Temporomandibular disorders in women

Symptoms and signs in populationbased studies

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ABSTRACT

The overall aim of this thesis was to investigate symptoms and signs of temporomandibular disorders (TMD) and orofacial pain in the Swedish female population in relation to some other health factors.

The thesis includes four cross-sectional studies. The specific aim of **Study I** was to analyze the relationship between chronic, severe orofacial pain in women aged 38 and 50 years and signs of depression, anxiety, sense of coherence (SOC) and oral healthrelated quality of life (OHRQoL). The aim of **Study II** was to analyze whether screening questions can be valid in estimating TMD prevalence in epidemiological research. The aim of the longitudinal **Study III** was to analyze the prevalence and incidence of radiographic signs of degenerative joint disorder (DJD) in the temporomandibular joint (TMJ). The aim of **Study IV** was to analyze whether osteoporosis has any relationship with radiographic or clinical signs of TMD in the elderly.

The results showed that 15 % of the women responded positively to questions about TMD-related pain in questionnaires (**II**). The validity of screening questions about TMD pain was considered acceptable (**II**). Of the almost 8 % who reported chronic, severe orofacial pain, it was noted that a larger proportion had signs of depression, anxiety, low SOC and poor OHRQoL. The likelihood of having severe orofacial pain increased if the SOC was low, if there were signs of depression, and if the OHRQoL was affected (**I**). Any clinical diagnosis of TMD was noted in 45 % of the women 38, 50 and 80 years of age, and a pain diagnosis in 21 %. The 80-year-old women rated their pain as less intense. A function diagnosis was found in around 31 % (**II** + **IV**). DJD in the TMJ, assessed on panoramic radiographs, was noted in 18 % at the age of 38 years, gradually increasing to 38 % at the age of 62 years and stable in older age groups at around 45 %. Usually, only one side was affected. The highest incidence of new DJD was seen between 55 and 65 years of age (**III**). Signs of osteoporosis had no association with DJD or a clinical TMD diagnosis (**IV**).

It can be concluded that screening questions are useful in indicating signs of TMD pain in middle-aged women. Orofacial pain that is frequent and intense has a relationship with psychosocial factors. TMD-related pain was reported by 15-20 % in women aged 38, 50 or 80 years, with the elderly reporting a lower intensity. The prevalence of DJD in the TMJ increases with age and the condition usually occurs around the age of 60. Osteoporosis seems to be unrelated to TMD.

Keywords: Degenerative joint disorder, Epidemiology, Oral health-related quality of life, Osteoporosis, Psychological distress, Radiography panoramic, Screening, Temporomandibular joint.

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Sammanfattning på svenska

Det övergripande syftet med avhandlingen var att öka kunskapen om förekomsten av smärta och funktionsstörning i käkarna inom en representativ del av den kvinnliga befolkningen i Sverige samt att undersöka möjliga samband med några andra hälsorelaterade faktorer. I avhandlingen ingår fyra tvärsnittsstudier. Syftet med Studie I var att analysera hur kronisk, frekvent och intensiv ansiktssmärta sammanhänger med 38- och 50-åriga kvinnor avseende tecken på depression, ångest, känsla av sammanhang (SOC) samt oral hälsorelaterad livskvalitet. Syftet i Studie II var att analysera om frågor som används i frågeformulär är användbara för att uppskatta hur vanligt ansiktssmärta och funktionsstörning i käkar är. Den longitudinella Studie III hade syftet att analysera hur vanligt radiologiska tecken på artros i käkled är samt när i livet som detta oftast drabbar kvinnor. Syftet i Studie IV var att analysera om osteoporos har något samband med radiologiska tecken på käkledsartros eller smärta och funktionsstörning i käkarna.

Resultaten visade att andelen medelålders kvinnor som svarade positivt angående ansiktssmärta i frågeformulär var 15 % (**II**). Frågornas validitet i förhållande till klinisk diagnos bedömdes vara acceptabel (**II**). Av de nästan 8% som angav kronisk, svår ansiktssmärta noterades en högre andel med tecken på depression, ångest, låg SOC samt sämre oral hälsorelaterad livskvalitet. Sannolikheten att ha svår ansiktssmärta ökade om SOC var låg, om det fanns tecken på depression samt om oral hälsorelaterad livskvalitet var påverkad (**I**). Klinisk diagnos på smärta eller funktionsstörning i käkar kunde noteras hos 45% av kvinnorna, 38, 50 och 80 år, varav en smärtdiagnos hos 21%. De 80-åriga kvinnorna bedömde smärtan som mindre intensiv än de yngre (**II+IV**). Tecken på artros i käkled, bedömd utifrån översiktsröntgen, noterades hos 18% vid 38 år, gradvis ökande till 38% vid 62 års ålder och runt 45 %, stabilt över tid i äldre åldrar. Oftast var enbart en sida drabbad. Den högsta andelen av nytillkomna formförändringar inträffade mellan 55-66 år (**III**). Förekomst av osteoporos hade inget samband med käkledsartros bedömd från översiktsröntgen eller diagnos på smärta eller funktionsstörningar i käkar. (**IV**).

Slutsatserna är att screeningfrågor är användbara bland medelålders kvinnor för att få en indikation om hur vanligt smärta, relaterad till käksystemet, är. Knappt en av fem medelålders och äldre kvinnor rapporterar smärta i käksystemet. Ansiktssmärta som är frekvent och intensiv har ett samband med psykosociala faktorer. Artros i käkled är vanligt förekommande och uppkommer vanligen runt 60-årsåldern. Osteoporos förefaller inte ha något samband med smärta och funktionsstörning i käksystemet.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. Bäck K, Hakeberg M, Wide U, Hange D, Dahlström L. Orofacial pain and its relationship with oral health-related quality of life and psychological distress in middle-aged women. Acta Odontol Scand. 2019 Aug doi: 10.1080/00016357.2019.1661512
- Bäck K, Hakeberg M, Hange D, Dahlström L. Validity of screening questions for temporomandibular disorders. Findings from the Population Study of Women in Gothenburg. Submitted.
- III. Bäck K, Ahlqwist M, Hakeberg M, Dahlström L. Occurrence of signs of osteoarthritis/arthrosis in the temporomandibular joint on panoramic radiographs in Swedish women. Community Dent Oral Epidemiol. 2017 Oct;45(5):478-484.
- IV. Bäck K, Ahlqwist M, Hakeberg M, Björkelund C, Dahlström L. Relation between osteoporosis and radiographic and clinical signs of osteoarthritis/arthrosis in the temporomandibular joint: a population-based, crosssectional study in an older Swedish population. Gerodontology. 2017 Jun;34(2):187-194.

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Abbreviations

AAOP	American Association of Orofacial Pain
BMD	Bone Mineral Density
CPI	Characteristic Pain Intensity
DC/TMD	Diagnostic Criteria/Temporomandibular Disorders
DJD	Degenerative Joint Disorder
DXA	Dual Energy X-ray Absorptiometry
HADS	Hospital Anxiety and Depression Scale
IASP	International Association for the Study of Pain
NPV	Negative Predictive Value
NRS	Numerical Rating Scale
OA	Osteoarthritis/arthrosis
OHIP	Oral Health Impact Profile
OHRQoL	Oral Health-Related Quality of life
OR	Odds Ratio
PPV	Positive Predictive Value
QoL	Quality of Life
RDC/TMD	Research Diagnostic Criteria/Temporomandibular Disorders
SOC	Sense of Coherence
TMD	Temporomandibular Disorders
TMJ	Temporomandibular joint

1 Introduction

The intention of this thesis was to contribute to the scientific knowledge about temporomandibular disorders (TMD) in the population. The first starting point for the thesis was to investigate whether other common health conditions, such as osteoporosis, served as a negative influence in the management of TMD-related pain.

The concepts of orofacial pain and TMD are closely interrelated [1]. Orofacial pain deals with pain in the oral and facial areas and the diagnoses of TMD pain from the masticatory muscles or the temporomandibular joint (TMJ) are regarded as orofacial pain. Pain is a part of the multidimensional concept of general health, which includes oral health [2, 3]. General health does not only refer to the absence of disease, but also the ability to recover from illness and other problems [3].

Persistent TMD-related pain may be associated with impaired general health and may lead to impaired quality of life [4-6]. Co-morbidity with common mental conditions, such as anxiety and depression, is often found, but much of the information comes from findings in patients in tertiary clinics with referred patients and not from population-based studies [7,8].

1.1 Epidemiology I

Epidemiology is the study of how often diseases occur in different groups of people and why. One of many definitions is 'the study of the distribution and determinants of health-related states or events' [9].

A very important component of epidemiology is the measured outcome in relation to a population at risk. Furthermore, there is also the assumption of a target population about which conclusions are to be drawn. In a majority of cases, observations can only be made on a study sample, which is selected in some way from the target population. To exemplify: in a survey of TMD and its possible associations with other conditions, the target population was all potential TMD sufferers. The study population was defined as all women from an urban area, and a sample of subjects was randomly selected for investigation from this study population. Further extrapolation to the target population; for example, men, remains a matter of judgment. This design is free from systematic sampling error. Furthermore, the epidemiological methodology changes continuously and is adapted from other disciplines, such as mathematics and statistics [10, 11].

The prevalence is the proportion of individuals with a defined condition in a defined population at a given point of time, and it can be captured with a cross-sectional approach. The incidence is the proportion of new cases of a condition within a defined timeframe. Incidence is often reported as the proportion of new cases or as an annual risk. Population-based longitudinal studies are therefore useful for the prediction of individuals at risk, information on associations, and expectations of progress. The observations primarily relate to groups of people.

When reporting a relationship between two conditions, a central issue is to find possible confounders; the confusion of effects. This means that the effect of a condition is mixed with the effect of another variable, leading to bias. When evaluating possible confounders, it is important to know the material and the subject. Many of the factors reported from health research involve socioeconomic status as a confounder [12, 13]. There are different ways to measure socioeconomic status [14]. Common determinants are educational level, social class, income and marital status. Education is an important factor with regard to employment status and income [15]. An assessment of the occupation as an indication of social class has been widely used in research, but since working life has differences between countries, cultures, and over time it has been found that social class is increasingly difficult to determine with this approach [14, 16].

Questionnaires about a number of different conditions are often used in large population-based surveys. To ensure that the burden to participants is not larger than necessary, it is important that the questions or instruments used are validated; i.e., that the researcher knows that the answer is reliable in relation to the condition of interest. Studies in tertiary clinics deal with care-seeking persons, and not a random sample. Data from both population-based groups and care-seeking groups with a higher prevalence are important to expand the understanding and treatment of TMD and orofacial pain [8, 17, 18].

1.2 Temporomandibular Disorders

Temporomandibular disorders (TMD) is a collective term that embraces a number of clinical problems that involve the masticatory muscles, the temporomandibular joint (TMJ) and associated structures [19, 20]. TMD have a musculoskeletal origin and relate to jaw function [19-21].

The most common complaint in care-seeking for TMD is pain, originating from the cheeks, the temporal area or the peri-auricular area. Other symptoms of TMD could be limitation of jaw movements or joint sounds following from intra-capsular derangement or degenerative bony changes in the TMJ [21].

