Temporomandibular disorders
Incidence, course, and risk factors

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To Per-Ivan, Andreas and Daniel
ABSTRACT

Temporomandibular disorders (TMD) embrace pain and dysfunction in the temporomandibular joint (TMJ) and jaw muscles. TMD is a prevalent condition in the population and constitutes a significant health problem. Knowledge of factors influencing the onset and course of TMD is important in preventive care and development of treatment strategies as well as in clinical decision making. The aim of this thesis was to gain knowledge of whether variations in dental occlusion, bruxism, spinal pain and gender predicted the development and course of TMD.

The study population comprised 371 undergraduate dental students. A questionnaire was used to obtain case histories. Clinical examination included the function of the TMJ, jaw muscles, maximal jaw mobility, the morphological occlusion, and contact patterns in centric and eccentric positions. The examinations were performed at start, and after 12 and 24 months. In total, 280 subjects were examined at all three occasions. The incidence of TMJ pain and dysfunction was high among both males and females. The course composed onset, recovery and maintenance resulting in a fluctuating pattern. Females were more likely to have persistent TMJ pain and dysfunction than males. The incidence and persistence of jaw muscle signs and symptoms was high and significantly more common in females. A similar fluctuating pattern as for TMJ pain and dysfunction was found. Crossbite predicted onset and persistence of TMJ pain and dysfunction; mandibular instability in centric positions predicted persistent TMJ pain and dysfunction, as well as persistent jaw muscle signs or symptoms. Reported bruxism increased the risk for TMJ pain and dysfunction but did not significantly affect the course of jaw muscle signs and symptoms. Spinal pain at baseline predicted the onset of jaw pain, headaches, and TMD pain. Signs of TMD at baseline predicted the onset of non-pain symptoms of TMD, jaw pain, headaches, and spinal pain.

In conclusion, the results in this thesis show high incidence rates for TMD, headaches, and spinal pain among dental students. Crossbite, mandibular instability, reported bruxism, as well as female gender were identified as contributing risk factors. Spinal pain and TMD mutually predicted each other, indicating common pathophysiological mechanisms and individual vulnerability. The findings support a multidisciplinary approach, and it is recommended that the status and function of the jaw system be considered in patients with spinal pain.

Key words: bruxism, dental occlusion, gender, headaches, longitudinal, myofascial pain, orofacial pain, prospective cohort, risk factors, spinal pain, temporomandibular joint
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### ABBREVIATIONS AND DEFINITIONS

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<tr>
<td>TMD</td>
<td>temporomandibular disorders</td>
</tr>
<tr>
<td>TMJ</td>
<td>temporomandibular joint</td>
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<tr>
<td>Bruxism</td>
<td>tooth grinding or clenching</td>
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<tr>
<td>Incidence</td>
<td>the number of new cases within a specified time period divided by the total number of individuals at risk at the beginning of the period</td>
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<td>Negative predictive value</td>
<td>the probability of not having a condition, given a negative test result</td>
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<td>Pain</td>
<td>“an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” by the International Association for the Study of Pain, IASP (Loeser and Treede, 2008; Merskey et al., 1994)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>the probability of having a condition, given a positive test result</td>
</tr>
<tr>
<td>Prevalence</td>
<td>the number of cases with a condition in a population, divided by the total number of individuals in the same population</td>
</tr>
<tr>
<td>Risk factor</td>
<td>a variable associated with an increased risk of disease or event</td>
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<tr>
<td>Sensitivity</td>
<td>the number of persons identified as having a condition divided by all with the condition</td>
</tr>
<tr>
<td>Specificity</td>
<td>the number of persons identified without a condition divided by all without the condition</td>
</tr>
<tr>
<td>Spinal pain</td>
<td>pain in the neck, shoulders, or back</td>
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This thesis is based on the following original papers, which will be referred to in the text by their Roman numerals:


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INTRODUCTION

Risk assessment

Knowledge and understanding of factors associated with the development and course of a disease or illness are fundamental for preventive care and treatment. Evaluation of a patient’s risk to develop or to progress in a disease as well as the probability to remain healthy or to recover is essential in the clinician’s daily decision making.

