Studies on the Associations between Dental Caries, Periodontal Disease and Different Systemic Conditions

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“The believers, in their mutual kindness, compassion and sympathy, are just like one body. When one of the limbs suffers, the whole body responds to it with wakefulness and fever.”

Mohammed (Peace & Blessings upon him)
Abstract

Studies on the Associations between Dental Caries, Periodontal Disease and Different Systemic Conditions

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Background and aims: Dental caries and periodontal disease are the two most common oral diseases in man. Evidence shows that they may be directly or indirectly related to each other and to other systemic conditions. The aims of this thesis were to study: 1) the root caries experience and risk in different periodontal disease severity groups, 2) the experience and risk of dental caries and the experience of periodontal disease in individuals with or without coronary artery disease (CAD), 3) the experience and risk of dental caries and periodontal disease in individuals with or without psoriasis and 4) clinical and biological indicators of dental caries and periodontal disease in adolescents with or without obesity.

Methodology: A total of 437 participants were examined cross-sectionally: 112 individuals with periodontal disease (Study I), 54 individuals with CAD +73 controls (Study II), 89 individuals with psoriasis + 54 controls (Study III) and 27 individuals with obesity + 28 controls (Study IV). Investigations included questionnaires, saliva sampling, radiographs, oral clinical examinations (Studies I–IV), assessment of plaque-pH changes following a glucose rinse, sub-gingival plaque sampling and the collection of samples from the gingival crevicular fluid (GCF) (Study IV). Two computer programs were used to illustrate the caries risk profiles (Studies I–III) and the periodontal disease risk profiles (Study III) after analysing the related data.

Results and conclusions: In Study I, the participants were grouped into three categories according to periodontal disease severity: gingivitis (n=44), mild to moderate periodontitis (n=33) and severe periodontitis (n=35). The prevalence of root caries or fillings in the three groups was 9%, 15% and 29%, respectively (ns). No significant differences in caries risk were observed between the three groups. Of the caries risk indicators examined, only the number of remaining teeth, gingival recession and the presence of one or more systemic conditions differed between the three groups (p<0.05). The difference in systemic diseases was no longer significant after controlling for confounders. In Study II, the mean number of remaining teeth in individuals with CAD and controls was 22 ± 7 and 26 ± 3, respectively (p=0.001). No significant differences in decayed or filled teeth or in caries risk were observed in individuals with or without CAD. However, the CAD group had lower salivary secretion, sub-optimal oral hygiene and used less fluoride. Fifty-two percent of the individuals with CAD, as opposed to only 11% of the controls, were regarded as moderate to severe periodontitis cases (p<0.05). In Study III, the psoriasis group included more overweight/obese individuals than controls (p<0.05). The mean number of remaining teeth in individuals with psoriasis and controls was 24 ± 4 and 26 ± 3, respectively (p=0.05). Psoriasis individuals had lower salivary buffer capacity and radiographic alveolar bone levels than controls (p<0.05). Differences with regard to the latter were no longer significant after controlling for confounders. No significant differences with regard to decayed or filled teeth, periodontal disease severity, or risk of caries and periodontal disease were observed between the groups. In Study IV, more caries and gingival inflammation were observed in adolescents with obesity. Of the clinical and biological indicators examined, salivary secretion rate was lower and sIgA levels were higher in the obesity group compared with controls. No differences between the groups were observed with regard to any of the remaining indicators, including plaque-pH changes, inflammatory markers in GCF and sub-gingival microbial profiles.

Keywords: coronary artery disease, dental caries, obesity, periodontal disease, psoriasis, risk assessment

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Preface

This thesis is based on the following four original papers, which are referred to in the text by their Roman numerals:


Introduction

Dental caries and periodontal disease are the two most common oral diseases in man. They may be related to each other in some way since they both occur in the mouth, particularly at teeth or tooth-surrounding tissues. They may also be related to health conditions that occur in other parts of the body. Dental caries and periodontal disease are thought to share common contributory factors with each other and with a number of chronic systemic conditions, such as cardiovascular diseases, diabetes and obesity (1). An overview of these two oral disease processes is required to obtain an understanding of the way they may relate to each other or to other systemic conditions.

Dental caries

Dental caries or tooth decay is one of the most common preventable diseases. It is reversible in its early stages and is recognised as the primary cause of oral pain and tooth loss (2). Caries refers to the localised destruction of susceptible dental hard tissues by acidic by-products from the bacterial fermentation of dietary carbohydrates (2). It is a chronic disease that progresses slowly in most people. It can be seen on smooth, pitted and fissured surfaces of the crown (i.e. coronal caries) and root (i.e. root caries) of a tooth. According to the World Health Organisation (WHO), 60-90% of school children worldwide have dental cavities (1). However, a marked decline in the prevalence of caries has been observed in developed countries. In Sweden for example, the mean number of decayed, missing or filled teeth in 12 year olds was 0.9 in 2008, while in developing countries (e.g. Saudi Arabia), the corresponding figure in 12 to 14 year olds, available since 2002 was 5.9 [Oral Health Database, Country/Area Profile Project (CAPP), Malmö University website].

Caries-related factors

Dental caries is a multifactorial disease. A number of lifestyle, environmental and hereditary factors contribute to its development. These include the frequent intake of fermentable carbohydrates, poor oral hygiene, high counts of cariogenic microorganisms, the inadequate use of fluoride and impaired salivary function (2).
**Dietary habits**

The high consumption of fermentable carbohydrates has been associated with the initiation and progression of caries (3). However, this association is not as evident nowadays as a result of the frequent use of fluoride toothpaste. Moreover, there are no studies showing that the reduction of sugar intake on its own affects the caries prevalence (4).

**Cariogenic microorganisms**

Endogenous bacteria residing in the dental biofilm, i.e. dental plaque, ferment dietary carbohydrates and produce acidic by-products as a result of the metabolic process. The acids cause the pH in plaque to drop below critical values, resulting in the demineralisation of tooth substances (5). Mutans streptococci are considered major pathogens in the initiation of caries due to their acidogenic and aciduric properties and their ability to adhere to the tooth surface and to other bacteria (6-8). Lactobacilli, which are highly acidogenic, are more common in deep caries lesions and indicate high fermentable carbohydrate consumption and disease progression rather than initiation (9).

**Use of fluoride**

The anti-cariogenic effect of fluoride is well documented. Fluoride acts by inhibiting demineralisation, enhancing remineralisation and inhibiting the bacterial metabolism (10). Experts agree that the use of fluoride toothpaste may be the main reason for the observed caries decline in developed countries, although other reasons should also be taken into account (11). Moreover, a high caries prevalence was observed in a number of populations residing in areas with water fluoridation (12). This may indicate that fluoride use alone may not be sufficient to overcome other caries-related factors.

**Saliva**

Saliva plays an important role in oral health maintenance and has several caries-preventive functions. These include a specific flushing effect, the maintenance of calcium super-saturation in plaque, the neutralisation of acids, raising the plaque pH and reversing the diffusion rate of calcium and phosphate towards the tooth surface (13). Saliva also contains a number of immunoglobulins (Ig) that specifically target cariogenic microorganisms, as in the case of secretory IgA (sIgA) and mutans
streptococci (14). Certain medications that are associated with a number of systemic conditions may reduce the salivary function (15), which may predispose to caries.

**Periodontal disease**

Periodontal disease refers to any disorder of the tissues surrounding and supporting the teeth, i.e. the periodontium. In principle, these disorders may be of developmental, inflammatory, traumatic, neoplastic, genetic, or metabolic origin (16). Those of inflammatory origin (i.e. gingivitis and periodontitis) are the most commonly discussed. The immune-inflammatory response, which develops in the periodontal tissues in response to the chronic presence of plaque, results in the destruction of the structural components of the periodontium. This ultimately leads to the common clinical signs of periodontitis (17). The host response is essentially protective, but both hypo- and hyper-responsiveness of certain pathways can result in enhanced tissue destruction. It is suggested that lifestyle, systemic and social environmental factors can disturb the optimal function of host defences, thereby modifying the final clinical presentation of periodontal disease (18). The WHO estimates that severe periodontal disease, which may result in tooth loss, is found in 5-20% of middle-aged adults worldwide (1). In a series of large-scale, cross-sectional studies over a period of 30 years in the city of Jönköping, Sweden, Hugoson et al. (19) showed that the percentage of subjects with severe periodontitis ranged between 3% and 13%. The latest available data from the WHO CAP project, collected in the 1990s, suggest that about 9% of the individuals in Saudi Arabia had deepened periodontal pockets at the time of examination and should seek periodontal treatment (Oral Health Database, CAPP, Niigata University website).

**Periodontal disease-related factors**

Periodontal disease is considered multifactorial in nature, with a number of factors contributing to its initiation and progression. These include poor oral hygiene, specific plaque bacteria, smoking, systemic conditions (e.g. diabetes), aging and a susceptible host (17).