1.2.1 Pain

Pain is a subjective experience and is linked to reactions, both psychological and emotional. The reactions occur regardless of whether or not there is tissue damage. A widely used definition of pain from The International Association for the Study of Pain (IASP) states that "pain is an unpleasant sensory and/or emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [22].

Pain is regarded as chronic, or long-lasting when it persists beyond the expected healing timeframe; longer than three to six months is a guideline [1, 23]. The underlying reasons for chronic pain are often difficult to trace. The consequences of pain in a psychosocial framework are complex and multifactorial, since there is a sensory part, an affective part, and a cognitive part [24, 25].

1.2.2 Musculoskeletal chronic pain

Musculoskeletal pain is normally the body's warning signal about a need for recovery and it is therefore not viewed as a disease. On the other hand, long-lasting pain affecting quality of life is common. About 20 % of the adult population in Europe report moderate to severe low back pain and 25 % report work-related neck/shoulder pain [26, 27].

The transition from an acute to a chronic pain condition is not fully understood and, hence, treatment is difficult [28]. A strong predictor is previous other chronic pain [29, 30]. Long-lasting pain produces changes in the CNS, affecting memory, among other functions [31].

Guidelines and definitions have been developed to identify altered central pain modulation after findings that chronic widespread pain is related to impaired modulatory mechanisms of neurobiological origin [31-33]. In addition, disability due to chronic pain may also be the result of psychological factors, such as fear avoidance, catastrophizing and depression [24, 34, 35].

1.2.3 Sex and gender differences in pain

The response to pain is different between men and women [36]. Musculoskeletal pain, including TMD, has a higher prevalence among women of reproductive age than in other age groups or in men [17, 25, 37]. The factors behind this are contradictory, but biological factors, such as sex hormones, endogenous opioid functions and different genotypes may influence the sensitivity and the level of pain severity in women [38, 39]. Psychosocial causes, for example stress exposure, also affect pain, which perhaps can be captured by the expression female gender instead of female sex [30, 40, 41].

1.2.4 TMD epidemiology and risk factors

TMD is a musculoskeletal disorder that is prevalent in the population [42]. The patient with acute pain in dental care is often suffering from toothache, whereas chronic pain is more often caused by TMD [43]. Overall, about 10 % of the adult population suffer from painful TMD with middle-aged women predominating [17, 44-48]. Complaints of TMD are rare during childhood, but during adolescence (12-19 years), the prevalence increases, especially in girls [49, 50]. An intra-capsular/disc derangement in the TMJ has been found to have a peak below the age of 30, whereas the degenerative bony changes in the TMJ seem to peak above the age of 50 [37]. Persistent TMD have been found to be twice as common in women as in men in the general population and in those seeking help for TMD, the predominance of women is even greater [8, 46, 51].

The annual incidence of TMD pain is reported to be in the range of 2-4 % and transition into more chronic symptoms has been seen in around half the studied groups [52, 53]. TMD can start as an acute condition with some cases turning into intermittent complaints, and it is common that reports of TMD fluctuate, both in adolescents and in adults [52, 54-57].

The etiology and risk factors of TMD are not clearly understood, but chronic TMD seem to have mechanisms that are interrelated with those who report suffering from other chronic musculoskeletal pain conditions, for example fibromyalgia, irritable bowel syndrome and low back pain [53,58-61]. However, the etiology may vary in different groups. Altered pain processing pathways in the nervous system, psychosocial factors, local trauma, bone and connective tissue disorders and negative mood are found to be predictors of TMD [21, 33, 53, 62-69].

1.2.5 Clinical diagnosis of TMD

Historically, the clinical examination and diagnostic system regarding TMD have undergone changes. In Scandinavia, there was rapid development in the 1960s and 1970s, to which, among many others, T. Krogh-Paulsen, U. Posselt, G.E. Carlsson and M. Helkimo contributed. A parallel network, the American Academy of Orofacial Pain (AAOP), has regularly published an international, diagnostic system which has covered many aspects of possible conditions [20]. There was a paradigm shift in the field in 1992, with the incorporation of psychosocial aspects in the TMD assessment, when the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) were developed for research purposes [46, 70]. The ongoing work with reliability and construct validity has transformed the diagnostic system into the Diagnostic Criteria for TMD (DC/TMD) [42, 71]. The DC/TMD criteria

have high sensitivity and specificity for the most common pain-related TMD diagnoses, as well as for some of the intra-articular disorders [72]. The dual-axis system with psychosocial evaluation has a natural position, both in modern TMD research, in clinical practice and in the system recommended by the AAOP. However, the definitions of orofacial pain are an ongoing project [1, 23].

The DC/TMD diagnoses are based on a clinical examination of the jaw-joint system with confirmation by self-reported symptoms during the last 30 days. An important difference between the RDC/TMD and the DC/TMD in diagnosing is that any provoked pain in the DC/TMD examination should be familiar to the subject [42].

The most common TMD diagnoses in samples from both population-based studies and tertiary clinics are related to jaw function, such as disc displacement with reduction, which is usually not painful. A clinical characteristic of disc displacement with reduction is a popping sound during jaw movement. The most common pain diagnosis found in studies is myalgia, pain located to the masticatory muscles [8, 46, 51, 73, 74].

1.3 Oral Health-Related Quality of Life

Quality of Life (QoL) is a concept outlining individual perceptions about positive and negative aspects of life. Life satisfaction deals with many things, including health [75]. In the medical field, the term Health-Related Quality of Life (HRQoL) is used [76]. Health problems and clinical conditions do not always impact QoL and individual attitudes may vary and are modified by different factors, for instance, adaptation, coping, and expectancy [77].

Impacted QoL is a common patient-reported research outcome and is evaluated with psychometric instruments. Within odontology, the term Oral Health-Related Quality of Life (OHRQoL) is used [2, 78]. This concept is considered to include the following main components: functioning (mastication, speech), pain/discomfort (acute, chronic), psychological aspects (appearance, self-esteem) and social aspects (intimacy, communication) [79, 80].

OHRQoL has been measured with different instruments. One of the most widely used since the 1990s is the Oral Health Impact Profile (OHIP) [81]. The OHIP is based on Locker's oral health model [82]. Initially, it included 49 questions but the shorter form, the OHIP-14, was developed after a few years [83]. The OHIP-14 is a well-validated version that has been translated into several other languages [84]. From 2006, a shorter version, the OHIP-5, has been used; however, not as widely as the OHIP-14. This version is also

validated and is considered to relate to the different dimensions in OHRQoL [85, 86]. The OHIP-5 consists of five questions concerning functional limitation, pain, psychological discomfort and physical disability. Symptoms of TMD and a reduced number of teeth are some of the known aspects of oral health that are often associated with poor OHRQoL, together with psychological distress, especially somatization and depression [4-6, 87, 88].

1.4 Psychological aspects

1.4.1 Anxiety and depression

Psychological distress is a general term that is used to describe unpleasant feelings or emotions that impact the level of functioning. Mental conditions, such as anxiety and depression, are common in the population. In a Swedish population study, Johansson et al. found anxiety in 14 %, and depression in 5-10 %, with a higher proportion among women, and with a common comorbidity of anxiety and depression [89]. There are some reports that socioeconomic status influences psychological distress [90]. Persons with TMD-related pain are found to exhibit more signs of depression and anxiety than those who are pain-free [91, 92].

Anxiety disorders are, in part, reactions to anticipation of a future threat. They are characterized both by fear and anxiety and typically include magnification of the danger the individual fears or avoids. Anxiety is often associated with muscle tension. The subject's body prepares for the expected future danger or resorts to avoidant behavior [93].

Depressive disorders have features of sadness, a sense of hollowness or irritable mood. The individual's capacity to function may be affected; for example, cognitive impairment accompanied by somatic changes, such as unexplained long-lasting pain or more vague, debilitating symptoms [93].

There are numerous instruments to measure anxiety and depression. A widely used combined instrument measuring both anxiety and depression, is the Hospital Anxiety and Depression Scale (HADS). The HADS was originally developed in 1983 as a screening instrument [94]. The purpose was to find subjects with clinically significant anxiety and depression in medical non-psychiatric patients.

1.4.2 Sense of Coherence.

The "salutogenic" theory is a social health-related theory, aimed at exploring the correlations between health, stress, and coping [95, 96]. The theory focuses on health rather than disease. Sense of coherence (SOC) is a central concept in

salutogenic theory and is a measure of the capability to use existing resources in order to overcome difficulties and cope with life stressors [95, 97]. The concept consists of three dimensions: comprehensibility, manageability and meaningfulness. SOC interrelates with common mental conditions and an individual with a low SOC often shows signs of anxiety and depression [98, 99].

Since the 1990s, the concept of SOC has been studied with the aim to explore possible associations with different aspects of health [100]. According to the salutogenic theory, the SOC develops during young adulthood. Studies have shown that high SOC scores are related to a higher socio-economic position, perceived good health, good OHRQoL and less chronic pain, including TMD [98, 100-104].

The relationship between HRQoL and SOC for many specific diseases reports a strong protective effect of the SOC against poor HRQoL; for instance, rheumatic disorders, irritable bowel syndrome and mental illness [105, 106]. Regarding OHRQoL, studies have shown that poor OHRQoL is associated with lower SOC scores. The association was independent of other explanatory factors of poor OHRQoL, such as poor self-reported oral health, irregular dental care and socioeconomic factors [102, 107].

1.5 Degenerative Joint Disorder

The most common low-inflammatory joint disease in the body is osteoarthritis/osteoarthrosis [108]. The condition, also called degenerative joint disorder (DJD), includes the acute phase (osteoarthritis), leading to a degenerative process in the joint. The more chronic phase of low-inflammatory osteoarthritis/osteoarthrosis is considered to be less painful [109], and the changes in the shape of the joint on a radiograph remain during the longer, not painful, state, osteoarthrosis [108-110]. Around 2-4 % of the population has the rarer high-inflammatory arthritic condition, with a rheumatic component and more long-lasting pain-related signs [108].

DJD most commonly affects the knee, hip and hand joints. Women are affected more often than men [108, 111]. Age, as in being older than 50 years, is another known risk factor. The etiology of DJD has not been fully elucidated, but biomechanical overload ("wear and tear"), genetics and general disorders are regarded as contributory factors. DJD affects the bone, supporting tissues and articular cartilage of the joint and the TMJ can also be involved [108, 112, 113].

There is no, or a weak, relationship between pain and signs of DJD in the TMJ on radiographs [111, 114]. Radiographically, DJD in the TMJ is characterized by findings, i.a., of osseous erosion, osteophyte formation, subchondral bone cysts, flattening of the articular surface, and sclerosis [115, 116].

Clinical diagnosis of DJD in the TMJ

A clinical diagnosis of not painful DJD (osteoarthrosis) in the TMJ is made from findings of crepitus during jaw movement. Reduced function may be present. In the RDC/TMD system, the diagnosis of osteoarthrosis is made from clinical findings of coarse crepitus and a painless joint [70]. In the DC/TMD system, the diagnosis is made on the basis of the combination of the subject's report of crepitus and clinical findings of crepitus [42]. The diagnosis in both systems can be verified by radiographic findings and it is reported that this increases the reported prevalence [117].