Determinants of disease development are more commonly referred to as risk factors. The term risk expresses the probability of a certain event occurring in a specific time period. Risk can be estimated by observing a population free from the specific condition at the beginning of the observation period, i.e., at risk. A risk factor may also contribute to the progress of the condition in focus. Clinical examinations or tests are used to establish a diagnosis among persons with illness. Ideally, affected persons should be correctly distinguished from unaffected persons and differentiated from those with other diseases without any mistake. A test with a high specificity produces a low proportion of false-positive results and a test producing a low proportion of false-negative results is described as having a high sensitivity. Predictive values, positive or negative, estimate the probability of a disease or condition to occur among people, given a certain test result or presence of a specific risk factor. The predictive values are highly dependent on the prevalence of the disease in focus (Altman, 1991; Scheutz, 2007).

Epidemiology is a fundamental methodology in health research and may be descriptive, analytic or interventive, focusing on distribution and determinants of health and disease in a population. A main purpose of epidemiology is to gain knowledge as to why certain individuals develop a particular disease or a specific condition while others do not. Prevalence is an estimate of the number or proportion of cases with a certain disease or condition in the population at a specific time. It is useful for descriptive purposes and for assessment of treatment needs. It may also be used to follow up changes in health status in a population over time and as a justification for allocation of resources for prevention or healthcare. The term incidence is related to onset of disease and explains the rate at which new cases occur in a population, making cause and effect analyses possible (Scheutz, 2007). Prevalence is a function of incidence and the duration of the disease. Knowing the natural course of a disease is thus one key in the decision making process.
In health care it is essential to study the correlation between exposure and effect and to relate it to strategies and costs for preventive care and treatment planning. For this purpose prospective studies are needed. However, so far very little has been published on risk assessments in the field of pain and dysfunction in the jaw-face system. Furthermore, most of the current knowledge is based on cross-sectional and case-control studies or simply based on clinical experience. A weakness of cross-sectional studies is the difficulty of establishing causal relationships between different factors. There are only a limited number of longitudinal studies published with a focus on the influence of certain factors on the incidence and persistence of temporomandibular disorders (TMD) (LeResche, 1997).

**Temporomandibular disorders**

*Terminology*

Temporomandibular disorders (TMD) is a widely used, all-embracing term for a number of conditions characterized by pain and dysfunction in the temporomandibular joint (TMJ), jaw muscles, and associated structures (Dworkin and LeResche, 1992; Okeson, 1996; 2008a). Since 1934, signs and symptoms of musculoskeletal disorders in the jaw-face have been assigned various terms, such as Costen’s syndrome, TMJ pain-dysfunction syndrome, functional TMJ disturbances, myofacial pain-dysfunction syndrome, occlusomandibular disturbances, mandibular dysfunction, internal derangements of TMJ, craniomandibular disorders and so on. The various terminologies reflect different concepts of etiology and pathogenesis, as well as assumed origin and source of these disorders over the course of nearly a century (Okeson, 2008a; Wänman, 1987).