*Oral hygiene*

Classical experimental gingivitis studies have shown that gingivitis is a reversible condition if adequate oral hygiene measures are implemented (20). The accumulation
of plaque or biofilm around teeth was designated as the primary cause of gingivitis, the removal of which led to the disappearance of clinical manifestations. It has also been suggested that unresolved gingivitis and the continued accumulation of plaque will eventually lead to periodontitis, an irreversible condition that requires more extensive treatment (21). Moreover, several studies have shown that the level of oral hygiene is correlated to the prevalence and severity of periodontitis (22). This vision was challenged by findings from other investigations. Only 20% of a remote population, deprived of regular dental care, suffered from severe periodontal breakdown (23). In fact, it was shown that a subset of patients under good periodontal maintenance and plaque control might still suffer from disease progression leading to tooth loss (24). Marsh (25) concluded that the overall effect of dental plaque is rather a function of a balance between pathogenic and other microorganisms that colonise the sub-gingival environment, in the presence of certain environmental conditions and a compromised host. Generally, it is agreed that maintaining acceptable levels of oral hygiene is a pre-requisite for periodontal stability.

Periodontopathic microorganisms

It is estimated that there are over 700 bacterial species identified in the oral cavity, about half of which are yet to be cultivated (26). These microorganisms essentially live in harmony, i.e. symbiosis, at different oral sites, including the gingival margin around teeth. As bacterial plaque continues to accumulate at the gingival margin, and in the presence of suitable anaerobic environmental conditions in the periodontal pocket, certain species may take the upper hand and infect the periodontal tissues. The infection of periodontal tissues by certain organisms is accompanied by the release of bacterial leukotoxins, collagenases, fibrinolysins and other proteases (27). Consequently, an inflammatory response is triggered. Several species have been associated with periodontal disease. In particular, Porphyromonas gingivalis, Tannerella forsythia and Spirochetes (e.g. Treponema denticola) were associated with tooth sites with periodontal disease progression (28). However, there have been reports of different sub-gingival microbial profiles in cases of chronic periodontitis, in different geographic areas (29). These differences suggest the possible influence of environmental, genetic and epi-genetic factors on such profiles and on the periodontal condition itself.
**Smoking**

In the 5th European Workshop in Periodontology, smoking was assigned as a true risk factor for periodontal disease progression (30). Numerous publications have pointed to the strong association between smoking and a deterioration in periodontal health. Over a 20-year observational period, smokers had significantly larger amounts of plaque, more gingival inflammation and faster progression rates of periodontal attachment loss than non-smokers (31). Linear regression analysis indicated that aging and light smoking were independently and significantly related to periodontal attachment loss (31). However, smoking and aging are still assigned as risk factors rather than causative factors for periodontal disease, as they are not sufficient to independently cause the disease (30).

**Systemic conditions**

Periodontal disease has been associated with a number of systemic conditions (32). In particular, diabetes in relation to periodontal diseases has been covered in the vast majority of the available evidence. In a meta-analysis of 23 publications comparing the periodontal conditions of diabetics and non-diabetics (33), diabetic individuals exhibited an increased severity, but a similar extent of periodontal disease than non-diabetics. The association between periodontal disease and the different systemic conditions is related mainly to the general state of chronic inflammation observed in these conditions. Systemic conditions, such as diabetes, are associated with an up-regulation of systemic inflammatory markers. This in turn leads to further activation of local inflammatory markers and, as a result, destruction of the periodontal connective tissues (32).

**Caries and periodontal disease risk assessment**

When it comes to multifactorial diseases, such as caries and periodontal disease, the assessment of risk of occurrence is far from straightforward. Risk may be defined as the probability that a harmful event will occur (34). Risk assessment is the means of organising and analysing all the available scientific information that has a bearing on the question under discussion (34). A risk factor, i.e. a true risk factor, is an environmental, behavioural, or biological factor confirmed by temporal sequence, usually in longitudinal studies (35). Risk factors are part of the causal chain or would at least expose the host to the causal chain. However, the removal of a risk factor may
not result in a cure, once the disease occurs. When the association between the exposure and the condition is determined through cross-sectional studies, the term “risk indicator”, i.e. potential, probable or putative risk factor, is used (35).

Figure 1. Four common risk assessment models for dental caries and periodontal disease: the Octagon (36) (upper left), the Cariogram (37) (upper right), the PRA polygon (38) (lower left) and the PPRD (39) (lower right)

A risk assessment model is one that considers multiple variables in order to identify one or more risk factors for the disease, so that likely points of intervention can be planned (35). A number of models have been graphically plotted for improved patient education and discussion. Some have even been developed into computer programs for easier use. The Octagon (36) and the Cariogram (40) are two examples of pedagogic caries risk assessment models that have been used to identify high caries risk individuals (Figure 1). Similarly, periodontal disease risk assessment models, such as the periodontal risk assessment (PRA) polygon (38) and the periodontal pentagon risk diagram (PPRD) (39) (Figure 1) have been used during periodontal maintenance in an attempt to identify patients at risk of disease recurrence. The application of risk assessment and risk assessment models in clinical settings may be
useful and has been recommended by major organizations (41, 42). Validation of the majority of risk assessment models as accurate models for predicting future disease has been conducted retrospectively on selected patient groups, in specific geographical areas. In reality, validation of any risk model is more complex and involves a number of steps performed in prospective studies, in different patient groups (43). This stresses on the need for further research to confirm the initial promising findings

**The relationship between dental caries and periodontal disease**

The study of the relationship between dental caries and periodontal disease has been an interesting topic in research. In a sample involving 227 schoolchildren, manifest caries lesions and dental fillings were significantly associated with gingival inflammation and periodontal disease progression over a three-year observation period (44). Another study of 4,777 Finnish adults revealed that 15% and 17% of the observed root caries was associated with gingival inflammation and with deepened periodontal pockets, respectively (45). Historically, skull remains from the Yayoi people, who dominated the Japanese archipelago between the 5th century B.C. and the 3rd century A.D., exhibited a significant correlation between root caries and alveolar bone loss (46).

Root caries differs from coronal caries due to the different location, anatomy, histology and chemical composition of the dental hard tissues. Root cementum contains about 30% organic material, compared with 2% in enamel. It has been shown that the critical pH for root cementum and dentin, i.e. the pH at which the cementum and dentin are dissolved, is 6.0-6.7, compared with 5.2-5.7 for enamel (47). A wider spectrum of microorganisms might be involved in the root caries process than in enamel caries (48). The risk of root caries development has been associated with the same main factors as for coronal caries, i.e. the host, the microflora and the diet (49). A systematic review of the available literature concluded that the most frequently reported root caries risk indicators were root caries prevalence at baseline, i.e. the past root caries experience, the number of teeth and dental plaque (50).

The relationship between periodontal disease and root caries in particular has been the focus of many research groups. Exposure of the root surface to the oral environment may occur for different reasons; one is following the loss of periodontal attachment in
advanced periodontal disease (51). The limited number of studies that looked into root caries in untreated patients with periodontal disease showed an increased prevalence and is listed in Table 1. Moreover, there are studies that found an increased prevalence and incidence of root caries among periodontally treated patients during the periodontal maintenance phase (52-55). Generally, there was large heterogeneity among the studies in terms of study design, included patients and the reporting of information related to the use of fluoride and general health. Also there weren’t any studies reporting on the relationship between root caries and periodontal disease severity.

Table 1. Studies mentioning the prevalence of root caries in untreated patients with periodontal disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Root caries prevalence</th>
<th>Methods used</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>El-Hadary et al., 1975 (56)</td>
<td>220 patients referred for periodontal treatment</td>
<td>Overall: 42%</td>
<td>Clinical + radiographic</td>
<td>No information regarding the severity of the periodontal conditions, use of fluoride or systemic health &lt;25 teeth: excluded</td>
</tr>
<tr>
<td>Hix and O’Leary 1976 (57)</td>
<td>124 moderate to advanced periodontitis patients referred for treatment</td>
<td>Root caries and/or fillings: 58%</td>
<td>Clinical + radiographic</td>
<td>Patients with systemic conditions or medication were excluded 50 brushed their teeth twice/day 90 did not use floss</td>
</tr>
<tr>
<td>Ravald and Hamp 1981 (58)</td>
<td>31 advanced periodontitis patients randomly selected from 195 consecutive patients referred for treatment</td>
<td>81%</td>
<td>Clinical + radiographic</td>
<td>No information regarding baseline use of fluoride or systemic health</td>
</tr>
<tr>
<td>Ravald and Birkhed 1991 (59)</td>
<td>147 periodontitis patients referred for treatment</td>
<td>80%</td>
<td>Clinical + radiographic</td>
<td>No information regarding the severity of the periodontal conditions, use of fluoride or systemic health</td>
</tr>
</tbody>
</table>

The link between oral and systemic diseases

The link between oral and general health has been suggested since early times, almost as early as history itself. The concept of local or systemic diseases secondary to a localised chronic infection (e.g. in the oral cavity) is usually called focal infection. Its origin can probably be traced back to the time of Hippocrates (60). In 1785, Stoll suggested a relationship between infection of the tonsils and some systemic diseases (61). In 1801, Rush reported that a patient suffering from arthritis of the hip was cured following the extraction of a tooth (62). The period of 1909-1937 has been regarded
as the focal infection era (63). In our time, the evidence linking oral infections, particularly periodontal disease, to other systemic conditions is substantial. It has even been suggested that the term “oral-systemic link” is a misnomer and that it should instead be referred to as the “perio-systemic link” (64). Various mechanisms and theories, including the focal infection concept, have been suggested in order to understand the association (65, 66). To say the least, oral diseases, such as periodontal disease and caries, share a number of contributory factors with several systemic conditions. Smoking, for example, is associated with periodontal disease and cardiovascular disease (67), while certain dietary habits are associated with caries and obesity (68).