The painful DJD phase (osteoarthritis) is associated with the clinical diagnosis of arthralgia or arthritis, most often not (yet) visible on a radiograph. In the RDC/TMD system the diagnosis of arthralgia requires pain on palpation of the TMJ and a pain history located to the joint area or pain during function. In the DC/TMD system, the diagnosis of arthralgia requires the subject's confirmation of familiar pain on palpation of the joint or during jaw movement. The diagnosis of arthritis in the DC/TMD requires additional history-taking and findings of swelling, edema and/or a lateral open bite. The treatment of painful joint signs and symptoms aims to shorten the painful phase and reduce the degree of change in the shape of the TMJ [112, 113].

Prevalence of DJD in the TMJ

When reporting the prevalence of any DJD, the information generally comes from population-based radiographic surveys [109]. The reports of the prevalence of DJD in the TMJ varies in the literature. Studies have reported frequencies of DJD between 22 % and 70 % [112, 115]. The divergence in data can be explained by the fact that the studies are often based on clinical patient material (tertiary clinics) and a mix of radiographic signs of DJD, clinical symptoms of DJD and the chosen radiographic method. The most reliable method to evaluate DJD in the TMJ is considered to be computed tomography (CT) [118]. Other methods could be cone-beam computed tomography (CBCT), Magnetic Resonance Imaging (MRI), panoramic radiograph (PAN) and tomographs, which all have their own justification and place as methods [114, 119-122].

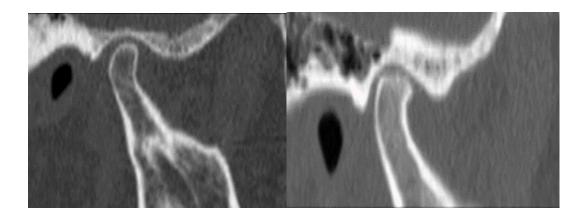


Figure 1 CT showing the TMJ.

To the left. CT showing the TMJ in a 92-year-old woman, not participating in the PPSWG, with no signs of arthrosis. The oral radiology specialist suspects signs of osteoporosis in the trabecular bone,. **To the right.** CT showing the TMJ with signs of arthrosis in a 48-year-old woman

1.6 Osteoporosis

Osteoporosis is a common disorder that is characterized by reduced bone mass, resulting in an increased risk of fragility fractures, especially in the hip. This systemic, metabolic disorder shows defects in the microarchitecture of the bone and the bone remodeling is changed; i.e., bone resorption exceeds bone formation [123-125]. Normal aging results in osteoporosis in both men and women. The shared risk factors include low body mass index, smoking, corticosteroid therapy, genetics and physical inactivity [126]. There are few subjective symptoms, except pain and disability from fractures. Around 21 % of the Swedish female population are classified as osteoporotic with increasing prevalence with age [123].

Women are usually more afflicted than men and it is generally believed to be related to estrogen deficiency after the menopause [123]. Even though osteoporosis and DJD both affect the bone quality, it is reported that the conditions are inversely connected [127, 128]. There are anthropometric differences in persons suffering from osteoporosis compared with DJD [127]. This is not shown regarding DJD in the TMJ, since the loading of the TMJ is not related to body composition.

The diagnosis of osteoporosis is established by measuring bone mineral density (BMD). The recommended method is dual energy X-ray absorptiometry (DXA) where the T-score is established, defined as the number

of standard deviations (SDs) above or below the mean BMD value for young (aged 25–45 years) adults of the same sex. A T-score below -2.5 is regarded as osteoporosis. Osteopenia, a milder form, is rated if the T-score is -1 to -2.5. The bone is considered normal at a T-score above -1. [124]

The relationship between oral health and osteoporosis is unclear. The skull bone may represent a different class of bone [129]. Individuals with osteoporosis may have an increased risk of oral manifestations. However, such a risk has not been definitively proven [130]. It has been found that a person with osteoporotic bone may have difficulty healing after an operation, due to medication, and more often has a reduced number of teeth [131, 132]. Regarding implant survival, periodontal disease, periapical lesions and DJD in the TMJ, the reports are inconclusive [133-138]. The visually sparse trabeculation and cortical erosion of the mandibular bone could be a predictor of the fracture incidence in other bones [139].

1.7 Epidemiology II

Screening methods are commonly evaluated on the basis of the reliability and validity of the test used. The difference between validity, the accuracy of the method, and reliability, the reproducibility of a certain method, is important [140].

1.7.1 Validity

There are different types of validity. The issue of whether the test measures what it is supposed to measure or not is called construct and content validity and is partly a subjective assessment.

The diagnostic accuracy of a test, such as a screening method, is commonly further evaluated with the criterion validity, in comparison with a reference test. The 'true positives' and 'true negatives' are calculated from a two-by-two table. The reported sensitivity is "the ability of an index test to define correctly a positive test result when disease is present", and the specificity is "the ability of a test to define a negative test result when disease is absent" [140, 141]. Positive and negative predictive values can be calculated from the values of sensitivity and specificity. The predictive values are affected by the prevalence.

The estimated 10 % with TMD pain is regarded as a relatively low prevalence. The validity analysis in these settings will probably show high specificity and a high negative predictive value (NPV). Studies have suggested that diagnostic tests for TMD should have a sensitivity of > 70 % and a specificity of > 95 % to be regarded as accurate for the condition [142, 143]. If the sensitivity is high,

the classification of the TMD pain is more particular, and with a lower sensitivity, the classification as "healthy" is more often wrong. If the TMD test is performed in a clinical setting, low sensitivity could prolong the suffering and low specificity could lead to unnecessary treatment.

In calculating the intrarater and interrater reliability, the Kappa value, calculated from the two-by-two table is commonly used. When analyzing the accuracy of an assessment method, for example a radiographic method, the Kappa value is reported together with the sensitivity and the specificity [11].

1.7.2 Assessment of TMD

Epidemiological research into TMD in population-based groups should distinguish between questions related to TMD pain and questions related to TMD function [45, 54, 144-146]. Hence, the criterion validity should be checked against two different reference standards, pain and function. Another issue is the ability to discriminate between TMD-related pain and pain from other structures. However, if a TMD screener is used in general practice, the main problem is to find the persons that could benefit from an extended examination and treatment or a referral. For this reason, the questions mainly refer to pain as this is the most common concern when patients seek help. Since about ten years, two validated sets of screening questions that focus on pain during the last month have been available, the Pain screener and the 3Q/TMD, where the validity is checked in relation to an updated clinical TMD diagnosis system [54, 144, 145]. Their ability to find subjects with TMD pain in general practice is regarded as good. The Pain Screener includes three or six questions about pain and the 3Q/TMD includes two questions about pain and one question about catching of the jaw. With a positive answer in the 3Q/TMD the subject reports a frequency of once a week or more.

From the 1990s, the TMD field has more often reported results from clinical examinations, but in epidemiological surveys, one or more questions were used [8, 45, 146-148]. One of the first epidemiological indices in the TMD field was Helkimo's index from 1974, with one part about the participant's evaluation of the impact of TMD, and another part with objective clinical findings, both pain and function [149]. Helkimo's index was widely used, also as a reference standard, when another set of screening questions in a mail survey was reported by Locker et al. in the 1980s [150]. These questions included the intensity and also the frequency of the pain with the aim to identify pain from the teeth, jaws, oral mucosa and temporomandibular joint without clinical examination. The validity analysis of the TMD questions by Locker et al. in relation to the reference standard showed good accuracy [151].

1.8 Rationale for the thesis

Epidemiological studies are needed to assess the different, potentially negative, consequences of chronic TMD. Many factors influence the prevalence of TMD pain; for instance, well-known factors such as female sex and other bodily pain. However, other aspects also interact with TMD, among them different social and psychological factors. Women are the key population in the majority of these conditions.

A better understanding of how psychological and health factors interact with TMD can lead to improvements in the understanding of women's assumptions in the treatment situation. In the long run, this may contribute to direct the attention to risk factors and, hence, to the well-being of both the individual and society. The screening questions in epidemiological research about TMD have, in some respects, unknown validity. This thesis further aims to elucidate the development of DJD over time.

2 Aim

The overall aim of this thesis work was to gain epidemiological knowledge about temporomandibular disorders (TMD) in a population-based group of women, with regard to the prevalence of signs and symptoms. A further aim was to evaluate methods and explore the possible relationship with some other common health conditions.

2.1 Specific aims

Paper I

To investigate the relationship between subjective symptoms of long-lasting TMDrelated pain and oral health-related quality of life, as well as psychological distress, in a population-based group of middle-aged women.

Hypothesis: Severe orofacial pain has an association with psychosocial factors, but the characteristics of the relationship may be different from that in patient-based samples.

Paper II

To explore the agreement between TMD-related screening questions used in questionnaires in epidemiological studies and in the 3Q/TMD, and a clinical diagnosis using the DC/TMD system in a population-based group of middle-aged women.

Hypothesis: Screening questions are an applicable method to identify women with signs of TMD-related symptoms within epidemiology.

Paper III

To determine the prevalence and incidence of radiographic changes in the temporomandibular condyle, regarded as signs of DJD/osteoarthrosis, in a representative population of middle-aged and older women.

Hypothesis: Signs of DJD are most common among older women.

Paper IV

To elucidate whether osteoporosis is linked to signs and symptoms of TMD, specifically signs of DJD, in a population-based cohort of elderly persons.

Hypothesis: There is no relationship between osteoporosis and DJD in the TMJ or other TMD signs.

3 Patients and Methods

3.1 Study population

This thesis is based on the ongoing Prospective Population Study of Women in Gothenburg (PPSWG), Sweden.

This systematic, cross-sectional and longitudinal study of middle-aged and elderly women was initiated in 1968. Uniquely, the study combined medical and dental health examinations of women. At the age of 70, the women in the PPSWG were also enrolled in a parallel study, the geriatric and gerontological population study called the H70.

The study area, Gothenburg, on the west coast of Sweden, is the second largest conurbation in the country. In 1968, the population was 680 000 and in 2016 it was 988 000 [152]. The total population of Sweden in 2016 was 9.9 million. Sweden is the world's 91st largest country, and situated in the northern part of Europe.

3.1.1 Prospective Population Study of Women in Gothenburg

The initial purpose in 1968 was to investigate anemia and health factors related to the menopause, and the PPSWG was one of few studies with only female subjects at the time. The study was based at the University of Gothenburg and included women aged 38-60 years. Regularly since then, new cross-sectional studies have been performed, at least every twelve years, inviting new women aged 38 and 50 years.

A systematic randomized sampling procedure was used to select women living in the area of Gothenburg from the Swedish Population Register. Women born on specific dates were invited (day 6, 12, 18, 24, 30). In 1968, the study invited 1462 women aged 38, 46, 50 and 60 years [153]. Follow-up examinations have been performed using the same procedure in 1980-81, 1992-1993, 2004-2005 and 2016-2017, with new, younger cohorts [154, 155].

The women selected from the Population register were sent an invitation letter. In later surveys, information was also given by phone. The women were offered a free health examination, including oral health. After accepting to participate in the study, they received a letter with a number of questionnaires. The health examinations were performed in premises arranged by the researchers. The participants met different medical and dental personnel. The examinations carried out included blood sampling, electrocardiography and panoramic radiographic examination of the jaws, among others. During the

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examination day, the women completed additional questionnaires. The systematic procedure and a high participation rate indicated that the PPSWG was representative of the female population in 1968-1992 [154]. The questionnaires have been changed as little as possible between each survey. The number of participating women and the participation rates in the dental examinations are shown in Table 1 and 2.