Since 1991, TMD has been the most established and used term. The Research Diagnostic Criteria for TMD (RDC/TMD) was created to provide a classification system that allowed for standardization and replication of research focusing on jaw muscle- and TMJ-related pain and dysfunction (Dworkin and LeResche, 1992). These criteria are still widely used, and several studies on reliability and validity have been conducted over the years (Emshoff et al., 2002; John et al., 2005; Lausten et al., 2004; Nilsson, 2007; Wahlund et al., 1998). The term TMD and the criteria have lately been criticized by some authors who suggested a need to update the criteria (Steenks and de Wijer, 2009) and even to terminate the use of the term TMD (Laskin, 2008). Nevertheless, this umbrella term describing different specific disorders related to function and signs and symptoms of the TMJ and jaw muscles is still widely used. As TMD currently is the most utilized and recognized term to summarize musculoskeletal disorder in the jaw-face
Prevalence
From the beginning of 1970 the prevalence of signs and symptoms associated with TMD has been analyzed in a number of epidemiologic studies in different populations (Agerberg and Carlsson, 1972; Egermark-Eriksson et al., 1981; Gesch et al., 2004; Helkimo, 1974b; Locker and Slade, 1988; Nourallah and Johansson, 1995; Pow et al., 2001; Shiau and Chang, 1992; Solberg et al., 1979). According to these studies and literature reviews (Carlsson, 1984; 1999), approximately one-third of the adult population reports symptoms and approximately 40–60% have signs of TMD. The treatment need owing to TMD in adults was recently estimated at 16% in a meta-analysis (Al-Jundi et al., 2008). The prevalence figure of treatment need itself indicates that TMD is a significant health problem. TMD occur already in childhood but the symptoms are mostly mild in character (Magnusson et al., 2005; Nilner and Lassing, 1981). The prevalence of TMD seems to increase with age and show a fluctuating pattern (Heikinheimo et al., 1989; Könönen and Nyström, 1993; Magnusson et al., 2005; Wänman, 1996). The highest prevalence of TMD symptoms is reported in the 20 to 40 age population (Okeson, 2008a) and after the retirement age the prevalence gradually decreases (Österberg et al., 1992).

Generally, females are more likely to experience a variety of recurrent pain conditions (Breivik et al., 2006). Underlying biological mechanisms of pain and the contribution of psychological and social factors warrant greater attention to women in pain research (Unruh, 1996). It has been suggested that the higher prevalence of chronic orofacial pain found in women is a result based on sex differences in generic pain mechanisms and of yet unidentified factors unique to the craniofacial system (Dao and LeResche, 2000). Gender differences in signs and symptoms of TMD are small in childhood (Magnusson et al., 2005; Nilner and Lassing, 1981), but from early adolescence, TMD has been reported at a slightly, but significantly higher prevalence among girls (Nilsson, 2007; Wänman and Agerberg, 1986a; b). In adults, females report more frequent, more severe, and lingering TMD symptoms and exhibit more clinical signs than males (Carlsson, 1999; Johansson et al., 2003; LeResche, 1997; Wänman, 1996). Female patients outnumber males in getting referrals to specialist clinics for TMD (Anastassaki and Magnusson, 2004). Different courses of TMD signs and symptoms in males and females were reported in a 10-year follow-up study (Wänman, 1996) and may in part explain why females are more likely to seek care (Carlsson, 1999). Gender differences and its influence on the course of TMD is still a topic of interest.
Etiology and risk factors

An etiological factor can be either necessary or sufficient. Absence of a necessary factor implies absence of effect, while presence of a sufficient factor is enough to cause an effect. No single cause accounts for all signs and symptoms of TMD, and studies trying to predict risk of TMD or the outcome of treatment have generally failed. Variables conventionally used to describe the functional status of the masticatory system have been reported to be, at best, of modest value in the estimation in healthy young subjects of the individual risk of developing TMD (Kirveskari, 2001). In addition, clinical, psychological, and illness behavior factors when used alone were found to be poor predictors of treatment outcome (Gerke et al., 1989). A general lack of knowledge of the mechanisms involved and the variability in individually contributing factors may be one reason for these results.

The etiology of TMD is considered multifactorial and may be viewed in the light of contributing factors. These factors can be divided into predisposing, initiating, and perpetuating factors. Predisposing factors may increase the risk of developing a condition; initiating factors may cause the onset or incidence of the condition; while perpetuating factors may contribute to the maintenance or persistence of the condition in focus (DeBoever and Carlsson, 1994; Okeson, 1996). As a complementary hypothesis, pain and dysfunction in TMJ and jaw muscles may be regarded as an outcome of the load subjected to these structures in relation to the tissues’ capacity to adapt to or restrain the load (Stegenga and de Bont, 2006; Wänman and Agerberg, 1991).