**Oral health in patients with cardiovascular disease**

Heart or cardiovascular disease is an umbrella term that refers to a wide range of acute and chronic medical conditions that affect one or more of the components of the heart, thus affecting its ability to function normally. The most common form of heart diseases are coronary artery diseases (CADs). CADs are due to the narrowing or blockage of the coronary arteries, i.e. atherosclerosis, that supply blood to the heart (69). According to the WHO, cardiovascular diseases are the number one cause of death globally (70). An estimated 17.3 million people died from cardiovascular diseases in 2008, representing 30% of all global deaths. Approximately 7.3 million of these were due to CAD. By 2030, almost 23.6 million people are expected to die from cardiovascular disease (70).

Several factors have been suggested as placing people at risk of developing heart disease. These include smoking, aging, male gender, unhealthy diet, physical inactivity, alcohol consumption and the factors comprising the so-called metabolic syndrome, i.e. type 2 diabetes, hyperlipidemia and abdominal obesity (71). There is a large body of epidemiological evidence, most of which is summarised in systematic reviews, indicating that individuals with periodontal disease run a higher risk of developing CAD than periodontally healthy individuals (72-74). On the other hand, there are only a few studies reporting the oral health of patients with coronary artery disease. Table 2 lists some of these studies, which generally show a compromised oral health status in patients with CAD compared with healthy controls. However, there was a large variation between the studies in the used methods and reported outcome.
**Table 2. Studies of dental and periodontal findings in individuals with coronary artery disease (CAD)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design and population</th>
<th>Methods used and outcome</th>
<th>Findings</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mattila et al. 1989 (75)</td>
<td>Case-control matched for age and gender</td>
<td>1) <strong>Total dental index</strong> calculated from clinical and radiographic methods (i.e. caries, periodontal pockets, periapical lesions and pericoronitis) 2) <strong>Pantomography index</strong> calculated from radiographic methods alone 3) Number of artificial teeth</td>
<td>Individuals with MI had significantly higher scores for both indices and more artificial teeth than controls</td>
<td>The test and control groups were divided into two separate subgroups, forming two series of separate comparisons</td>
</tr>
<tr>
<td>Mattila et al. 2000 (76)</td>
<td>Case-control matched for age and social status</td>
<td>1) <strong>Clinical periodontal sum score</strong> (i.e. probing depth, gingival bleeding, suppuration, furcations) 2) <strong>Clinical and radiographic sum score</strong> (i.e. angular bony defects added to previous score) 3) <strong>Panoramic tomography score</strong> (i.e. caries, angular defects, periapical lesions, pericoronitis) 4) <strong>Radiographic periapical and periodontal score</strong></td>
<td>No significant differences between test and control in any of the specified scores</td>
<td>The test group included 30 individuals with a history of acute MI, 31 with recent acute MI and 24 with CAD but no MI. The recruitment of controls was not clear.</td>
</tr>
<tr>
<td>Meurman et al. 2003 (77, 78), Janket et al. 2004 (79)</td>
<td>Case-control matched for age, gender and area of residence</td>
<td>1) <strong>Total dental index</strong> and 2) <strong>Modified dental index</strong></td>
<td>Fewer remaining teeth and more decayed teeth, retained roots and periapical lesions in CAD individuals No differences in any of the constructed indices</td>
<td></td>
</tr>
<tr>
<td>Persson et al. 2003 (80)</td>
<td>Case-control Accounted for gender, smoking, socioeconomic status</td>
<td>Clinical + radiographic</td>
<td>Proportion of alveolar bone loss at different periodontal diagnosis cut-off categories was significantly higher in the acute MI group No difference in number of teeth, root canal treated teeth or periapical lesions</td>
<td></td>
</tr>
<tr>
<td>Renvert et al. 2004 (81)</td>
<td>Case-control matched for age, gender and social status</td>
<td>Clinical + radiographic</td>
<td>Individuals with acute MI had more plaque and bleeding on probing, but less gingival recession. The groups had similar remaining teeth, probing depth and radiographic alveolar bone loss Acute MI was associated with higher scores of the periodontal risk model</td>
<td></td>
</tr>
</tbody>
</table>
Psoriasis is a chronic, immune-mediated inflammatory skin disease with a genetic basis and environmental triggering factors. The pathophysiology is complex, with interactions between the innate and adaptive immune systems (85). Psoriasis is found worldwide, with a frequency of 1–3% in Northern Europe. It is equally common in males and females (86). Usually, the elbows, knees and/or the scalp are involved. Several forms of psoriasis have been reported, with plaque psoriasis being the most common. Chronic plaque psoriasis is characterised by sharply demarcated, erythematous and squamous lesions. Psoriasis in general has been associated with compromised quality of life. In addition, several co-morbidities have been reported. These include diabetes, cardiovascular disease, metabolic syndrome, inflammatory bowel diseases and malignancy (87-89). Between 1% and 39% of patients with psoriasis develop a related rheumatic disease, termed psoriatic arthritis (PsoA) (90).

Several reports on oral health in individuals with psoriasis can be found in the literature, mostly from case reports and from a few case-control studies. A previous study of 200 consecutive patients with psoriasis reported that 10% of the individuals had changes in their oral mucosa, 9.5% had fissured tongues, 3.5% had angular cheilitis and 1% had geographic or smooth tongues (91). Moreover, individuals with psoriasis had significantly more fissured and geographic tongues than controls (92).
Yamada et al. (93) reported that exacerbations of the psoriasis condition were accompanied by gingival epithelial changes and periodontal bursts. Generally, intra-oral manifestations of psoriasis may range from the presence of irregular erythematous lesions with raised yellow to white borders to frank ulcerations and desquamative gingivitis (94). With regard to dental and periodontal findings in individuals with psoriasis, only two comparative studies were found, which suggest a compromised dental and periodontal status in individuals with psoriasis and psoriasis arthritis (Table 3). Further studies in the field may be expected, as streptococcal throat infections in particular are thought to trigger the psoriasis disease onset and can even cause exacerbation of the pre-existing chronic plaque psoriasis (95). It has also been suggested that psoriasis arthritis may predispose to dry mouth and Sjögren’s syndrome (96), which have in turn been associated with a higher caries experience (97).

Table 3. Studies of dental and periodontal findings in individuals with psoriasis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design and population</th>
<th>Methods used and outcome</th>
<th>Findings</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Körönen et al. 1990 (98)</td>
<td>Case-control Test: 1050 psoriasis (Ps) Control: 400 psoriasis arthritis (PsoA)</td>
<td>Questionnaire Self-reported number of remaining teeth and use of removable dentures</td>
<td>&lt; 65 yrs: Ps had more teeth than PsoA Young adults: Females in the Ps group wore more dentures Old adults: Males in PsoA group wore more dentures</td>
<td>There was no negative (i.e. non-psoriasis) control group No information regarding severity of psoriasis conditions</td>
</tr>
<tr>
<td>Preus et al. 2010 (99)</td>
<td>Case-control matched for age and gender Test: 155 Ps Control: 155 non-Ps regular dental clinic attendees</td>
<td>Radiographic</td>
<td>Ps had lower alveolar bone levels and fewer remaining teeth No differences in individuals with or without PsoA</td>
<td>No information regarding severity of psoriasis conditions</td>
</tr>
</tbody>
</table>
**Oral health in individuals with obesity**

In 2008, the WHO estimated that there were more than 1.5 billion adults worldwide who were overweight, i.e. with a body mass index (BMI) of >25 kg/m². Out of these, around 500 million were obese, i.e. with a BMI of >30 kg/m² (100). Today, there is no doubt that obesity is a rapidly growing global health problem, with alarming signs already being noticed early in life. In 2010, nearly 43 million children under the age of 5 were considered overweight (100). By definition, obesity is the degree of excess weight that is associated with adverse health consequences (101). It has been nominated as a potential risk factor for several chronic conditions, such as type 2 diabetes, dyslipidemia, hypertension and CAD (102). An expert panel confirmed abdominal obesity as a central part of the metabolic syndrome; a cluster of multiple risk factors for CAD (103). A hyperinflammatory trait that is associated with changes in circulating free fatty acids and adipose tissue-derived inflammatory markers, i.e. adipokines, is thought to be the driving force behind the more serious health conditions that proceed obesity (104).

In the last 10 years, there has been an explosion of studies investigating the impact of obesity on oral health. Nationwide registries have revealed an increased prevalence of periodontitis among young adults with obesity (105). A positive association between measures of body composition and increasing severity of periodontal disease has also been demonstrated (106). Systematic reviews have confirmed the association between periodontal disease and obesity in different age groups (107-109). With this compelling amount of available evidence, obesity was eventually regarded as a putative risk factor for periodontitis (30). A number of narrative reviews have looked into possible mechanisms in an attempt to explain the association (110, 111). The so-called hyperinflammatory trait may be one direction to examine (112). Other researchers suggest that the psychosocial status of obese individuals would negatively influence lifestyle habits, such as oral hygiene, directly affecting periodontal health (113). With regard to dental caries in relation to obesity, positive associations were reported (114, 115). Researchers suggest that caries and obesity share the same cluster of lifestyle factors, including dietary habits (116). Currently, there is no consensus on the association between caries and obesity. Moreover, the only available systematic review yielded inconclusive results (117). Table 4 lists some studies of oral health in
young individuals with overweight/obesity, generally pointing at a more compromised status. However, the studies differed considerably in many aspects.