	2016-17	2004	1992-93	1980-81	1968-69
Born	age (n)	age (n)	age (n)	age (n)	age (n)
1908					60 (78)
1914				66 (125)	54 (172)
1918				62 (295)	50 (390)
1922				58 (305)	46 (421)
1930			62 (268)	50* (323)	38 (356)
1942			50* (98)	38 (109)	
1954		50* (293)	38 (66)		
1966	50* (310)	38 (207)			
1978	38 (263)				
Total	38-50 (573)	38-50 (500)	38-62 (432)	38-66 (1157)	38-60 (1417)
Invited	843**	848	604	1591	1622
Participation rate	68.0 %	59.0 %	71.5 %	72.7 %	87.4 %

Table 1. Number of women, cohorts younger than 70 years of age, participating in the dental part of the PPSWG, including year of birth and age. (*including women who have moved to Gothenburg after the previous study). The total number of invited women and the participation rates are shown. **In 2016, 1038 women were invited, but 195 could not be reached. If these women are included, the participation rate was 55 %.

In the subsequent surveys, after 1968, the same women have been re-invited, in a longitudinal design. New cohorts of 38-year-olds have been invited and in the cohorts of 50-year-olds, women who had moved to the area after the previous survey were also invited with the same inclusion criteria.

The PPSWG comprised physical, social and psychological circumstances, hence, providing information on general and oral health in middle-aged and older women. The study has been able to establish knowledge about changes over time in both individuals and in the population, and also possible determinants in illnesses noted in older ages.

3.1.2 H70/Geriatric and Gerontological Population Study

This, still on-going, study was initiated in 1971 with a cohort of men and women, aged 70 years [156]. The purpose was to contribute to the knowledge of normal aging processes and of normal social and medical conditions within the age group. Longitudinal studies have been performed in cohorts of high

age [157]. The sampling procedure was the same as in the PPSWG. Women from the PPSWG older than 70 years of age participated in 1992, 2000, 2005 and 2010 as a part of the H70 study. Participation rates in the dental examinations are shown in Table 2.

	2010	2005	2000	1992	1980
Born	Age (n)	Age (n)	Age (n)	Age (n)	Age (n)
1908			92 (2)	84 (16)	72 (41)
1914			86 (20)	78 (70)	
1918		87 (124)	82 (101)	74 (201)	
1922	88 (48)	83 (178)	78 (143)	70** (275)	
1930	80 (173)	75 (225)	70 **(248)		
Total	80-88	75-87 (527)	70-92 (514)	70-84 (562)	72 (41)
Invited (n)	516	807	1103	954	64
Participation rate	23.4%	65.3%	46.6%	59.0 %	64.1%

Table 2. Number of participating women in the dental part of the PPSWG and H70 after 1992. Age cohorts 70 years and older, including year of birth and age (**including women who have moved to Gothenburg after the previous study). The number of invited women as well as the participation rates are shown.

3.1.3 Non-participation analysis

To analyze possible differences between participants and non-participants, information from the local fiscal authority together with inpatient and outpatient records were obtained. Some of the information could also be collected through telephone calls or by mail. Income, marital status, mortality, number of teeth and smoking habits were included in the analyses [154, 155, 158]. Among the non-participants in 1968/69, single women were over-represented [153]. A larger proportion of the non-participating women were smokers but showed no significant differences concerning socioeconomic status. [154, 158]. The non-participants, aged 38 and 50 years, in 2004/05 had lower income and more often a background of immigration [155].

Dental status has been followed longitudinally. The non-participants in the follow-up studies were reported to have fewer teeth and the remaining teeth had fewer restorations [158, 159].

In the analysis of the aging participating cohorts, the initial participants were largely characteristic of the general population, even after a long follow-up period [154]. The long-term survival was lower among the initial refusers than the initial participants. In 2000-2001, 64 % of the original participants were alive [160].

3.2 Study methods and measurements

Within the oral health part of the PPSWG, the participants have responded to questionnaires followed by a dental screening examination and further supplemented with a panoramic radiograph. In 2016, there were 127 questions in the oral health questionnaire.

As a part of the questionnaires used in the 1992, 2004 and 2016 surveys, the women made an assessment of subjective pain in the jaws and/or head during the last month, based on studies published by Locker et al. in the 1980s with good accuracy in relation to the reference standard used [151]. The PPSWG questionnaires had four questions about pain in the jaw, face and head. One question about stiff jaws as a sign of milder TMD symptoms was also added. The women rated the questions about pain in the jaw, face and head from three aspects. Firstly, they rated the frequency (never/once a month/once a week/many times per week/daily); secondly, they evaluated the intensity on a 0-100 numerical rating scale (NRS), where 100 is the worst, and thirdly, they rated for how long the pain was noted (less than a week/one week to one month/one to six months/over six months); see formulations in Table 3 and the Swedish version in Appendix. Since three evaluations were made for each pain question, a positive answer did not have obvious characteristics. As a consequence, four groups with varying inclusion criteria, especially regarding pain frequency, were formed and analyzed in Study I and II, see Table 4.

Questions about symptoms during the past month

- 1 Are your jaws and muscles tired/tender/stiff when waking up or moving the lower jaw? (yes/no)
- 2 Do you have pain in your jaw when you chew?
- 3 Do you have pain in your face in front of the ear?
- 4 Do you have pain in your jaw when you open wide?
- 5 Do you have headaches?

Questions 2-5 about pain were three-folded. Firstly, rating how often the pain was noted (never/once a month/once a week/ many times per week/daily). Secondly, rating the intensity on a 0-100 numeric rating scale (NRS) where 100 is the worst. Thirdly, rating for how long the pain was noted (less than a week/one week to one month/one to six months/over six months).

Table 3. The questions, used in the PPSWG, Paper I and II. Based on different combinations of frequencies, intensity and chronicity, four groups were put together: "any TMD symptom", "TMD pain", "TMD pain and headaches" and "severe orofacial pain".

3.2.1 Paper I

In a cross-sectional design, the paper reports on women aged 38 and 50 years in the PPSWG studies in 2004 and 2016. The number of included women is related to the number of completed instruments.

Orofacial pain was measured as a part of the larger self-reported questionnaire on oral health; see Table 3 and 4. Women with reported long-lasting pain of the jaw and head, with a frequency of many times a week or daily, and an intensity ≥ 40 on the NRS were included in the group "severe orofacial pain". The women with severe headaches in the group had simultaneously "any TMD symptoms", otherwise not included in the "severe orofacial pain" group.

Oral Health-Related Quality of Life, OHRQoL, was measured with the fiveitem Oral Health Impact Profile (OHIP-5); see Appendix for the Swedish version [85, 161]. Each item in the OHIP-5 has five choices on an ordinal rating scale: 0 (never) up to 4 (very often), to indicate the degree of severity and the influence on the woman's life. The OHIP-5 has a sum of scores between 0 and 20. Higher values indicate poorer OHRQoL. The mean score was calculated and the OHIP-5 was also dichotomized into good OHRQoL (scoring 3 or 4 on no more than one item) vs. poor OHRQoL (scoring 3 or 4 on at least two items) [162].

Sense of Coherence, SOC, was measured with a questionnaire. The version used is the SOC-13; see the Swedish version in Appendix [95-97]. Each item was scored on a scale from 1-7 points, giving a total range of 13 to 91 points for the SOC score. A higher score indicates a stronger sense of coherence. There are no known cut-off scores. The SOC was also divided into tertiles; three groups based on the individual scores in the total group [104].

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS); see Appendix for the Swedish version [94, 163]. It comprises seven questions on anxiety and seven questions on depression, each with four choices, giving scores from 0-3, maximum 21, on HADS-A and HADS-D, respectively. Anxiety (HADS-A) and depression (HADS-D) are scored separately and higher scores indicate a higher degree of psychological distress. Mean scores, as well as a commonly used cut-off score, ≥ 8 , were used to indicate psychological distress [164].

Marital status was self-reported and stated as not living together (i.e., living alone, unmarried, divorced, widowed or married but not living together), or living together (i.e., co-habiting, married or in a partnership).

Educational level was self-reported and based on years of school attendance. Three levels; low (1-9 years), medium (10-12 years), and high level (\geq 13 years) of education were reported.

	Any TMD symptom	TMD Pain & Headaches		Severe Orofacial Pain Long-lasting and NRS ≥ 40	
		TMD headaches	TMD pain	Severe TMD headaches	Severe TMD pain
TMD symptom - Positive answer on question 1	Yes	Yes		Yes	
TMD pain - Any positive answer on question 2-4, with different frequencies	Yes, ≥ once a month	Yes, ≥ once a month	Yes, ≥ once a week	Yes, ≥ once a month	Yes, many times a week/daily
Headache - Positive answer on question 5		Yes≥ Once a week		Many times a week/daily	
	Paper I and II	Paper II		Paper I	

TMD pain and headaches (II). Positive to TMD pain, question 2-4 in Table 3, added with positive to headache, question 5 (criterion: frequency \geq once a week) and simultaneous "any TMD symptom". **Severe orofacial pain (I).** Long-lasting pain = pain noted longer than one month and \geq 40 on the NRS. Positive in questions 2-4 in Table 3 (criterion: frequency), added with positive to headache question, question 5, with the criterion of frequency \geq many times a week and simultaneous "any TMD symptom".

Table 4 The four groups that was set up from the PPSWG questionnaire; "any TMD symptom", "TMD pain", "TMD pain and headaches" and "severe orofacial pain" that were analyzed in Paper I and II. See formulations of the questions in Table 3.

3.2.2 Paper II

This paper reports on women, 38 and 50 years old, in a cross-sectional design, in a subsample from the PPSWG study in 2016.

A power analysis at a 0.8 % level, sensitivity minimum 0.5, and an estimated prevalence of 10 %, revealed a preferred sample size of 200.

Screening questions for TMD 1, were measured as a part of the larger selfreported questionnaire on oral health, see Table 3 and 4. In relation to reported frequency of pain, three different groups were set up and analyzed. In the "any TMD symptom" group, any positive answer to four questions in Table 3 about TMD symptoms and pain was included, the criterion being once a month or more often. Included in the group "TMD pain" were positive answers to any of the three TMD pain questions but with the frequency criterion once a week or more often. In the "TMD pain and headaches" group, the women with headache once a week or more often were added to the TMD pain group if they reported symptoms of any TMD at the same time. The intensity was rated on an NRS scale of 0-100.

Screening questions for TMD II were measured in the form of the 3Q/TMD and asked verbally [145]. Each of the three questions should be answered with a yes or no. The questions were formulated as follows: Q1: 'During the past month, did you have pain in your temple, face, jaw or jaw joint once a week or more?'; Q2: 'During the past month, did you have pain once a week or more when you open your mouth or chew?'; Q3: 'During the past month, did your jaw lock or become stuck once a week or more?'. The questions were analyzed in different combinations. See the Swedish version in Appendix.