Over the years a variety of etiological or contributing risk factors have been proposed. Some of these factors are related to dental occlusion (Egermark et al., 2003; Mohlin et al., 1980; Mohlin and Thilander, 1984), behavioral factors such as tooth grinding or clenching (Magnusson et al., 2000), micro trauma caused by repeated overloading of the jaw system (Okeson, 1996), joint hyper-mobility (Hirsch et al., 2008; Westling, 1989), or external trauma (Pullinger and Seligman, 1991b). A series of articles have described the functional relationship between the temporomandibular and cranio cervical neuromuscular systems (Eriksson et al., 2000; Hägman-Henrikson et al., 2006) and impaired jaw function following a whiplash trauma (Eriksson et al., 2007; Grönqvist et al., 2008). Trauma following endotracheal intubation (Martin et al., 2007) or third-molar extraction (Huang and Rue, 2006) has also been disclosed as a possible risk factor to TMD. Furthermore, psychological factors and depression (Slade et al., 2007), social and general health factors (Johansson et al., 2004), inflammatory diseases (Helenius et al., 2005; Wenneberg and Kopp, 1982) and pain in the neck (Ciancaglini et al., 1999) or back (Wiesinger et al., 2007), or widespread pain (John et al., 2003) have all been regarded as risk
or contributing factors. Recently, the importance of neurobiological mechanisms (Svensson and Graven-Nielsen, 2001) and genetic factors has also been emphasized (Diatchenko et al., 2005), and a biopsychosocial model has been proposed to explain the etiology of TMD (Gatchel et al., 2007; Suvinen et al., 2005). This model seems suitable to embrace conditions such as TMD at a population level, but may be less useful when it comes to judging the individual cases (Greene, 2006).

**Dental occlusion, bruxism and spinal pain**

Among possible risk factors of significance for the development of TMD and of special interest for the dental profession are those related to dental occlusion and bruxism. The significance of variations in the dental occlusion as a contributing factor to TMD is controversial, and the question is still debated. In an editorial, methods used in studies rejecting the occlusal hypothesis were questioned (Alanen, 2002). An opposite argument, in response, was to consider if it would make any difference in the care of TMD patients if occlusion were dismissed or included as an etiologic factor (Greene, 2002). Dental occlusion has in some population-based studies been found to be associated with signs and symptoms of TMD (Egermark-Eriksson et al., 1990; Henrikson et al., 1997; Landi et al., 2004; Mohlin et al., 1980; Pullinger et al., 1993; Wänman and Agerberg, 1991). However, others have not confirmed these relationships, and the importance of occlusion in relation to TMD has been questioned (Clark, 1991; Clark et al., 1999; Droukas et al., 1984; Koh and Robinson, 2004; Pullinger and Seligman, 1991a; Seligman and Pullinger, 1991a; b; Suvinen et al., 2005; Witter et al., 1994). Most studies have been cross-sectional, and, consequently, few firm conclusions can be drawn regarding causal relationships as these studies do not indicate the direction of the correlation. Hence, some occlusal variations may be a consequence of TMD rather than its cause (Pullinger and Seligman, 2000). In prospective studies, elimination of occlusal interferences was reported to reduce the incidence of TMD in subjects who underwent occlusal adjustments repeatedly in comparison to mock adjustment (Kirveskari et al., 1989a; Kirveskari et al., 1989b; Kirveskari et al., 1998) and subjects with an earlier history of TMD were found to be more vulnerable to changes in the dental occlusion (Le Bell et al., 2006). Since the literature is not conclusive, there is still a need for longitudinal studies (Mohlin et al., 2007). It seems to be an open question whether variations in dental occlusion may act as a predisposing, initiating, or perpetuating risk factor to the development of TMD pain and dysfunction or if it should be disregarded.