Table 4. Studies of dental and periodontal findings in adolescents with overweight/obesity

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design and population</th>
<th>Methods used and outcome</th>
<th>Findings</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larsson et al. 1995 (118)</td>
<td>Cross-sectional Cohort of 181 15-yr olds</td>
<td>Clinical + radiographic</td>
<td>Positive correlation between body mass index (BMI) and caries</td>
<td></td>
</tr>
<tr>
<td>Reeves et al. 2006 (119)</td>
<td>Cross-sectional Cohort of 2,452 13-21 yr olds Data from the 3rd National Health and Nutrition Examination Survey (NHANES III)</td>
<td>Clinical Periodontitis definition: &gt;1 site with at least 3 mm of probing depth and loss of periodontal attachment</td>
<td>111 individuals had periodontitis 13-16 yrs: Not at risk of periodontal disease 17-21 yrs: At risk of periodontal disease</td>
<td>Only non-smokers were included</td>
</tr>
<tr>
<td>Alm et al. 2008 (120)</td>
<td>Cross-sectional Cohort of 402 15 yr olds</td>
<td>Radiographic</td>
<td>Adolescents with high BMI had more approximal caries than those with low BMI</td>
<td></td>
</tr>
<tr>
<td>Modéer et al. 2010 (121)</td>
<td>Case-control matched for age and gender Test: 65 with obesity Control: 65 normal-weights Mean age=14.3 yrs</td>
<td>Clinical + radiographic + saliva samples</td>
<td>Adolescents with obesity had more decayed surfaces, plaque and bleeding on probing, and lower salivary secretion rate</td>
<td></td>
</tr>
<tr>
<td>Modéer et al. 2011 (122)</td>
<td>Case-control matched for age and gender Test: 52 with obesity Control: 52 normal-weights Mean age=14.5 yrs</td>
<td>Clinical + radiographic + gingival crevicular fluid (GCF) samples</td>
<td>Adolescents with obesity had more gingival inflammation, pathological periodontal pockets and GCF levels of IL-1β and IL-8 No difference in alveolar bone levels</td>
<td></td>
</tr>
<tr>
<td>Honne et al. 2011 (115)</td>
<td>Cross-sectional Cohort of 463 13-15 yr olds</td>
<td>Clinical</td>
<td>Adolescents with obesity had more caries than normal-weights</td>
<td></td>
</tr>
<tr>
<td>Franchini et al. 2011 (123)</td>
<td>Cross-sectional Cohort of 98 10-17 yr olds</td>
<td>Clinical</td>
<td>Individuals with obesity had more gingivitis</td>
<td></td>
</tr>
<tr>
<td>Alm et al. 2011 (124)</td>
<td>Repeated cross-sectional Cohort of 671 children (followed from age of 1 to 20 yrs)</td>
<td>Clinical + radiographic</td>
<td>Adolescents at the age of 15 yrs with overweight or obesity had higher caries prevalence</td>
<td></td>
</tr>
<tr>
<td>Zeigler et al. 2012 (125)</td>
<td>Case-control matched for age and gender Test: 29 with obesity Control: 58 normal-weights Mean age=14.6 yrs</td>
<td>Clinical + radiographic + saliva samples + sub-gingival plaque samples</td>
<td>Adolescents with obesity had more plaque and gingival inflammation and lower secretion rate No signs of alveolar bone loss 32 out 40 bacterial species were higher in adolescents with obesity</td>
<td>No information with regard to probing pocket depth Sub-gingival plaque samples collected by means of a single sterile paper point at two tooth sites</td>
</tr>
</tbody>
</table>
Remarks

It appears from the available literature on the different conditions of interest that there was considerable variation between studies in terms of study designs, methodology and accounting for different relevant factors. Consequently, a variation in the reported conclusions may also be observed. Although it is almost impossible to reach a consensus regarding the optimal methodology to be used when investigating a certain topic, this thesis will explore the associations between dental caries, periodontal disease and a number of inflammatory systemic conditions, i.e. CAD, psoriasis and obesity, in a straightforward comparative manner. Recognised up-to-date methodology will be used and common risk indicators will be accounted for. Ultimately, the included investigations would form starting points for future research, in order to help formulate suitable, case-specific prevention programmes that focus on oral health promotion and education and that stress on the importance of frequent dental recall visits. Generally, the first step in conducting effective oral disease prevention programmes in the general population and in specific patient groups, such as those suffering from certain systemic conditions, is to determine the prevalence and characteristics of the oral disease in the targeted population. Assessing the disease experience gives an overview of the prevalence and points for necessary action. Determining the risk, on the other hand, helps to locate points of intervention for the prevention of new cases or for reducing the progression of existing ones.
Aims

The aims of the four parts comprising this thesis were to study:

- the root caries experience and risk in different periodontal disease severity groups (Study I),
- the experience and risk of dental caries and the experience of periodontal disease in individuals with or without coronary artery disease (Study II),
- the experience and risk of dental caries and periodontal disease in individuals with or without psoriasis (Study III) and
- clinical and biological indicators of dental caries and periodontal disease in adolescents with or without obesity (Study IV).
Material and Methods

Ethical considerations

The local ethics committees at the 6 different institutions involved approved the protocols for the four included studies. All the participants were informed about the nature of the studies and gave their written informed consent prior to participation. They were also assured confidentiality with regard to the collected information and were informed about any necessary treatment they ought to seek according to the findings following the different examination procedures. All the respondents were given the choice of not participating or withdrawing from the studies at any time point.

Study samples

A total of 437 participants were included in the different studies comprising this thesis. Table 5 summarises the designs, the sample sizes and types and the study populations of the four studies.

Table 5. Characteristics of the four studies included in the present thesis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample size (N)</th>
<th>Sample type</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Cross-sectional</td>
<td>112</td>
<td>Consecutive</td>
<td>Patients referred for treatment of periodontal disease</td>
</tr>
<tr>
<td>II</td>
<td>Case-control</td>
<td>127</td>
<td>Consecutive</td>
<td>Patients with coronary artery disease (n=54)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vs. Controls with no history of coronary artery disease (n=73)</td>
</tr>
<tr>
<td>III</td>
<td>Case-control</td>
<td>143</td>
<td>Consecutive</td>
<td>Patients with psoriasis (n=89)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vs. Controls with no history of psoriasis (n=54)</td>
</tr>
<tr>
<td>IV</td>
<td>Case-control</td>
<td>55</td>
<td>Consecutive</td>
<td>Adolescents with obesity (n=27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vs. Controls with normal weight (n=28)</td>
</tr>
</tbody>
</table>

Study I

The participants were recruited from those referred to the Periodontics Clinic, College of Dentistry, King Saud University (KSU) in Riyadh, and from the Periodontics Division of the Dental Centre, King Fahd Armed Forces Hospital (KFAFH) in Jeddah, Saudi Arabia. Both clinics are considered major referral centres for the treatment of patients with periodontal disease in the central and north-western regions of Saudi Arabia. The patients were referred from private clinics or from other
departments/divisions within the same centre. They were referred either during the initial phase of treatment or prior to undergoing prosthodontic rehabilitation. Twenty patients were excluded for not fulfilling the inclusion criteria; 10 had only localised periodontal conditions, four had fewer than 20 teeth remaining, four had received periodontal treatment form a hygienist or periodontist within the past six months and two did not have any signs of periodontal disease.

**Study II**

The participants were recruited from one of two centres: the North West Armed Forces Hospitals (NWAFH) in Tabuk, and the King Fahd Armed Forces Hospital (KFAFH) in Jeddah, Saudi Arabia. The cardiology clinics at both hospitals are major referral centres for both the western and north-western regions of Saudi Arabia and they accommodate approximately 6,000 outpatients and 1,500 inpatients each year. The test group included coronary artery disease patients who were either admitted to the hospital through the Department of Cardiology due to angina pectoris or myocardial infarction and were scheduled for catheterisation (n=37, NWAFH), or who were visiting the department for a follow-up after having undergone a recent surgical intervention (n=17, KFAFH). Control individuals with no history of coronary artery disease were recruited from those visiting the acute dental care clinic at the same hospital and were not regular dental clinic attendees. Details on excluded participants can be found in Paper II.

**Study III**

The participants were adults over 40 years of age, who responded consecutively to an advertisement from the Department of Dermatology at the Sahlgrenska University (SU) Hospital in Gothenburg, Sweden. The test group comprised respondents who have been diagnosed with psoriasis for at least 10 years. Both individuals who were undergoing therapy and individuals who were untreated were included. Those to be allocated to the control group for comparison should not have a diagnosis of psoriasis and should be of similar age and gender. Control participants included individuals who responded to a similar advertisement as mentioned above, friends of the psoriatic participants or interested hospital personnel. Details about the dermatology clinic and excluded participants can be found in Paper III.
Study IV

The test participants were adolescents with obesity, who were recruited from the Obesity Clinic at the Queen Silvia Children’s Hospital, Göteborg, Sweden. Controls were healthy, normal-weight, age- and gender-matched individuals, recruited from test individuals’ friends or classmates in order to assume similar lifestyle habits and socio-economic status. Details about the obesity clinic and excluded participants can be found in Paper IV.