Clinical examination. All participants underwent the standardized clinical examination according to the DC/TMD protocol, axis I [165, 166], and two groups were set up. One group included individuals with any pain diagnosis (myalgia, myofascial pain, headache related to TMD, arthralgia, arthritis), and a second group included the women with any TMJ dysfunction diagnosis (disc displacement with and without reduction, DJD). The women could be included in both groups, depending on their diagnoses. The pain diagnosis group was used as the reference standard in the validity analysis. The intensity of the pain was rated with the CPI [167, 168].

3.2.3 Paper III

This paper reports on the panoramic radiographs from the women in the PPSWG dental examinations in 1968-2011. It is a repeated, cross-sectional and longitudinal cohort study in women aged 38-84 years.

Panoramic radiographs (PAN). The radiographs were evaluated in digital form, and all analog radiographs from the PPSWG were scanned. The presence of flattening (loss of smooth convexity), osteophyte (bony process on the anterior condyle) and erosion (area with diminished cortical density) was evaluated as positive (1) or negative (0) on each side. A summarized assessment, "radiographic normal condyle" or "radiographic signs of DJD", was noted for each radiograph. In the dichotomization, any of three possible alterations of the mandibular condyles could be present and included if both TMJs were rated as readable. Co-training and calibration were performed by an oral radiology specialist, co-author Margareta Ahlqwist (MA), before the evaluations were made.

Computed Tomography (CT). Evaluations of radiographic signs of a change in the shape of the TMJ on CTs for 60 women, aged 38 years and older and not connected to the PPSWG, were made by MA [118]. The corresponding PANs were evaluated by KB, in the same way as with the PANs from the PPSWG. The radiographs were performed and evaluated in 2014-2015.

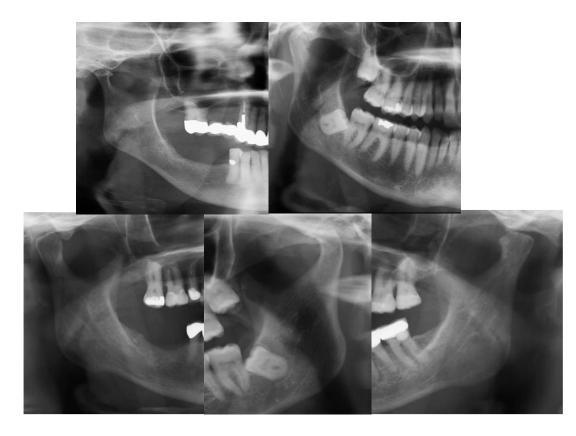


Figure 2. Examples of condylar alterations on panoramic radiographs.

3.2.4 Paper IV

In a cross-sectional design, this paper reports on a subsample of men and women, born in 1930, and aged 75 and 80 years, from the PPSWG and the H70 study in 2005 and 2010, respectively.

Osteoporosis was measured in the form of whole-body Bone Mineral Density (BMD) with dual-energy X-ray absorptiometry (DXA), in the form of T-scores. In the analysis, the inclusion criterion in the group regarded as having low BMD was a T-score of \leq -1 (osteopenia/osteoporosis) [169]. The T-score groups (< -2.5 (osteoporosis), -2.5 - -1 (osteopenia), and > -1 (normal BMD) were also analyzed.

Panoramic radiographs (PAN) The radiographs were evaluated in the same way as in Paper III, resulting in a dichotomous variable, where signs of radiographic change in the condylar form (DJD) were noted.

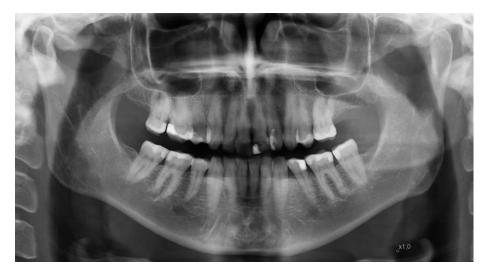


Figure 3. Panoramic radiograph (PAN) performed in 2010 on a woman aged 80 years. Assessed as having no alteration.

Clinical examination The participants in 2010 underwent a clinical examination according to the RDC/TMD [70]. According to the criteria, the diagnosis of osteoarthrosis, RDC III c, assumes no inflammatory disorder, a painless joint and coarse crepitation and/or positive tomographic findings. As tomograms were not performed, one group with clinical findings of osteoarthrosis and/or condylar alteration, as judged from panoramic radiographs, was formed and named the 'arthrosis group'. Two groups were

set up with the persons with a clinical RDC/TMD diagnosis. One group with any pain diagnosis (myofascial pain, arthralgia, arthritis) and one group with any function diagnosis (disc displacement with and without reduction, osteoarthrosis (DJD)).

3.3 Statistics

The statistical analyses in all papers were made with SPSS (versions 19 - 24) and included descriptive statistics, determination for normality, proportions, standard deviation and 95 % confidence intervals (CI). The chi-square test was used for categorical data and a significance level of p < 0.05 was used.

Paper I. Positives in the group "severe orofacial pain" were analyzed in relation to the non-case group. The t test was used for continuous data. A Bonferroni correction, using alpha less than 0.0036, was applied.

A multivariable logistic regression analysis was performed using an enter procedure. The dependent variable was the "severe orofacial pain" group and the independent variables the dichotomized HADS-A, HADS-D, age, examination year, marital status and education (3 levels). The OHIP-5 and SOC-13 were included in the regression analysis as continuous variables. The variables were checked using the Spearman correlation and cross-tabulation. Associations were presented as odds ratios.

Paper II. The t test was used in the analysis of mean values of continuous data. In the validity analysis, the reference standard was the DC/TMD pain diagnosis group. Sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV) and likelihood ratios were calculated for the groups of women with reports of TMD-related pain from the PPSWG questionnaires and from the 3Q/TMD.

Paper III. Intrarater reliability and interrater reliability were calculated with kappa statistics. One hundred and fifty PANs were randomly selected for a second independent evaluation by both KB and MA, two months after the first evaluation.

In the evaluation of the PAN radiographic method to detect signs of condylar alterations, the CTs of the TMJ were used as the reference standard. Sensitivity and specificity were calculated.

The incidence was calculated both as the cumulative proportion in each age cohort that was evaluated as developing condylar alterations between two examination years, and also with life tables, using the actuarial method.

Paper IV. The relationships between the osteopenia/osteoporosis group and the radiographic condylar alterations group, the arthrosis group and an RDC/TMD diagnosis were analyzed. The t test was used in analyzing continuous data.

The radiographs were evaluated on two occasions by the two authors, KB and MA. If no consensus was achieved between these two, a third evaluation was performed.

3.4 Ethics

The Regional Ethical Review Board in Gothenburg, Sweden, has approved the surveys performed by the Population Study of Women in Gothenburg, Sweden (D-nr 65-80, 179-92, Ö402-99, S377-99, S227-00 S069-01, 123-04, 134-05, T453-04, Ö564-03, 075-09, T257-09, 258-16).

Participation in the studies was voluntary. After information verbally and in writing about the purpose of the studies, all participants provided written informed consent. All participants were given an individual code that is administered by the University of Gothenburg. The participants were assured that they could withdraw from the study at any time, without explaining the reason why, and that this would not influence their future medical or dental care.

4 Results

All reported statistical results in this section are statistically significant (p < 0.05), unless otherwise stated. There are no significant differences between the cohorts aged 38 years and 50 years, unless otherwise stated.

4.1 Number of participants

In **Paper I**, 1059 women, 464 aged 38 years and 595 aged 50 years, examined in 2004 or 2016, were included. In **Paper II**, 239 women participated in the clinical examination. The subsample included 104 women aged 38 years and 135 women aged 50 years. In **Paper IV**, 114 men and women were included in the radiographic analysis. In the clinical examination there were 48 women and 40 men, 80 years of age. In **Paper III**, the radiographs from 2383 female participants in the different examination years were evaluated. In the analysis of prevalence and incidence, 4501 PAN's, of the total of 5234 radiographs, were used.

4.2 Symptoms of TMD. Paper I, II, IV

The "severe orofacial pain" group, reported in Paper I, had a prevalence of 7.7 % with a mean pain intensity on the NRS of 60. The women had a frequency of pain many times a week or daily, and three quarters of them had experienced the pain longer than six months. Of the total of 82 women included in the group, 35 had pain located only to the face. Women aged 50 years reported more symptoms; however, not significantly more.

The two sets of screening questions for TMD from the PPSWG and the 3Q/TMD, used in the subsample in Paper II, are shown in Figure 4, with the PPSWG groups "any TMD symptom", "TMD pain" and "TMD pain and headaches". The proportion of the "any TMD symptom" group in Paper I was 29.4 % (95 % CI 26.6-32.1). When analyzing a higher frequency of pain, as in "TMD pain" and "TMD pain and headaches" groups in Paper II, a mean pain intensity of 51 on the NRS was found. In the 3Q/TMD, a positive answer to Q3 was more common among the 50-year-olds.

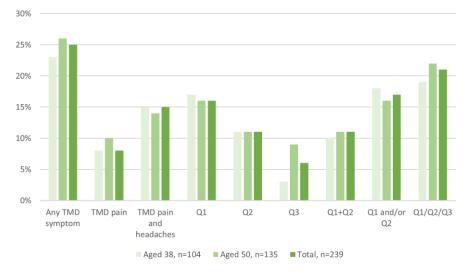


Figure 4. Proportions of positives in the PPSWG groups, and of positive answers to the 3Q/TMD reported by 239 middle-aged women in Paper II.

In Paper II, a validity analysis of the screening questions was performed. The groups from the PPSWG questionnaires and the 3Q/TMD were analyzed in relation to a reference standard, a clinical diagnosis of TMD pain. The specificity was high and the sensitivity moderate in all groups. When judging the best accuracy in relation to the reference standard, prevalence, pain estimates, PPV, NPV and likelihood ratios were considered. Among the PPSWG groups, the "TMD pain" and "TMD pain and headaches" groups were highlighted, and among 3Q/TMD, the Q1 and/or Q2 group. See Table 5.

In the validity analysis of the screening questions in relation to a pain diagnosis, the sensitivity of any combinations of positive to the pain questions in 3Q/TMD, Q1 or Q2, was between 0.46 and 0.65. The specificity was between 0.91 and 0.98. The number of women having a TMJ dysfunctional diagnosis, such as disc displacement with reduction with intermittent locking and disc displacement without reduction with limited opening was five and, therefore, the validity analysis of the Q3 question was not performed. In the validity analysis, the groups "TMD pain and headaches", 14.6 %, and "Q1 and/or Q2", 16.7 %, were regarded as comparable. The "Q1 and/or Q2" group in relation to "TMD pain and headaches": sensitivity: 0.80, specificity: 0.98, see Table 5.