Bruxism refers to subconscious, nonfunctional grinding or gnashing of teeth (Okeson, 2008a). Its etiology has been considered multifactorial and mainly regulated centrally, not peripherally (Lobbezoo et al., 2006). Both tooth grinding and clenching are observed during sleep and should be
differentiated from daytime bruxism, which is mainly considered a behavior related to stress and strain or anxiety (Lavigne et al., 2003; Lavigne et al., 2007). The consequences of sleep bruxism may include tooth destruction, jaw pain, headaches or limitations of mandibular movement, as well as tooth-grinding sounds. Reported bruxism may also involve the feeling of being “tense” (Svensson et al., 2008). The role of bruxism as an initiating risk factor in TMD has been questioned (Barbosa Tde et al., 2008), and the scientific evidence of its influence on TMD (DeBoever and Carlsson, 1994; Lobbezoo and Lavigne, 1997), and craniofacial pain (Svensson et al., 2008) has been rated weak. A call for longitudinal epidemiologic, clinical or experimental studies with the aim to establish or refute the relationship between bruxism and various subgroups of TMD (Lobbezoo and Lavigne, 1997) was one motive of this research project.

Associations between TMD, headache, and cervical pain (Rantala et al., 2003; Storm and Wänman, 2006); TMD and headache (Ballegaard et al., 2008; Glaros et al., 2007); TMD and neck pain (Ciancaglini et al., 1999; Wänman, 1995); TMD and back pain (Wiesinger et al., 2007); headache and back pain (Hagen et al., 2006; Von Korff et al., 2005); and neck pain and back pain (Hagen et al., 2006) have been reported in cross-sectional studies and indicate comorbidity between pain conditions at different locations. Previous chronic pain elsewhere and poor physical health was reported to predict ”new” chronic back pain (Smith et al., 2004), and onset of TMD pain was found to be significantly increased for persons with other pain conditions at baseline (Drangsholt and LeResche, 1999; John et al., 2003; Macfarlane et al., 2004; Von Korff et al., 1993). It has been suggested that individuals who develop TMD pain in adolescence are latent vulnerable to experiencing pain that is not unique to the orofacial region (LeResche et al., 2007). Recently, long-term back pain was found to be associated with musculoskeletal disorders in the jaw-face, together with a reciprocal dose-response-like relationship between severity of spinal pain and TMD (Wiesinger et al., 2007; 2009). The results thus indicate that these conditions may share common risk factors or that they may influence each other. However, this phenomenon has not been fully addressed in controlled prospective cohort studies, and further research on the temporal sequence of spinal pain and TMD are needed.
AIMS

The general aim of this thesis was to gain knowledge of whether dental occlusion, bruxism, spinal pain and gender are possible risk factors predicting the development of temporomandibular disorders.

The specific aims were

- to evaluate incidence and course of temporomandibular joint (TMJ) pain and dysfunction during a 2-year period (Papers I, IV)
- to test the null hypothesis that presence and course of TMJ pain and dysfunction were not dependent on bruxism and variations in dental occlusion (Papers I, IV)
- to evaluate incidence and course of jaw muscle signs and symptoms during a 2-year period (Papers II, IV)
- to test the null hypothesis that presence and course of jaw muscle signs and symptoms were not dependent on bruxism and variations in dental occlusion (Papers II, IV)
- to study the course of TMD in relation to gender (Papers I, II, IV)
- to study if pain in spinally innervated areas predicted incidence of TMD and headaches during a 2-year period (Paper III)
- to study if signs and symptoms in the jaw-face predicted incidence of headache and spinal pain during a 2-year period (Paper III)
MATERIAL AND METHODS

Study design

The study had a 2-year prospective observational design with registrations at baseline, and after 12 and 24 months. Different methods were used to evaluate associations between possible risk factors and signs and symptoms of TMD:

- Cross-sectional analysis of baseline variables and 1-year-period prevalence of TMD signs and symptoms (Papers I, II).
- Case-control study within a 2-year prospective cohort (Papers III, IV).

Paper I
Temporomandibular joint conditions were scrutinized. Focus of interest was the prevalence, 1-year incidence and course of TMJ signs and symptoms. The study analyzed if age, gender, awareness of bruxism and variations in dental occlusion influenced the 1-year-period prevalence of TMJ pain and dysfunction.