Questionnaire

Studies I–IV

All participants answered a self-administered, structured, closed-ended questionnaire about general health conditions and medication, smoking habits, dietary habits, oral hygiene and the use of fluoride.

Oral clinical examination

Studies I–IV

Examinations were carried out using an optimal light source, a dental mouth mirror and a graded periodontal probe. Clinical measurements included the registration of plaque according to Sillness and Löe (126) (Studies I and II) and O’Leary (127) (Studies III and IV), utilising the periodontal probe with no disclosing solution. Marginal gingival bleeding was assessed by applying gentle pressure with the probe along the gingival margin (128) (Studies I–IV). Probing pocket depth, bleeding on probing (Studies I-IV) and gingival recession (Studies I–III) were also registered. These parameters were recorded from four tooth sites, i.e. mesial, distal, facial and lingual. The mid-buccal clinical attachment level was determined in Study II. The registration of plaque and marginal gingival bleeding was made in six representative teeth, i.e. 16, 12, 24, 36, 32 and 44 (Studies I–III), or in two crossed upper and lower quadrants, selected by means of a coin-flip (Study IV). The remaining periodontal measurements were taken from all teeth except third molars.

Dental caries was registered with modifications to the WHO criteria (129). The number of teeth and tooth surfaces with coronal caries or restorations (Studies I–IV), the number of teeth with decayed or filled root surfaces and the number of remaining
teeth (Studies I–III) were registered. Cariological measurements were taken from all teeth except third molars. Caries in a filled surface was scored as caries. White spot lesions were scored as caries (Study IV). Molars and premolars were considered to have five surfaces and the remaining teeth four surfaces. Crowned posterior teeth were scored as five filled surfaces. Caries activity and tooth wear were not registered.

**Oral radiographic examination**

*Studies I–IV*

In Study I, a full set of periapical and bitewing radiographs was available for most referred periodontal disease patients. In Studies II–IV, four bitewing radiographs were taken. Additional periapical radiographs were taken when needed (Studies II and III). All radiographs were evaluated using a light desk and a magnifying viewer. Radiographs were used to assess approximal caries and determine the alveolar bone level in relation to the tooth. Both initial (i.e. a caries lesion in the enamel that has not reached the enamel-dentine junction, or one that reaches/penetrates the enamel-dentine junction but does not extend into the dentine) and manifest (i.e. a caries lesion that clearly extends into the dentine) caries were recorded from approximal tooth surfaces (130). In all studies, the total prevalence of clinical and radiographic caries (initial + manifest), at all tooth surfaces, was reported. Alveolar bone loss was assessed in relation to the tooth root length (131) (Study I) and in relation to the distance from the cement-enamel junction to the alveolar bone crest (132) (Studies II–IV).

**Periodontal case definitions**

Based on clinical and radiographic findings, gingivitis was defined as the presence of gingival bleeding without the associated loss of alveolar bone (17). Periodontitis, on the other hand, was the loss of alveolar bone in conjunction with gingival bleeding (17). The number of involved sites determined the extent of the periodontal condition, i.e. “localised”: <30% of the sites involved, or “generalised”: >30% of the sites involved (132). Categorisation according to the severity of periodontal conditions in the different studies depended on the intended purpose, the available radiographs and for reasons of comparisons with other relevant studies.
Study I

Full-mouth radiographs were available for this study. To allow for comparisons between three distinct periodontal disease groups, alveolar bone loss in relation to root length was evaluated around all teeth and the sub-categories that were used were modified from Hugoson and Jordan (133). Those exhibiting no signs of interproximal attachment loss, yet presented with gingival recession at buccal aspects due to improper toothbrushing habits were allocated to the gingivitis group.

Study II

In Study II, where only bitewing radiographs were available, and to allow for comparisons with other available studies of patients with coronary artery diseases, alveolar bone loss was determined according to the distance from the cement-enamel junction to the alveolar bony crest, in the posterior region [sub-categories modified from Hugoson and Jordan (133)].

Study III

In Study III, again only bitewing radiographs were taken, and there were no previous studies that report the periodontal condition of patients with psoriasis to compare with. The aim was therefore to define periodontal disease cases based on the latest suggested criteria, which can be used in larger periodontitis surveillance studies. The distinction of periodontal disease categories was based on modifications to the Centre of Disease Control and Prevention and American Academy of Periodontology’s recent case definitions (134, 135), accounting for the presence of alveolar bone loss, measured from the cement-enamel junction to the alveolar bony crest in millimetres, and bleeding on periodontal probing in at least two non-adjacent interproximal sites on two different teeth, assessed from the distal aspect of the canine to the mesial aspect of the second molar.

Periodontal risk assessment (PRA)

Study III

The PRA web application was used to illustrate the periodontal disease risk profile (38). Nine selected, periodontitis-related parameters are entered into the web application (details on the nine parameters can be found in Paper III).
After entering the nine parameters, a hexagon-shaped diagram appears on the screen, with each corner representing a parameter or a combination of parameters (an example of a PRA polygon can be found in Paper III). The surface area of the diagram, the size of which is dependent on the entered values, is calculated automatically. As the size of the surface area increases and approaches the outer limits of the polygon representing unfavourable values, the risk of periodontal disease increases.

**Caries risk assessment**

*Studies I–III*

The Cariogram computer program was used to illustrate the caries risk profile (37). Nine selected, caries-related parameters are scored and entered into the program (details on these nine parameters can be found in Papers I, II and III). The scores are based on a numerical scale from 0 to 3 (or 0 to 2), with 0 being the most favourable score and 3 being the least favourable. In Study II, the Cariogram analysis was performed twice: once entering the parameter “related diseases”, and once without. In Study III, the parameter “related diseases” was set at 0 in the control group and 2 in the test group.

The program calculates the risk of future caries based on the nine parameters, using a built-in algorithm. After entering at least seven out of the nine parameters, a pie chart with five sectors appears on the screen (examples of the Cariogram pie-chart can be found in Papers I, II and III). The green sector represents the “actual chance (%) of avoiding new cavities”, the size of which is determined by the other sectors. As the size of the green sector decreases, the risk of caries increases. Each of the remaining four sectors represents a combination of the entered parameters (details can be found in Papers I and II).

**Cariogenic diet**

*Study IV*

A modified dietary assessment that focuses on meal frequency and the amount of 33 specific sugary and snack products commonly consumed by teenagers in Sweden today was carried out (136). These products included common brands of chocolate bars, biscuits, cakes, potato chips, dried fruits, soft drinks and hot beverages. Each
product was scored from 0 to 21 based on the daily/weekly frequency. The mean of all 33 products gave the dietary assessment score.

**Saliva**

*Studies I–IV*

Unstimulated whole saliva samples were collected for estimation of the secretion rate (137) (Studies III and IV). The participants were asked to bend the head slightly forward while sitting on the dental chair and face the floor. They were instructed to open their mouths and allow saliva to drip into a measurement tube for 5 min. The stimulated salivary secretion rate was estimated according to the method described by Heintze et al. (137) (Studies I–IV). The participants were asked to chew on a piece of paraffin wax for 1 min until it softened and then spit the stimulated saliva into a measurement tube while chewing for 5 min.

In Studies I and II, the salivary buffer capacity was estimated by means of a commercial colour strip (CRT® Buffer, Vivacare, Schaan, Liechtenstein), while in Studies III and IV, the original method described by Ericsson (138) was used.

Counts of two cariogenic bacteria in saliva, i.e. mutans streptococci and lactobacilli, were determined on selective agar media (139, 140). In Studies I and II, double-sided, dip-slide commercial kits comprising the special agar plates were used (CRT® Bacteria, Vivacare). In Studies III and IV, basic agar plates were used.

In Study IV, concentrations of sIgA were determined from the stimulated saliva samples using enzyme-linked immunosorbent assays (ELISA) (141).

**Plaque-pH**

*Study IV*

The plaque-pH was determined before (0 min) and at 2, 6, 10, 15, 20 and 30 min after rinsing with 10 mL of 10% glucose solution for 1 min. Indicator strips measuring a pH value in the range of 4 to 7 were used in the interproximal area between teeth 14 and 15 (Spezialindikator, Merck, Darmstadt, Germany) (142). The area under the curve (AUC), representing the change in pH over 30 min after the glucose rinse, was calculated using a computer program (143).
Gingival crevicular fluid (GCF) volume and inflammatory markers

Study IV

GCF samples were obtained from four sites in the premolar-molar region, i.e. the mesial periodontal pockets of teeth 14, 26, 34 and 46. The GCF volume and the concentration of a number of inflammatory markers that are believed to be associated with periodontal disease and/or obesity were determined. Following isolation with cotton rolls, removal of supra-gingival plaque and drying with compressed air, a special filter strip (Periopaper®, Interstate Drug Exchange, Amityville, NY, USA) was gently inserted 1-2 mm into the pocket for 30 s (144). Samples visibly contaminated with blood or saliva were discarded. The GCF volume was determined using a pre-calibrated, fluid-measurement device (Periotron 8000, Harco Electronics Limited, Winnipeg, MB, Canada). The volume was calculated by interpolation from a standard curve for distilled water and expressed as µL GCF. The four GCF samples were placed in separate Eppendorf tubes and stored at -80°C until analysed. Concentrations of nine inflammatory cytokines/adipokines were determined using commercial Bio-Plex Cytokine Assay panels (Bio-Rad Laboratories, CA, USA) and were expressed as pg/mL. The nine inflammatory markers were interleukin (IL) -1β, IL-6, IL-8, tumour necrosis factor (TNF) -α, Leptin, Resistin, plasminogen activator inhibitor (PAI) -1, Adiponectin and Adipsin. The mean values for each marker for the four GCF samples were taken to represent the individual as a unit.