_	Sensitivity	Specificity	PPV	NPV	Positive likelihood ratio	Negative likelihood ratio
PPSWG						
TMD pain	0.35	0.98	0.85	0.86	22.6	0.66
n = 20	(0.22-0.49)	(0.97-1.0)	(0.69-1.0)	(0.81-0.90)	(6.9-73.8)	(0.53-0.81)
TMD pain and						
headaches	0.52	0.95	0.71	0.89	7.6	0.56
n = 35	(0.38-0.66)	(0.92-0.98)	(0.56-0.86)	(0.84-0.93)	(5.1-19.2)	(0.37-0.68)
3Q/TMD						
Q1 and/or Q2	0.62	0.95	0.75	0.91	11.9	0.36
n = 40	(0.49-0.76)	(0.91-0.98)	(0.62-0.88)	(0.87-0.95)	(6.3-22.7)	(0.27-0.57)
Reference standard: 48 women in the DC/TMD pain diagnosis group						
TMD pain and headaches/	0,57	0.98	0.80	0.93	28.5	0.40
Q1 and/or Q2	(0.39-0.75)	(0.97-1.0)	(0.64-0.98)	(0.88-0.98)	(7.6-72.4)	(0.27-0.53)
TMD pain and headaches in relation to Q1 and/or Q2						

TMD pain and headaches in relation to Q1 and/or Q2

Values are given with 95% CI

Table 5. Sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), positive likelihood ratio and negative likelihood ratio, for the screening questions. Reference standard was 48 women in the DC/TMD pain diagnosis group. The table also shows the values for the "TMD pain and headaches group" in relation to the "Q1 and/or Q2" group.

4.3 Clinical diagnosis of TMD. Paper II, IV

Clinical TMD diagnoses, that is, signs of TMD, were obtained in Paper II and IV from women aged 38, 50 and 80 years. The groups with a pain diagnosis and a function diagnosis are shown in Table 6.

The most frequent diagnosis among the middle-aged women was disc displacement with reduction, 24 %, while the most frequent diagnosis in the 80-year-olds was DJD, 17 % (diagnosis IIIc in the RDC/TMD).

A diagnosis of muscular origin was found in 16 % of the 38-year-olds, in 14 % of the 50-year-olds and in 20 % of the 80-year-olds. The 38-year-olds had lower proportions of DJD and arthralgia.

The evaluated intensity of pain on the CPI had a higher mean value in the middle-aged women (51, SD 9) than in the 80-year-olds. Within the

pain diagnosis group, the proportion with a CPI \geq 50 was 58 %, 76 % and 14 %, respectively, in the three age cohorts.

In relation to the non-case group, the pain diagnosis groups had a lower mean opening capacity value; however, not significantly lower among the women aged 38 and 50 years. All middle-aged women with an opening capacity less than 40 mm had a pain diagnosis.

There were no significant differences in proportions between men and women aged 80 years with regard to having any RDC/TMD diagnosis or having a pain diagnosis; however, a higher proportion of the elderly women had signs of DJD.

	38 years old	50 years old	80 years old
Participants (n)	104	135	48
Any diagnosis	43, 41.3 %	66, 48.9 %	20, 41.7 %
	(31.9-50.8)	(40.5-57.3)	(27.7-55.6)
Pain diagnosis ¹	19, 18.3 %	29, 21.5 %	11, 23.0 %
-	(10.9-25.7)	(14.6-28.4)	(11.0-34.8)
Function diagnosis ²	33, 31.9 %	51, 37.8 %	10, 20.8 %
5	(22.8-40.7)	(29.6-46.0)	(9.3-33.2)
Combined pain ¹ and function ²			
diagnosis	9, 8.6 %	14, 10.4 %	1, 2.1 %
-	(3.3-14.1)	(5.2-15.5)	(0-6.2)

Values are given with n, %, (95% CI)

¹Pain diagnoses are myalgia, myofascial pain, referred pain, arthralgia, arthritis.

²Function diagnoses are disc displacement with reduction, disc displacement without reduction, degenerative joint disorder (DJD)/osteoarthrosis

Table 6. The pain diagnosis and function diagnosis groups in women, aged 38, 50 and 80 years. The examination was performed according to the DC/TMD system in cohorts aged 38 and 50 years and according to the RDC/TMD in the 80-year-old cohort.

4.4 Degenerative Joint Disorder. Paper II, III, IV

To facilitate the reading of the following paragraph, the RDC/TMD diagnosis IIIc, osteoarthrosis, in Paper IV will be referred to as the degenerative joint disorder (DJD) diagnosis, almost similar to the DC/TMD diagnosis of DJD in Paper II.

A clinical diagnosis of the non-painful diagnosis of DJD in Paper II and IV was found in 3 % of the 38-year-olds, 14 % of those aged 50 years and in 17 % of the 80-year-olds. When the clinical diagnosis among the women aged 80 years was supplemented with women with signs of radiographic condylar alteration (arthrosis group), their prevalence increased to 48 %.

A clinical diagnosis of painful arthralgia or arthritis was found in 5 % of the 38-year-olds, in 13 % of the 50-year-olds and in 4 % of the 80-year-olds.

Radiographic findings of condylar alterations/DJD in Paper III were found in 18 % at the age of 38 years, 27 % at the age of 50 years and then gradually increasing. At ages older than 70 years, the prevalence was stable around 45 %. Bilateral findings were uncommon. Flattening was the most prominent finding. Both flattening and osteophytes increased over the years while erosion was a rare finding. There was no difference in prevalence between the cohorts born at the beginning or in the middle of the century. The incidence rate between the examination years was between 15 and 24 % and was found to be highest around the age of 60.

In the evaluation of the PAN radiographic method, the sensitivity was 0.59 and the specificity was 0.91. The intrarater reliability of interpreting PAN was $\kappa = 0.76$ and the interrater reliability was $\kappa = 0.63$.

4.5 Other health conditions. Paper I, IV

Headache of any frequency was reported by 52.5 % of the 1059 women in Paper I, and 53 % of these women had headache once a month, the others more often. There was a significant relationship between reports of "any TMD symptom" and reports of headache.

Oral health-related quality of life, reported in Paper I as the mean score on the OHIP-5, was found to be higher in the group with long-lasting severe orofacial pain than in the non-case group. The mean score was 4.5, SD = 3.8, effect size 0.46. The mean score on the OHIP-5 in the total group was 2.2 (SD=2.5). In the five questions/items of the OHIP-5, the severe orofacial pain group had a greater proportion of the highest scores (3 or 4) than the non-case group. Figure 5 shows the proportion of women with high scores (3 or 4) on two or more of the five questions. In the regression analysis, the OHIP-5 revealed a significant association with severe orofacial pain, with an OR of 1.2.

Sense of coherence, the mean value on the SOC-13 score in Paper I, was found to be higher in the group with long-lasting severe orofacial pain. The mean score was 59, SD = 14.2, effect size 0.45. Figure 5 shows the proportion of

women with a score of ≤ 66 (the lowest third in the total group). These significantly different proportions are only presented here and not in Paper I. The mean score on the SOC-13 in the total group was 69.9 (SD = 12.1). In the regression analysis, SOC-13 revealed a significant association with severe orofacial pain, with an OR of 0.95.

Anxiety, rated as the mean score on the HADS-A in Paper I, was found to be higher in the group with long-lasting severe orofacial pain. The mean score was 8.1, SD = 4.6, effect size 0.38. Figure 5 shows the proportion of women with signs of anxiety (score ≥ 8). The mean score on the HADS-A in the total group was 4.8 (SD=5.1). In the regression analysis, signs of anxiety were not significant in explaining the aspect of severe orofacial pain.

Depression, rated as the mean score on the HADS-D in Paper I, was found to be higher in the group with long-lasting severe orofacial pain. The mean score was 5.8, SD = 4.2, effect size 0.39. In the regression analysis, women with signs of depression (score ≥ 8) were twice as likely as women without signs of depression to exhibit severe orofacial pain. Figure 5 shows the proportion of women with signs of depression. The mean score on the HADS-D in the total group was 3.1 (SD = 3.1).

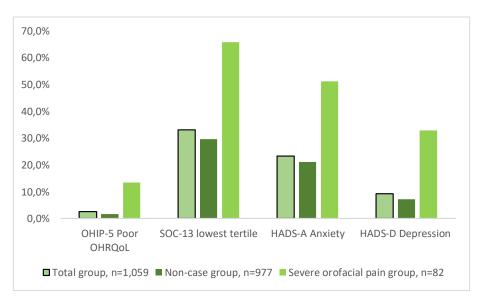


Figure 5. Proportions of poor OHRQoL (score 3 or 4 on more than two items on the OHIP-5), low SOC (within the lowest tertile in the total group), signs of anxiety (HADS-A, score ≥ 8), and signs of depression (HADS-D, score ≥ 8) in Paper I, in 1059 middle-aged Swedish women in the total, non-case and severe orofacial pain group.

In the regression analysis in Paper I, the level of education, marital status, age and participation year were not significant in terms of explaining severe orofacial pain. The proportion of women in the total group with high **education** was 60 % with the highest numbers among the 38-year-olds in 2016. Of the women in Paper I, 48.8 % were **living with a partner**.

Osteoporosis, signs of low BMD, in Paper IV was found in 47.6 % of the women aged 80 years, significantly more often than in men with 21.6 %. No association in relation with radiographic signs of DJD or clinical diagnoses of TMD was found.

5 Discussion

The basis for this thesis was to report on findings of TMD in a populationbased female sample and the relationship with other conditions. The screening questions were designed with the intention to recognize individuals with different impact from pain. The different frequencies of reported TMD pain seemed to influence the accuracy between positive answers to the questions and a DC/TMD pain diagnosis.

Findings of depression, low OHRQoL and low SOC scores were related to an elevated risk of experiencing severe orofacial pain. The pattern from prevalent frequent pain symptoms resembles other musculoskeletal pain conditions. Findings of anxiety did not result in an elevated risk of orofacial pain and this aspect may be a part of the psychological conditions leading to care-seeking behavior.

TMD pain was reported in the screening questions by 10-16 % of the middleaged women. Middle-aged and elderly women had a clinical TMD diagnosis of the same degree, but the pain was regarded as milder in intensity by the elderly women.

DJD in the TMJ and osteoporosis, two common conditions in older ages with approximately the same proportions, do not seem to have any relationship. Radiographic alterations in the TMJ gradually increased during adult life, with only one side affected in most cases. The incidence rate was highest in the older middle-aged women.

5.1 Methodological considerations

The systematic sampling method in the PPSWG is considered to be a good method. The participation rates in the studies up until 1992 were high. In the two latest studies, in 2004 and 2016, with the 38-year-old and 50-year-old cohorts, the participation rate has declined.

Participation rate in epidemiological research in general are calculated to be 40-60%, with these figures applying to dial surveys [170]. Therefore, the participation rate in the two surveys in 2004 and 2016 can be regarded as acceptable. In the PPSWG, the women are asked to attend at least half a day, plus the time required to fill out the questionnaires. There is no economic compensation, and this may influence the willingness to participate. On the other hand, the free health examination, including dental health, may be motivating. Also, many women appreciate the idea of contributing to knowledge about both health and illness. Lissner et al. have highlighted the

importance of home visits to the elderly cohorts to avoid non-participation among those with poor health [160]. This was also applied to the dental part of the PPSWG, with the consequence of there being no PANs for some subjects, although a clinical dental screening examination was performed.