Paper II
The prevalence, 1-year incidence and course of myofascial pain (signs and symptoms in the jaw-face-temple region) were examined. Age, gender, awareness of bruxism and variations in dental occlusion were analyzed in relation to the 1-year-period prevalence of jaw muscle signs and symptoms.

Paper III
The research question was: Do pain and dysfunction in the jaw-face region predict pain in the spinal area or vice versa? The study population was classified into five different case-control groups with regard to the onset (incidence) of non-pain TMD symptoms, jaw pain, headaches, spinal pain, or TMD pain (RDC/TMD), respectively. Subjects without a stated symptom at baseline who reported onset of that symptom during the following 2 years were categorized as cases, and those without the specific symptom during the whole study period as controls. The significance of baseline variables such as spinal pain, headaches, and signs and symptoms of TMD for the incidence of respective symptoms were analyzed.

Paper IV
The research questions were related to risk factors associated with the 2-year cumulative incidence and persistence of signs or/and symptoms of TMD. Baseline factors used as independent variables were age, gender, reported
bruxism, perceived tooth contact patterns at jaw closing, and clinically registered morphological and functional variations in the dental occlusion.

**Study population**

The study population comprised all students enrolled in the dentistry program at Umeå University during the period of 1998–2005. In total, 371 individuals (142 males and 229 females) out of 372 accepted to take part in the 2-year prospective study. At baseline the mean age was 23 years, with the range of 18–48 years. After the first year, 63 (30 males and 33 females) and after the second year another 28 individuals (14 males and 14 females) dropped out, due to interruption of their education. The proportion of men was significantly higher among the dropouts, compared to the study population. There were no other significant differences between the dropouts and the study population regarding prevalence of variables examined at baseline. At the 1-year follow-up 308 individuals were re-examined and in total 280 individuals were examined at all three examinations. The age and gender distribution is presented in **Table 1**. Ninety-eight percent of the study population was Caucasian. The Ethics Committee at Umeå University approved the project, and the students gave their informed consent to participate.

**Table 1.** Age and gender distribution, at baseline, at 1-year follow-up and at 2-year follow-up among the participants in a 2-year prospective study (**Papers I–IV**).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td><strong>Baseline</strong></td>
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<tr>
<td>Mean age (SD)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>371</td>
<td>142 (38%)</td>
<td>229 (62%)</td>
</tr>
<tr>
<td>22.6 (5.5)</td>
<td>24.7 (5.9)</td>
<td>21.8 (3.7)</td>
<td></td>
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<tr>
<td><strong>1-yr follow-up</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Mean age (SD)</td>
<td></td>
<td></td>
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<tr>
<td>(Papers I,II)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>n</td>
<td>308</td>
<td>112 (36%)</td>
<td>196 (64%)</td>
</tr>
<tr>
<td>23.8 (4.8)</td>
<td>25.6 (5.9)</td>
<td>22.8 (3.8)</td>
<td></td>
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<tr>
<td><strong>2-yr follow-up</strong></td>
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<tr>
<td>Mean age (SD)</td>
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<tr>
<td>(Papers III,IV)</td>
<td></td>
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<tr>
<td>n</td>
<td>280</td>
<td>98 (35%)</td>
<td>182 (65%)</td>
</tr>
<tr>
<td>24.6 (4.6)</td>
<td>26.4 (5.3)</td>
<td>23.6 (3.8)</td>
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</table>