Sub-gingival microbiota

Study IV

A pooled sub-gingival plaque sample was obtained from the mesial periodontal pocket of the six Ramfjord teeth, i.e. 16, 21, 24, 36, 31 and 44, for the determination of the sub-gingival microbiota. After the removal of supra-gingival plaque, sub-gingival plaque samples were collected using individual sterile Gracey curettes. The samples were placed in a single Eppendorf tube containing 0.1 ml of buffering solution and 0.1 ml of 0.5 M NaOH was added to each tube. The samples were then stored in 6°C. The plaque samples were analysed using the checkerboard DNA–DNA hybridisation technique (145) for the detection of 18 microbial species, which are commonly tested for in periodontal disease and caries. The 18 species were Porphyromonas gingivalis, Prevotella intermedia, Pacifastacus nigrescens,
*Tannerella* forsythia, *Fusobacterium nucleatum*, *Aggregatibacter actinomycetemcomitans*, *Treponema denticola*, *Poliana micra*, *Campylobacter rectus*, *Eikenella corrodens*, *Selenomonas noxia*, *Streptococcus intermedius*, *Streptococcus sanguinis*, *Streptococcus mutans*, *Veillonella parvula*, *Capnocytophaga ochracea*, *Streptococcus oralis* and *Actinomyces oris*.

**Statistical analysis**

Means, standard deviations (Studies I–IV) and 95% confidence intervals (Studies III and IV) were used to describe the different study samples. To assess differences between the various groups in terms of continuous variables, a two-samples t-test (Studies I–IV) and analysis of variance (ANOVA) (Studies I–III) were used. Fisher’s exact test, Pearson’s chi-square (Studies I–IV) and the Wilcoxon rank test (Study IV) were utilised for categorical variables. Multiple linear regression analysis (Studies I–IV) and logistic regression analysis (Studies I and II) were used to test for significance in relation to continuous and categorical variables, respectively while controlling for possible confounders. The significance level was set at 5% for most statistical analyses. When comparing the test and control group with regard to a number of inflammatory markers and sub-gingival microbes (Study IV), the significance level was set at 1% to avoid the risk of multiple inference. Intra-examiner (Studies I–III) and inter-examiner (Study IV) reliability testing were performed with regard to selected variables and the kappa value was calculated in each study. The analyses were performed using the SAS® statistical software, version 8.2 (SAS Institute Inc., Cary, NC, USA) (Studies I and II) and IBM® SPSS®, version 20 (IBM, Armonk, New York, USA) (Studies III and IV).
Results

Study I

Caries experience in relation to periodontal disease severity

The prevalence of coronal caries or fillings was 94% for the 112 referred patients and it was almost constant between the three periodontal disease groups. For root caries or fillings in the gingivitis, mild-moderate periodontitis and severe periodontitis groups, the prevalence was 9%, 15% and 29%, respectively (not significant-ns). Figure 2 shows the mean number of decayed teeth in the three groups.

![Bar chart showing mean number of teeth with coronal and root caries in the three periodontal disease severity groups](image)

Figure 2. Mean (± standard deviation) number of teeth with coronal and root caries in the three periodontal disease severity groups. No significant differences between the groups were observed using ANOVA. G= gingivitis group, MP= mild-moderate periodontitis group, SP= severe periodontitis group

Caries risk indicators in relation to periodontal disease severity

The severe periodontitis group had fewer remaining teeth (24 ± 4) than the other two groups (27 ± 2, p<0.05). The severe periodontitis group also had more teeth with gingival recession (13 ± 11) than the mild-moderate periodontitis (7 ± 9) and gingivitis (1 ± 4) groups (p<0.001). No significant differences were detected between the three periodontal disease groups with regard to the remaining caries risk indicators, apart from the presence of one or more systemic condition(s), from which half the studied sample were suffering. Systemic conditions reported by the...
participants included diabetes, hypertension, hypothyroidism, asthma and associated medication. The percentage of subjects with such conditions increased with increasing periodontal disease severity (p<0.05). However, when controlling for the confounders age, gender and smoking by means of multiple linear regression analysis, the association with periodontal disease severity was no longer significant.

Caries risk profiles in relation to periodontal disease severity

According to the Cariogram computer program, the mean chance of avoiding cavities (Chance-AC) in the gingivitis, mild-moderate periodontitis and severe periodontitis groups was 67%, 64% and 58%, respectively (ns). Figure 3 shows the distribution of individuals in the three periodontal disease groups according to the different caries risk categories. From the total of all three groups, a number of indicators contributed to the increased risk in those with Chance-AC<40%, with sub-optimal use of fluoride being the most significant (p<0.001).

Figure 3. The distribution of individuals from the three periodontal disease severity groups with regard to the different caries risk categories according to the Cariogram computer program. No significant differences between the groups were observed using Pearson's chi-square.
Chance-AC= chance of avoiding cavities according to the Cariogram computer program, G= gingivitis group, MP= mild-moderate periodontitis group, SP= severe periodontitis group
Study II

Caries experience and coronary artery disease

Figure 4 shows the significant difference in the number of decayed teeth between individuals with coronary artery disease (CAD) and controls. However, the difference was no longer significant after controlling for the possible confounders medical centre, smoking, diabetes and other systemic conditions by means of multiple linear regression analysis. In both groups, the mean number of teeth with root caries and/or fillings was 1.1.

![Figure 4](image.png)

Figure 4. Mean (± standard deviation) numbers of teeth with caries and fillings in individuals with coronary artery disease (CAD) and controls. Values in **bold** are statistically significant at the 0.05 level using two-sample t-test.

Cariological parameters, risk indicators and coronary artery disease

More individuals from the CAD group reported smaller amounts of daily sugar consumption compared with the non-CAD group (63% and 26% respectively, p<0.001). Significantly more CAD subjects were not using any fluoride products, including toothpaste, compared with controls (70% and 41% respectively, p<0.01). The test group also included more individuals with diabetes (56%) or other systemic conditions such as renal and thyroid dysfunctions (50%) than the control group (5% and 20% respectively, p<0.001). A larger percentage of individuals from the CAD group had a low stimulated salivary secretion rate, i.e. <1.1 ml/min, compared with controls (52% and 30% respectively, p<0.05). Individuals from the CAD group had
more gingival recession \( (p<0.05) \). The differences were no longer significant after controlling for confounders by means of multiple linear regression analysis (Table 6).

Table 6. Differences between CAD and non-CAD subjects with regard to certain carioloigical and periodontal parameters and risk indicators after controlling for medical centre, smoking, diabetes and other systemic conditions by means of multiple linear regression analysis.

BoP = bleeding on probing. PPD = probing pocket depth, CAL-b = clinical attachment level at buccal aspect. \( p \) values presented in bold fonts are statistically significant.

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of remaining teeth</td>
<td>0.027</td>
</tr>
<tr>
<td>Teeth with recession</td>
<td>0.071</td>
</tr>
<tr>
<td>Plaque-harbouring sites (%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sites with BoP (%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Number of sites with PPD &gt;6 mm</td>
<td>0.681</td>
</tr>
<tr>
<td>CAL-b (mm)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

**Caries risk profiles and coronary artery disease**

According to the Cariogram computer program, the mean chance of avoiding cavities (Chance-AC) in the CAD and non-CAD groups was 31\% and 40\%, respectively \( (p<0.05) \). After adjusting for the Cariogram parameter “related diseases”, the corresponding figures were 32\% and 39\%, respectively (ns). Figure 5 shows the distribution of individuals in the two groups according to the different caries risk categories.

![Figure 5](image_url)

Figure 5. The distribution of individuals from the CAD and control groups with regard to the different caries risk categories according to the Cariogram. No significant differences between the groups were observed using Pearson’s chi-square. Chance-AC= chance of avoiding cavities according to the Cariogram, CAD= coronary artery disease.
Periodontal disease experience and coronary artery disease

Figure 6 shows the distribution of individuals, with and without CAD, according to the different periodontal disease severity categories. The control group included more individuals in the healthy-gingivitis categories, while the CAD group had more individuals in the moderate-severe periodontitis categories (p<0.001).

![Figure 6. The distribution of individuals from both the test and control groups with regard to the different periodontal disease categories. The differences between the groups were statistically significant at the 0.001 level using Pearson’s chi-square.](image)

Periodontal parameters, risk indicators and coronary artery disease

Individuals from the CAD group had fewer teeth and more plaque-harbouring sites, bleeding on probing sites and sites with deep pockets than controls (p<0.05). Table 6 shows the significance levels between the groups after controlling for the possible confounders medical centre, smoking, diabetes and other systemic conditions by means of multiple linear regression analysis.
**Study III**

**Caries experience and psoriasis**

Figure 7 illustrates the mean numbers of decayed and filled teeth in individuals with and without psoriasis. No differences between the two groups were observed.