Cohorts of women aged 38 and 50 years may differ with regard to the menopause; hence, the pain experience may be decreased in the older cohort, as mentioned in the introduction about the relationship with hormonal effects. In the analyses in Paper I and II, there were no such differences, the 50-year-olds reported more symptoms, although not significantly more, than the 38-year-old women. In 1992, 15 % of the 50-year-old women had experienced the menopause, but this analysis remains to be performed in the 2004 and 2016 surveys. The menopausal age in cohorts with a high proportion of women with earlier or active hormonal therapy is unclear. There seems to be a trend of increasing menopausal age [171]. Furthermore, in Sweden, a woman aged 50 years, just as a woman aged 38, may perceive work-related stress with high mental demands on time and with responsibility for children under 18 [172].

The chosen criteria for the severe orofacial pain group reported in Paper I were in line with the aim to find the subjects with a pain experience that probably influenced their life. To find high-impact pain cases in epidemiological studies, many factors have to be considered, especially when choosing psychometric tests, screening questions and whether a clinical examination should be performed or not [173]. The criteria for choosing the rating \geq 40 on NRS aimed at catching the expression "moderate to severe pain". If the 0-100 NRS is divided into 3, 4 or 5 categories instead of a continuous scale, the NRS 40 excludes the lower categories ones and catch the higher ones [174-176]. Within the field of TMD, von Korff's graded chronic pain scale (GCPS) is widely used and the included CPI uses 50 as the distinction between grade I and II, whereas others have considered using \geq 30 [145, 167, 174].

The radiographic method with panoramic radiographs has obvious drawbacks. Only condylar changes can be evaluated with any confidence and with good specificity but low sensitivity. The temporal components are assessed with insufficient accuracy. In diagnosing DJD, the reference standard is usually CT and signs of DJD are flattening, osteophytes and erosion. In the definition of DJD/OA, especially of the knee, Kellgren's definitions are often used [108]. There are no clear definitions of the noted alterations in the shape of the TMJ, but remodeling is seen, in part, as a result of normal function [118]. The discussion about the best or acceptable technique and criteria is ongoing. When studying a PAN, due to the low sensitivity, it is not possible to distinguish between remodeling and more definite signs of DJD. There are ethical considerations with the radiation dose if CT is used in a population-based sample [120]. In an epidemiological survey there are also practical and economic issues that could favor PAN. Generally, when studying the prevalence of DJD in other joints in the body, radiographic changes are reported. If a clinical examination is added, the aim is to report the difference in prevalence between painful and not painful joint signs.

5.2 Assessment and prevalence of TMD

The validity analysis showed that reports of TMD pain in two different sets of screening questions could be regarded as being accurate in relation to the reference standard. The analysis was positive, both with regard to the questions formulated earlier (PPSWG), and those formulated more recently (3Q/TMD). The prevalence of TMD pain in middle-aged women could be estimated to be 14 - 16 %.

The analysis showed an acceptable probability that a pain diagnosis was not present when the answer to the pain questions was negative. There was high specificity and a high NPV but a moderately low negative likelihood ratio. The probability that a pain diagnosis was present when the answer to the pain question was positive was regarded as acceptable. The PPV and the positive likelihood ratio were high, even though the sensitivity was low.

When comparing the two sets of questions about TMD-related pain, the PPSWG questions are more detailed, with five questions instead of two and with more choices than the 3Q/TMD. For this reason, they are more difficult to comprehend and analyze. Other epidemiological screening instruments, with more questions, mix questions about pain, function and impact from behavior [45, 146]. Another alternative is to choose a single question, as in the large US study published in 2008; however, the Pain Screener with high sensitivity recommends a minimum of three questions [144, 147].

In recent population-based studies from Sweden and Finland, positive answers to Q1 and/or Q2 from middle-aged women are reported with a prevalence of 15 % and 25 %, respectively [73, 177]. The studies by Lövgren et al., regarding the validity analysis of the 3Q/TMD, report findings similar to those in the present study [178].

TMD include functional disturbances and not only pain. This includes noise from the TMJ during jaw movement, such as clicking and crepitation. TMD also cover conditions that hamper jaw function. To identify those conditions, questions other than pain-related are required. The Q3 in the 3Q/TMD is constructed by experts in the field, and the intention of Q3 was to find subjects with intermittent or definite TMJ locking. In Paper II, the validity analysis of

Q3 could not be performed, since there were few women with these TMJ dysfunctions. The women with positive answers to Q3, most of them 50-year-olds, referred to functional limitation, but its nature is unknown.

The findings of radiographic alterations as signs of DJD in the longitudinal Paper III increased with age; one in five at ages around 40 years and two in five at ages around 60, where the highest incidence was found. This is in line with earlier findings, both in other joints and regarding the TMJ [179]. The underlying reasons for DJD is unknown, since it is not an inflammatory disorder. It could be speculated that findings of DJD in the younger cohorts could be caused by other mechanisms than in older ages. In the reported suggestions for criteria for DJD by Ahmad et al., remodeling is regarded as a reaction to normal function or age but due to the low sensitivity of a PAN, this will probably not be shown [118].

The findings in Paper IV, that the prevalence of DJD increased when a radiographic analysis completed the clinical diagnosis, is in line with other findings [117]. The radiographic evaluations were considered to be performed with acceptable reliability and validity.

There are reasons to believe that the TMD clinical examinations were made with sufficient stringency. Using RDC/TMD criteria, as in Paper IV, intraexaminer reliability is regarded as adequate [180]. The DC/TMD was chosen in Paper II due its reported reliability and validity for the most common TMD diagnoses. It was considered that the DC/TMD could be used as the reference standard also for the criterion validity analysis since the system is structured in detail [72].

Among the 20 % with a pain diagnosis, myalgia was the most common, with elderly women reporting less impact. As mentioned in Paper II, other studies with reports by middle-aged women have a slightly lower prevalence but a tendency of increasing awareness of the jaw system over time [47, 73, 74, 145]. Chronic pain is common in elderly, but TMD in the elderly seem to be a minor issue [37, 181-183]. As mentioned, this may reflect an increased coping ability with age. Additionally, it could reflect the effect of changed hormonal levels in women after the menopause, since, in this study, there were no gender difference regarding TMD diagnoses. The diagnosis of muscular pain in the elderly would probably have had a lower reported prevalence if the women had been examined in the DC/TMD system instead of the RDC/TMD.

Based on the findings from all three clinically examined age groups, it seems that an opening capacity below 40 mm is related to a pain diagnosis. The diagnoses of DJD and arthralgia differed between the 38, 50 and 80-year-old women. The escalated prevalence of arthralgia among the 50-year-olds, as a

sign of possible ongoing formation of DJD, is in line with other studies in relation to incidence age as well as increasing findings of DJD with age [46, 117, 184, 185].

5.3 Psychological and other health aspects

The observed prevalence of TMD and orofacial pain among the women can be related to biological, psychological and social factors [60]. The biological factors, as discussed earlier, are genetic variations and hormonal factors [62, 186]. The social context and general health status may contribute to both TMD and related psychological distress [59,162]. This could affect the treatment of persons with these conditions [28, 187]. The findings in Paper I indicate that women with orofacial pain and HADS scores pointing to signs of anxiety or depression and the SOC score had a significant relationship. However, the effect sizes showed low-to-moderate strength. Findings from the regression analysis regarding the severe orofacial pain group were that signs of anxiety were not significant, in contrast to the OHIP score, the SOC score and signs of depression. The relationship between pain and psychological distress, such as anxiety and depression, is bi-directional. Psychological distress is a risk factor for experiencing pain and pain is a risk factor for psychological distress [188-190]. Treating one of these conditions may contribute to milder symptoms in the other. On the other hand, it is found that depression can influence the outcome of the treatment [33, 188, 189]. Knowing the patient and the different psychological factors provides an opportunity to customize the treatment [28, 191].

As previously found, catastrophizing and somatization are high-risk conditions to experience chronic pain [24, 34, 64, 192]. If treatment could be addressed to the probable cause of pain, together with the apparently most severely affected psychological dimension in a personalized way, the improvement in quality of life, could perhaps be even greater [28, 68, 193]. Pain is one of the most frequent symptoms in care-seeking for TMD and impacts QoL negatively [6, 8, 46]. Pain intensity is recognized as one of the dominant factors and in most circumstances, its assessment relies primarily on the patient's selfreporting, as in the NRS and CPI. It is difficult to capture what constitutes meaningful improvement of pain to an individual patient and it is not known what the "clinically most significant" reduction in pain relief among TMD patients is. The most frequently reported outcome of relief in musculoskeletal pain is suggested to be a reduction ≥ 2 points on a 0-10 scale, or a 33-37 % overall reduction in pain intensity [194, 195]. The setting up of the severe orofacial pain group in Paper I aimed at capturing the women with moderate and severe chronic pain and the mean values on the NRS were 60. On the other hand, the mean value in the subsample from 2016 in Paper II with broader

inclusion criteria was 51. This relatively small difference in evaluated mean intensity between the groups could be an indication that a middle-aged woman recognizes (frequent) pain only when it is of high intensity. The pain intensity among younger women is unknown.

The severe orofacial pain group in Paper I had an association with depression and low SOC scores. The salutogenic perspective (measured by SOC) refers to the use of general resilience and encouraging measures to gain and preserve good health [100]. Among middle-aged women, a stronger SOC was related to a lower risk of severe orofacial pain. It is possible to speculate that lower SOC scores reflect difficulties to cope successfully with pain and that higher SOC scores reflect a strength to cope with threats and stressors rather than problems and illness. There are no guidelines for the interpretation of the individual's SOC level and SOC is formed by life experiences [95, 100]. Interventions to decrease depression and anxiety or increase coping ability may be seen as a good health investment [35]. As shown in Paper I, the association between orofacial pain and psychological distress in the population is similar to that in comparable clinical groups [7, 92, 196]. The aspect of signs of anxiety did not have a significant relation with orofacial pain in the regression analysis and this feature might be linked to care-seeking behavior.

Orofacial pain was found to affect OHRQoL, independently of socioeconomic factors. Reports have found that both the OHIP 5 and the OHIP 14 cover the aspects of OHRQoL in TMD equally well [5, 85]. It is of value to report further on the associations between TMD and OHRQoL in population-based studies [78]. Moreover, van der Meulen et al. reported that OHIP 14 was the version to be applied in TMD cases, but recommended more research [87]. In view of the burden of questions in the PPSWG—127 questions about oral health with the addition of others in the medical part—the shorter OHIP-5 version was preferred.

After whole-body BMD measurements for signs of osteoporosis and crude radiographic evaluations of the condyles for signs of DJD, no association could be found. The clinical TMD examinations did not indicate a correlation either. These findings are in line with the hypothesis and also with the results from general studies of the relationship between osteoporosis and DJD [127]. The study by Klemetti et al., relating to clinical diagnoses of orofacial pain and levels of bone density found no associations either [138]. The findings of osteoporosis/osteopenia in 46 % of the elderly women were in line with the expected prevalence at this age [123].

5.4 Limitations and strengths.

A limitation of this thesis is that the observations are limited to women of this age in Sweden. Furthermore, due to the cross-sectional design, the associations cannot be seen as causal. In Paper I, II and IV, pain from other conditions were not controlled for. If the results are generalized to other groups, caution must be observed. In Paper I, it may be speculated that the effect of socioeconomic status has been underestimated [13]. However, with respect to age and gender, the prevalence of psychological distress in the group of 1059 women was similar to that in other epidemiological studies. In the subsample in Paper II, the PPSWG questionnaire was answered separately but the 3Q/TMD and DC/TMD examination were performed verbally. The three different, yet related sets of questions, followed one another in a rather limited timespan. This may have led to an increasing focus on facial pain among the women and, hence, impacted the prevalence of positive findings in the study [197].