**Case history**

Case histories were collected via a questionnaire before the clinical examinations (at baseline, and after 12 and 24 months). The questions focused on presence and frequency of temporomandibular joint (TMJ)
symptoms (reported clicking, pain, locking), jaw muscle symptoms (reported tiredness, stiffness, pain in the jaw muscle region), difficulties in opening or closing the jaw, presence and location of headaches (right temple, left temple, forehead), neck pain, shoulder pain, and back pain. The frequency of each symptom was stated on a 5-grade scale (never; once or twice a month; once a week; several times a week; daily). In the analysis, frequent symptoms were defined as those reported to occur once a week or more often. The questionnaire also included questions regarding awareness of tooth grinding or clenching, cheek or tongue biting, frequent use of chewing gum, and perceived tooth contact pattern at jaw closing. The subjects made a decision on four statements: the teeth contact equally on both sides; the teeth contacts more distinctly on the left hand side; the teeth contact more distinctly on the right hand side; the teeth contact more distinct on the front teeth. At the baseline examination the time frame for the questions was occurrence of symptoms during the previous month, and at the follow-ups the time frame was occurrence of symptoms during the past year.

Clinical examination

The clinical examinations were performed at the start of the students’ education (baseline), after one year (1-year follow-up), and after two years (2-year follow-up), by two experienced TMD specialists (SM and AW). The clinical examinations followed a standardized protocol, in accordance with routine methods used in the Department of Clinical Oral Physiology at Umeå University. The examiners were blinded to the participant’s responses to the questionnaire. Each examiner did examine the same subjects at the follow-ups as at baseline. The subjects were in a supine position during the examination. The following variables were registered:

Temporomandibular joint (TMJ) signs

- TMJ clicking sounds. Presence of reproducible TMJ clicking sounds on jaw opening and closing movements were registered by palpation and auscultation without the use of a stethoscope.
- TMJ locking. Locking of one or both sides of the TMJ was registered if the jaw opening was less than 25 mm or if a deviation of 5 mm or more occurred when opening wide.
- TMJ pain to palpation. The TMJ was palpated laterally and posteriorly through the auditory meatus. Pain was registered when the palpation elicited a palpebral reflex in the eye or a protective reflex.
- TMJ pain on movement. Pain was registered on free movements (opening wide, laterotrusion, protrusion).
- TMJ pain on joint loading. Each subject was requested to bite hard for 30 seconds on double wooden spatulas (2 mm), placed in the first molar region on the right side with the procedure then repeated on the left
side. Elicited pain in the contralateral joint was registered as TMJ pain on joint loading.

**Muscle signs**
- Pain to palpation was registered if the muscle palpation elicited a palpebral reflex or a withdrawal reaction for the following sites: the tendon, anterior, and posterior part of the temporal muscles, the superficial and deep parts of the masseter muscles, the lateral pterygoid region, the medial pterygoid muscles, the digastric muscles, the sternocleidomastoid muscles, the region of neck muscles, the ascending part of the trapezius muscles, the underarm muscles, thumb muscles, and calf muscles.
- Clench symptoms. Each subject was asked to clench the teeth hard for 30 seconds in the intercuspal position. Development of pain or fatigue in the face or jaws during the clenching task was registered as clench symptoms.

**Number of teeth (0-32)**

**Range of movement of the mandible**
Measurements were made for maximal opening, maximal lateral movements to the left and right, and maximal protrusion (Agerberg, 1974).

**Morphological occlusion**
- Sagittal occlusion (Angle classification) was judged at the canines and the molars on both sides. If the molar occlusion deviated from neutral occlusion distally or mesially by more than half a cusp width, it was classified as distocclusion or mesiocclusion, respectively.
- Vertical occlusion. Frontal open bite was registered if overbite was ≤ 0 mm and no contacts were present between upper and lower incisors; edge-to-edge bite if overbite was = 0 mm and contacts were present between upper and lower incisors; deep bite if the overbite was ≥ 5 mm.
- Transversal occlusion was judged in the canine-premolar and molar segments. Crossbite was registered if the buccal cusps of the upper teeth occluded lingually with the buccal cusps of the lower teeth; scissors bite was registered if the lingual cusps of the upper teeth occluded buccally with the buccal cusps of the lower teeth.
- Overjet and overbite were measured to the nearest mm with a ruler in intercuspal position (ICP).