![Graph showing mean numbers of decayed and filled teeth](image)

Figure 7. Mean (± standard deviation) numbers of teeth with caries and fillings in individuals with psoriasis and controls. No significant differences between the groups were observed using two-samples t-test.

**Cariological parameters, risk indicators and psoriasis**

Psoriasis individuals had a lower salivary buffer capacity than non-psoriasis individuals (5.2 ± 1.4 and 5.9 ± 1.3, respectively, p<0.01). This difference remained significant after controlling for possible confounders by means of multiple linear regression analysis (Table 7). Individuals with psoriasis arthritis had lower unstimulated secretion rates than non-psoriasis arthritis individuals, and lower stimulated secretion rates than non-psoriasis controls (p<0.05).

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary BC (pH)</td>
<td>0.011</td>
</tr>
<tr>
<td>Number of remaining teeth</td>
<td>0.018</td>
</tr>
<tr>
<td>Alveolar bone level</td>
<td>0.104</td>
</tr>
</tbody>
</table>

Table 7. Differences between psoriasis and non-psoriasis individuals with regard to certain cariological and periodontal parameters and risk indicators after controlling for smoking, diabetes, age, gender, body mass index, cardiovascular and other systemic diseases and medication by means of multiple linear regression analysis.

p = p value, BC = buffer capacity

P values presented in **bold** fonts are statistically significant.
Caries risk profiles and psoriasis

According to the Cariogram computer program, the mean chance of avoiding cavities (Chance-AC) was 52 ± 21% in the psoriasis group and 56 ± 20% in the control group (ns). Figure 8 shows the distribution of individuals in the two groups according to the different caries risk categories.

![Bar chart showing caries risk profiles](image)

Figure 8. The distribution of individuals from both the test and control groups with regard to the different caries risk categories according to the Cariogram computer program. No significant differences between the groups were observed using Pearson’s chi-square.

Chance-AC = chance of avoiding cavities according to the Cariogram computer program.

Periodontal disease experience and psoriasis

Figure 9 illustrates the distribution of individuals, with and without psoriasis, according to the different periodontal disease severity categories. No differences between the two groups with regard to any of the categories were observed.
Figure 9. The distribution of individuals from both the test and control groups with regard to the different periodontal disease categories. No significant differences between the groups were observed using Pearson’s chi-square.

**Periodontal parameters, risk indicators and psoriasis**

The psoriasis group included more overweight or obese individuals than the control group (78% and 59%, respectively, p<0.05). The psoriasis group also had fewer teeth and lower radiographic alveolar bone levels than controls (p<0.05). The differences with regard to the latter were no longer significant after controlling of confounders (Table 7).

**Periodontal disease risk profiles and psoriasis**

According to the periodontal risk assessment (PRA) web application, the mean PRA polygonal surface area in the psoriasis and non-psoriasis groups was 42.5 ± 24.2 and 27.6 ± 20.5, respectively (p<0.001). Figure 10 shows the distribution of individuals in the two groups according to the different periodontal risk categories.
Figure 10. The distribution of individuals from both the test and control groups with regard to the different periodontal risk categories according to the PRA web application. No significant differences between the groups were observed using Pearson’s chi-square.
Study IV

Caries experience and obesity

Figure 11 illustrates the significant difference in the number of decayed teeth between adolescents with obesity and controls. Similarly, the mean number of decayed surfaces in the obesity and the control groups was 3.4 ± 6.6 and 0.8 ± 1.1, respectively (p<0.05). This difference remained significant after controlling for the possible confounders smoking, age, gender and medication by means of multiple linear regression analysis.

![Bar chart showing decayed and filled teeth in obesity and control groups.](chart.png)

Figure 11. Mean (± standard deviation) number of teeth with caries and fillings in individuals with obesity and controls as shown on bitewing radiographs. Values in bold are statistically significant at the 0.05 level using two-sample t-test.

Cariological parameters, risk indicators and obesity

Both adolescents with obesity and controls presented with similar dietary patterns and daily use of fluoride. However, adolescents with obesity had a lower stimulated salivary secretion rate (1.55 ± 0.63 mL/min) than controls (2.05 ± 1.05, p<0.05). The differences remained significant after controlling for confounders such as medication by means of multiple linear regression analysis, bearing in mind that 30% of the test individuals were on medication. Similarly, the obesity group exhibited remarkably higher concentrations of sIgA than controls after controlling for confounders (p<0.001).
Overall, no significant differences between the groups were observed in terms of plaque-pH drop after the 1-min rinse with the 10% glucose solution. A more pronounced plaque-pH drop was observed in the obesity group following the glucose rinse (ns) (see Figure 2 in Paper IV). However, the area under the constructed pH-time curve (AUC) was similar in both groups (Figure 12).

![Figure 12. Mean (± standard deviation) area under the constructed pH-time curve in individuals with obesity and controls. No significant differences between the groups were observed using two-samples t-test.](image)

Periodontal parameters, risk indicators and obesity

Both groups presented with similar numbers of plaque-harbouring sites and very few sites with deep probing depths. The obesity group, however, had more sites with bleeding on probing, which was statistically significant after controlling for confounders by means of multiple linear regression analysis (p<0.001).

The mean volume of gingival crevicular fluid (GCF) was 0.2 µL in both groups. No significant differences in any of the assessed inflammatory markers in the GCF were observed between the groups (see Table 2 in Paper IV).

Both the obesity and the control groups presented with similar sub-gingival microbial profiles. All plaque samples showed high proportions of *S. oralis, P. gingivalis* and *F. nucleatum*. No significant differences between the groups with regard to any of the assessed bacterial species were observed (see Figure 3 in Paper IV).
Discussion

Study I

Root caries experience and risk in individuals with periodontal disease

In Study I, the prevalence of root caries and/or fillings was 29% in individuals with severe periodontitis and was 17% in the three periodontal disease groups all together. When looking at the available literature (Table 1), the prevalence figures reported from other periodontal disease populations prior to periodontal treatment varied between 35% and 81% (56-59). This variation coincided with variations in study designs and populations, the recruitment and exclusion of participants and the accounting for and reporting of periodontal disease severity and caries contributory factors, such as the use of fluoride and systemic health. In Study I, 25 of the 35 severe periodontitis individuals reported using fluoride toothpaste regularly on a daily basis. In addition, the study sample may have included individuals from high water-fluoride areas in Saudi Arabia (146). However, assumptions related to fluoride do not coincide with the high coronal caries experience, also reported in Study I. It is also worth mentioning that patients with less than 20 teeth were initially excluded. It can be argued that those patients may have had root caries and/or fillings in their remaining teeth. Nevertheless, the exclusion criteria were based on what would fit the scope of the study. Finally, the sample in Study I comprised a wide range of age groups, including those below 25 years of age. It can be assumed that the young age of some of the participants was the reason for the observed lower prevalence of root caries. However, we anticipated that young participants might present with gingival recession due to vigorous oral hygiene practices. Reports confirming this statement have already been published in Saudi Arabia, showing the impact of the improper use of toothbrushes and chewing sticks (i.e. Miswaks) on the prevalence of gingival recession early in life (147-149).

No difference in caries risk was observed between the three periodontal disease groups according to the Cariogram risk assessment model. Although the Cariogram has been shown to be useful in predicting coronal and root caries (150), one of its shortcomings is that it relies on a fixed number of caries-related factors in its assessment of the caries risk. According to the systematic review by Ritter and co-
workers (50), there are around 95 clinical and non-clinical variables that have been tested as root caries risk indicators. In Study I, significantly fewer teeth were observed in the severe periodontitis group and the prevalence of gingival recession significantly increased with increasing periodontal disease severity. The prevalence of root lesions also tended to increase in relation to severity. It can be speculated that different risk profiles would have been illustrated if, for example, the number of teeth, gingival recession and past root caries experience had been accounted for in the assessment.

*Study II*

**Oral disease experience and risk in individuals with coronary artery disease**

In Study II, individuals with CAD had significantly fewer teeth and more sites with plaque, bleeding on probing and moderately deep periodontal pockets than controls, after controlling for confounders. These findings are in agreement with those from other studies (77, 82). It was also observed, both in our study and in another case-control investigation (82), that the CAD group included significantly more individuals with moderate to severe periodontitis than the control group. There are studies, however, which have reported similar numbers of teeth in individuals with or without CAD (80, 151). These somewhat conflicting findings may be related to the differences in study designs and populations and the methods that were used, as the reasons for tooth loss were rarely reported. As in most of the studies, the individuals included in Study II were recruited consecutively from two specific institutions, in one geographic area. Consequently, extrapolation of results to other settings should be performed with caution.