Defining alterations in the TMJ with PAN, as in Paper III and IV, is not the recommended method, as stated earlier. On the other hand, it is unlikely that a population-based study would get ethical approval to perform CT, in view of the large and repeated number of evaluated (healthy) TMJs. In Paper IV, the frequencies of the conditions of osteoporosis and osteoarthrosis, were considered to be high enough to indicate a statistical power in the whole group of men and women, even though there was a risk of type II errors. The BMD examination was performed with other medical considerations but with a random selection of the participants in the H70.

A positive characteristic of the studies was that the PPSWG did not focus on TMD, as the surveys are population-based with the main focus on health. There were moderate to high participation rates in addition to the systematic random selection of a large number of women. Moreover, the cross-sectional design was repeated over a long time period.

6 Conclusion

The overall conclusion of this thesis is that TMD pain was found in 15 % of a representative sample of women aged 38 and 50 years. More frequent and intense orofacial pain was reported by 8 % of the women. A clinical diagnosis of TMD pain was found in 20 % of the women aged 38, 50 and 80 years. The elderly rated a lower pain intensity. The proportion of a clinical diagnosis of DJD was lower than the findings of radiographic alterations. Screening questions aimed at finding subjects with TMD pain in epidemiological surveys were found to have sufficient accuracy. Orofacial pain was associated with more signs of psychological distress and a poorer oral health-related quality of life. TMD and osteoporosis do not appear to be associated.

Paper I. Orofacial pain was associated with poorer OHRQoL and signs of psychological distress. In interpreting the value of the SOC, women with orofacial pain also appear to have a poorer adaptive capacity. The aspect of anxiety may be linked to care-seeking behaviour.

Paper II. Positive answers to screening questions about TMD-related pain in questionnaires and in the 3Q/TMD were indicative of a pain diagnosis from the DC/TMD system in middle-aged women.

Paper III. The prevalence of radiographic signs of DJD in the TMJ evaluated on PAN, including remodeling, increases substantially with age. Around one in five middle-aged women and almost every second woman of older age had some radiographic alteration in the TMJ. The highest proportion with new findings of OA was found among older middle-aged women.

Paper IV. The prevalence of osteopenia/osteoporosis does not appear to be of importance for radiological or clinical findings of DJD in the TMJ.

7 Future perspectives

Further investigations of these cohorts of women could elucidate additional secular trends in TMD symptoms as well as in the other psychometric instruments.

A longitudinal study of the reported pain and the possible relationship with the menopause would provide new insights. In epidemiological research, reports are often performed on cohorts of 10 years, starting at 20 years of age. A conclusion to be made in relation to the menopausal age is that the reports on the women could benefit from another breakdown age. The ages before and after 55 might be a better choice in order to show the possible age differences related to the menopausal age in women.

Further research on the prevalence and criteria of DJD, as well as the underlying reasons, is important.

A discussion about the preferred information to be obtained about TMD in epidemiological research is also important. What do we want to know about function and how do we ask about that? TMD pain is obviously one of the most important parts. It appears that positive answers in the 3Q/TMD Q1 and/or Q2, completed with an evaluation on a 0-10 NRS, may be a suitable combination of questions in large epidemiological surveys.

Further analysis of OHRQoL is important. The dichotomized value could perhaps be used in evaluating TMD treatment outcome. How does OHRQoL change in a longitudinal analysis of TMD?

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Appendix

OHIP-5

Följande fem frågor syftar till att utvärdera i vilken utsträckning ditt munhälsotillstånd påverkar din allmänna livssituation.

1. Har du känt att dina smakupplevelser har försämrats beroende på problem med dina tänder eller munhåla?

- o Aldrig
- o Sällan
- o Ibland
- o Ofta
- o Mycket ofta

2. Har du haft smärta från munhålan?

- o Aldrig
- o Sällan
- o Ibland
- o Ofta
- o Mycket ofta

3. Har du upplevt svårigheter att äta någon föda beroende på problem med dina tänder eller munhåla?

- o Aldrig
- o Sällan
- o Ibland
- o Ofta
- o Mycket ofta

4. Har du känt dig generad beroende på problem med dina tänder eller munhåla?

- o Aldrig
- o Sällan
- o Ibland
- o Ofta
- o Mycket ofta

5. Har du haft svårt att genomföra dina vanliga sysslor beroende på problem med dina tänder eller munhåla?

- o Aldrig
- o Sällan
- o Ibland
- o Ofta
- Mycket ofta

HADS

Dessa frågor har ställts samman för att hjälpa oss att förstår hur du mår. Läs igenom varje påstående och sätt ett kryss i den ruta som bäst beskriver hur du har känt dig den senaste veckan. Fundera inte för länge över dina svar; din spontana reaktion inför varje påstående är förmodligen mer korrekt än ett svar som du tänkt på länge.

1. Jag känner mig spänd eller "uppskruvad"

- För det mesta
- o Ofta
- Då och då
- o Inte alls Aldrig

2. Jag uppskattar samma saker som förut

- Precis lika mycket
- o Inte lika mycket
- Endast delvis
- Nästan inte alls

3. Jag får en slags känsla av rädsla som om någonting förfärligt håller på att hända

- o Alldeles bestämt och rätt illa
- o Ja, men inte så illa
- Lite, men det oroar mig inte
- Inte alls

4. Jag kan skratta och se saker från den humoristiska sidan

- Lika mycket som jag alltid kunnat
- o Inte riktigt lika mycket nu
- o Absolut inte så mycket nu
- o Inte alls

5. Oroande tankar kommer för mig

- Mycket ofta
- o Ofta
- Då och då men inte så ofta
- Bara någon enstaka gång

6. Jag känner mig glad

- Inte alls
- Inte ofta
- o Ibland
- För det mesta

7. Jag kan sitta i lugn och ro och känna mig avspänd

- o Absolut
- Oftast
- Inte ofta
- Inte alls

8. Jag käner mig som om jag gick på "lågt varv"

- Nästan jämt
- Mycket ofta
- o Ibland
- o Inte alls

9. Jag får en känsla av rädsla, som om jag hade "fjärilar i magen"

- o Inte alls
- Någon gång
- o Rätt ofta
- Mycket ofta

10. Jag har tappat intresset för hur jag ser ut

- o Absolut
- Jag bryr mig inte så mycket om det som jag borde
- Jag kanske inte bryr mig om det riktigt så som förut
- Jag bryr mig lika mycket om det som förut

11. Jag känner mig rastlös som om jag måste vara på språng

- Verkligen mycket
- En hel del
- Inte så mycket
- Inte alls

12. Jag ser fram emot saker och ting med glädje

- o Lika mycket som tidigare
- Något mindre än tidigare
- Klart mindre än jag brukade
- Nästan inte alls

13. Jag får plötsliga panikkänslor

- Verkligen ofta
- o Rätt ofta
- Inte så ofta
- o Inte alls

14. Jag kan njuta av en bra bok, ett bra TV- eller radioprogram

- o Ofta
- o Ibland
- Inte så ofta
- Mycket sällan

KASAM (SOC 13)

Här är några frågor som berör skilda områden i livet. Varje fråga har 7 möjliga svar. Var snäll och markera den siffra som bäst passar in på ditt svar. Siffran 1 eller 7 är svarens yttervärden. Om du instämmer i det som står under 1, så ringa in 1:an; om du instämmer i det som står under 7, så ringa in 7:an. Om du känner annorlunda, ringa in den siffra som bäst överensstämmer med din känsla. Ge endast ett svar på varje fråga.

1. Har du en känsla av att du inte riktigt bryr dig om vad som händer runt omkring dig?

1	2	4	5	6	7	
Mycket sällan eller aldrig					Mycket ofta	
2. Har det hänt att du blev överraskad av beteendet hos personer som du trodde du kände väl?						
1	2	4	5	6	7	
Har aldrig hän	ar aldrig hänt Har ofta hänt					
3. Har det hänt att människor som du litade på har gjort dig besviken?						
1	2	4	5	6	7	
Har aldrig hän	t				Har ofta hänt	
4. Hittills har ditt liv:						
1	2	4	5	6	7	
Helt saknat må och mening	àl				Genomgående haft mål och mening	
5. Känner du dig orättvist behandlad?						
1	2	4	5	6	7	
Mycket ofta					Mycket sällan eller aldrig	

6. Har du en känsla av att du befinner dig i en obekant situation och inte vet vad du ska göra?						
1	2	4	5	6	7	
Mycket ofta					Mycket sällan eller aldrig	
7. Är dina dagliga sysslor en källa till:						
1	2	4	5	6	7	
Glädje och dj tillfredsställel	-				Smärta och leda	
8. Har du mycket motstridiga känslor och tankar?						
1	2	4	5	6	7	
Mycket ofta					Mycket sällan eller aldrig	
9. Händer det att du har känslor inom dig som du helst inte vill känna?						
1	2	4	5	6	7	
Mycket ofta					Mycket sällan eller aldrig	
10. Även en människa med stark självkänsla kan ibland känna sig som en "olycksfågel". Hur ofta har du känt det så?						
1	2	4	5	6	7	
Aldrig					Mycket ofta	
11. När något har hänt, har du vanligtvis funnit att du:						
1	2	4	5	6	7	
Över- eller undervärderade dess betydelse					såg saken i dess rätta proportion	

12. Hur ofta känner du att det inte är någon mening med de saker du gör i ditt dagliga liv?

1 2 4 5 6 7 Mycket sällan Mycket ofta eller aldrig

13. Hur ofta har du känslor som du inte är säker på att du kan kontrollera?

2 4 5 6 7 1 Mycket ofta

Mycket sällan eller aldrig

TMD screening frågor

PPSWG TMD I i artikel II

1. Brukar du bli trött, öm eller stel i tuggmusklerna och käkarna när du vaknar på morgonen eller när du rör på underkäken? Ja/nej

2. Har du under den senaste månaden känt smärta från käken vid tuggning?

3. Har du under den senaste månaden känt smärta i ansiktet strax framför örat?

4. Har du under den senaste månaden känt smärta vid stor gapning?

5. Har du under den senaste månaden känt huvudvärk?

Fråga 2-5 har inga ja/nej utan följdfrågor. A. Hur ofta? (aldrig/någon gång per månad/någon gång per vecka/). B. Intensitet värderas på en sifferskala 0-100 där 100 är värst. C. Hur länge? (mindre än en vecka/1 vecka-1 månad/1-6 månader/mer än 6 månader).

3Q/TMD TMD II i artikel II

1. Har du den senaste månaden haft ont i tinningen, ansiktet, käklederna eller käkarna en gång i veckan eller oftare? Ja/nej

2. Har du den senaste månaden haft ont när Du gapar eller tuggar en gång i veckan eller oftare? Ja/nej

3. Har du den senaste månaden haft låsningar eller upphakningar i käken en gång i veckan eller oftare? Ja/nej