala kariesutvecklingen.

## *7.4 Konklusion*

Resultaten från denna avhandling påvisar att riskfaktorer för kariesutveckling hos barnet under tonårsperioden kan identifieras redan under moderns graviditet. Baserat på våra fynd bör förebyggande åtgärder, avseende riskfaktorer för karies hos det blivande barnet, riktas till de blivande föräldrarna redan på mödravården.

Barn till utlandsfödda föräldrar bör betraktas som riskpatienter för karies. Fynden indikerar att nuvarande profylaxprogram inom den organiserade barn- och ungdomstandvården är otillräckliga och bör omformas för att nå ut till denna målgrupp.

Vidare visar resultaten att munhygienvanorna hos dagens ungdomar är otillräckliga och behöver förbättras för att minimera framtida utveckling av karies och parodontala sjukdomar.

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