In Study II, it was observed that the number of teeth with root caries or fillings was similar in the CAD and non-CAD groups. In another radiographic investigation (84), the number of teeth with root caries or fillings was significantly higher in the test group than in controls. It should be clarified that all radiolucent lesions in Study II were re-checked clinically to confirm or reject a caries diagnosis. It is therefore possible that some lesions in the study by Friedlander and co-workers (84) may have been overestimated, due to the lack of clinical confirmation in that study.
There are almost no studies that have utilised pedagogic models for assessing the risk of oral diseases in individuals with CAD. Only Renvert and co-workers (81) demonstrated that individuals with acute myocardial infarction (MI) ran a higher risk of developing periodontal disease or further periodontal disease progression than controls, using the functional periodontal pentagon risk diagram (PPRD). In Study II, individuals both with and without CAD ran a high-medium risk of developing future caries according to the Cariogram model, with no differences observed between the groups. However, significant differences were observed with regard to a number of caries risk indicators. For example, individuals with CAD used less fluoride, had lower salivary secretion and had more plaque than controls. On the other hand, non-CAD individuals consumed higher amounts of sugar, had higher counts of salivary mutans streptococci and presented with more decayed teeth than CAD individuals. The differences in caries risk indicators, in spite of the similar risk profiles, indicate that the overall risk is the result of interplay between several different parameters rather than a single parameter. This also underlines the fact that similar risk levels may be due to relatively different underlying risk indicators/factors.

**Study III**

**Oral disease experience and risk in individuals with psoriasis**

In Study III, individuals both with and without psoriasis had a similar experience and risk of dental caries. This could be expected, as the two groups generally had similar dietary habits, comparable levels of oral hygiene and regularly used fluoride toothpaste. The psoriasis group, however, had a significantly lower salivary pH than controls. Psoriasis arthritis individuals, in particular, demonstrated lower stimulated salivary secretion rates. It is worth mentioning that the interest in psoriasis arthritis individuals with regard to caries was based on earlier findings (96, 152), which suggest a reduced salivary function in those individuals. The salivary function is in fact an important line of defence against caries (13) and should be considered when formulating preventive programmes. However, as the overall risk is related to a combination of risk indicators/factors, the lower salivary pH or secretion did not appear to play a crucial role in the findings from Study III.

The psoriasis and the control groups also had a similar experience and risk of periodontal disease. However, fewer remaining teeth and lower radiographic alveolar
bone levels were observed in the psoriasis group compared with controls. These findings are in line with another recent investigation (99). Interestingly, the differences in radiographic alveolar bone levels were no longer significant after controlling for confounders. Radiographic findings alone reflect only the history of periodontal disease. In Study III, no significant differences between the groups were found with regard to periodontal diagnosis based on both clinical and radiographic findings. One explanation for the similar periodontal status that was observed may be the comparable levels of oral hygiene observed in both the psoriasis and non-psoriasis groups.

When going back to the literature, it has been reported that exacerbations of the psoriasis condition were accompanied by periodontal bursts (93). In Study III, the included psoriasis cases were of mild to moderate severity at the time of examination and were undergoing therapy. Whether a more pronounced experience or a higher risk of caries or periodontal disease would be observed in more severe, untreated psoriasis cases, or whether different findings would have been observed if the participants had been followed longitudinally, remain as questions for future research to answer.

**Study IV**

Clinical and biological indicators of caries and periodontal disease in adolescents with obesity

In Study IV, a significantly lower salivary secretion rate was observed in adolescents with obesity than in normal-weight controls after controlling for possible confounders. This is in line with another investigation involving the same age group (121), but is in contrast to another study of younger children (153). One reason may be that 30% of the test individuals included in Study IV were on certain medication, which may affect the salivary secretion (154). Moreover, adolescents with obesity had more decayed tooth surfaces than normal-weight controls, which is in agreement with the findings by Modéer et al. (121). This can be partially attributed to the reduced salivary secretion rate, since the participants in both groups used fluoride toothpaste regularly and had similar dietary habits based on the questionnaire and the simplified dietary assessment. However, the misreporting of dietary information by individuals with obesity cannot be ruled out. A number of studies have shown that individuals
with obesity consume more carbohydrates and have more caries than controls (155, 156, 120).

Individuals with obesity also had higher levels of sIgA than the control group. It has been suggested that sIgA is the main immunoglobulin against mutans streptococci, the bacteria mostly associated with the initiation of dental caries (14). However, the differences between the groups with regard to salivary counts of mutans streptococci were not statistically significant. Thus, the higher sIgA levels may rather be due to the general state of dysimmunoglobulinemia, i.e. unstable levels of immunoglobulins, reported in individuals with obesity (157).

Following the glucose rinse, the pH-drop was more pronounced in the obesity group than in controls (see Figure 2 in Paper IV). This may be explained by the lower salivary secretion (p<0.05), the relatively lower salivary buffer capacity (ns) and the somewhat higher counts of salivary mutans streptococci (ns), that were observed among individuals with obesity. It should be mentioned that the “strip method” (142), used in the present investigation, measures somewhat superficial plaque-pH. Lower values and a more pronounced pH-fall could have been expected if, for example, the telemetric method had been used and the individuals had avoided tooth brushing 2-3 days before the day of the test (158).

The obesity group had more gingival inflammation than the control group, despite the fact that both presented with similar amounts of plaque. These findings differ from those from other investigations, where adolescents with obesity had more gingivitis and more plaque than controls (123, 122). Unlike plaque records, it is known that marginal gingival bleeding reflects how frequently oral hygiene measures are performed (159). It can be assumed that the individuals with obesity focused on toothbrushing and plaque control prior to their oral examination but not necessarily as frequently or efficiently at other times. However, repeated measurements of plaque and gingivitis are needed to assess an individual’s compliance with oral hygiene instructions. Such an assessment is not possible with a cross-sectional examination.

No differences between the groups were observed in terms of GCF volume. Although the same conclusions were reached by Modéer et al. (122), the overall GCF volume reported in their study is double that observed in Study IV. This suggests relatively less gingivitis in our study sample, as it is known that the GCF volume is directly
correlated with gingival inflammation (160). It also supports the hypothesis that the reported gingival inflammation may be transient and is induced by irregular plaque control rather than being chronic in nature or influenced by the systemic condition per se. Furthermore, no differences were observed between the groups with regard to the levels of inflammatory markers in the GCF. This is in contrast to what is mentioned in the literature, where differences in the levels of inflammatory markers in the GCF, in relation to healthy and unhealthy periodontal sites, are expected (161-163). For example, leptin and adiponectin are two hormone-like proteins, secreted primarily by adipose tissue cells, i.e. adipocytes. Leptin suppresses the appetite and increases energy expenditure, while adiponectin has anti-inflammatory properties (164). Leptin was also found to act on bone metabolism (165). It is thought that both leptin and adiponectin are gradually reduced if gingival health changes into gingivitis and then progresses to more severe periodontitis (162, 163). On the other hand, classical cytokines, such as TNF-α and IL-6, are pro-inflammatory and contribute to systemic inflammation, insulin resistance and poor health outcomes (166). It was found that both TNF-α and IL-6 increase with increasing periodontal disease severity (167, 168). It should be noted that the individuals recruited in Study IV suffered, at most, from gingivitis and that deep periodontal pockets and alveolar bone loss were rarely found in either group.

Similar sub-gingival microbial profiles were observed in adolescents with and without obesity. This is in contrast to what has recently been reported, where 23 of 40 species were three times higher in adolescents with obesity (125). These included species such as P. intermedia, P. gingivalis, and T. forsythia, which are recognised putative periodontal pathogens, associated with deep periodontal pockets in adolescents (169). In the present investigation, deep pockets were rarely present in any of the individuals, while no information regarding pocket depth was mentioned in the study by Zeigler and co-workers (125). Moreover, the samples in Study IV were collected using sterile curettes from the six Ramfjord teeth. In the study by Zeigler and co-workers (125), sterile paper points were used to collect the samples from one lower molar and one upper incisor. It is known that pocket depth, sampling technique and the number and distribution of sampled sites may all influence the information obtained from microbial sampling (170). Having said this, an overgrowth of T. forsythia in healthy sulci and in gingivitis pockets in individuals with
overweight/obesity was also reported in a large cross-sectional study (171). Although these authors used sterile curettes to collect sub-gingival samples from the entire dentition, they stated that an important limitation of the study was that it was not originally designed as a case-control investigation. The sample comprised individuals who were enrolled in multiple trials and were not recruited specifically for that study. Comments of this kind limit the conclusions that can be drawn. Generally, and despite the presence of several plausible explanations, the question of why individuals with obesity may exhibit an altered oral microbial flora compared with individuals with normal weight is yet to be clarified.
Conclusions

The main conclusions from this thesis were that:

- no differences in root caries experience or risk were observed in the different periodontal disease severity groups. Of the caries risk indicators examined, the number of remaining teeth decreased and the number of teeth with gingival recession increased with increasing periodontal disease severity (Study I),

- both individuals with and without coronary artery disease were of relatively high caries risk, with no differences in caries experience or risk observed between the two groups. However, individuals with coronary artery disease demonstrated lower salivary secretion rates, sub-optimal oral hygiene and were using less fluoride. The coronary artery disease group also had fewer teeth and more severe periodontal disease than the control group (Study II),

- no differences in the experience or risk of dental caries and periodontal disease were observed among individuals with or without psoriasis. However, the psoriasis group exhibited lower salivary buffer capacity and had fewer teeth than the control group (Study III) and

- more caries and gingival inflammation were observed in adolescents with obesity. Of the clinical and biological indicators examined, salivary secretion rate was lower and sIgA levels were higher in the obesity group compared with controls. No differences between the groups were observed with regard to any of the remaining indicators (Study IV).
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