**Functional occlusion**
- Occlusion in ICP. Mandibular stability in ICP was measured in the molar segments with a double-folded plastic foil (Arti-Fol, 0.008 mm, Bausch Articulating Papers, Inc., Nashua, NH, USA) if the molar teeth bilaterally could keep a firm grip on the foil during moderate clenching.
effort. Mandibular instability in ICP was registered if the molar teeth on one side or both sides could not keep a firm grip on the foil or could only do so during hard clenching.

- Occlusion in retruded contact position (RCP). RCP was obtained passively with the mandible guided by the examiner, and the side of the first contact on guided hinge closure was registered (Helkimo et al., 1971).

- Lateral slide in centric: The horizontal, vertical, and lateral distance between RCP and ICP was measured with a ruler to the nearest 0.5 mm.

- Eccentric occlusion. Contact pattern was registered at 3 mm and 9 mm lateral excursions as anterior guidance, cuspid guidance, group function, molar guidance, balanced occlusion, balanced occlusion at moderate clenching, or mediotrusive side interference (MI) on the left and right sides respectively. MI was defined as a single tooth contact between the maxillary and mandibular teeth on the mediotrusive side, inhibiting any contact on the laterotrusive side.

Classifications were made in accordance with

- Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) axis I; group I a, myofascial pain and III a, arthralgia (Dworkin and LeResche, 1992)

- Anamnestic Dysfunction Index (Ai) and Clinical Dysfunction Index (Di) (Helkimo, 1974a)
The distribution of baseline variables is presented in Table 2 (Papers I-IV)

**Table 2.** Percentage distribution and variation of baseline variables for all participants included in Papers I-IV.

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Papers I-II n=308</th>
<th>Papers III-IV n=280</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>36</td>
<td>35</td>
</tr>
<tr>
<td>Females</td>
<td>64</td>
<td>65</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤21 years</td>
<td>56</td>
<td>57</td>
</tr>
<tr>
<td>&gt;21 years</td>
<td>44</td>
<td>43</td>
</tr>
<tr>
<td>Parafunctions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tooth clenching</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>Tooth grinding</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Bruxism</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>Cheek biting</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Gum chewing</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>Pain conditions*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headaches</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Neck pain</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Shoulder pain</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Back pain</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Spinal pain</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td>Sagittal occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutroclusion</td>
<td>88</td>
<td>87</td>
</tr>
<tr>
<td>Distocclusion</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Mesiocclusion</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Vertical occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal overbite</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Open bite</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Edge-to-edge bite</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Deep bite</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Transversal occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal bite</td>
<td>90</td>
<td>89</td>
</tr>
<tr>
<td>Crossbite unilateral</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Crossbite bilateral</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Scissors bite</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Malocclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any divergence from normal occlusion</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Overjet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5mm</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Occlusion in ICP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandibular instability</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Perceived unequal stability</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>Occlusion in RCP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral contact</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>Bilateral contact</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Lateral slide in centric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1mm</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Eccentric occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI at 3 mm lateral excursion</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>MI at 9 mm lateral excursion</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Any MI present</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Symptoms of TMD*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ai &gt;0</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Signs of TMD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Di &gt;0</td>
<td>46</td>
<td>46</td>
</tr>
</tbody>
</table>

*Symptoms reported to occur once a week or more often
MI = mediotrusive side interference
Ai = Anamnestic Dysfunction Index , Di = Clinical Dysfunction Index (Helkimo, 1974a)
Statistical methods

All statistical analyses were performed using the Statistical Package for Social Sciences, (SPSS, Inc., Chicago, IL, USA). Associations between data at nominal level were performed with chi-square test (Papers I, II). Analyses of changes between baseline and follow-ups were tested with McNemar test (Papers I, II, IV) and marginal homogeneity test (Paper I).

Associations between presence, incidence, and persistence of TMD signs and symptoms, pain at other locations, and baseline factors were assessed in binary logistic regression models. Independent variables significantly associated to dependent variables in the univariate analyses were assessed in multiple regression models and a backward stepwise likelihood ratio procedure. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. Results were considered statistically significant if the CI did not include 1. In the logistic regression models adjustments were made for age and gender (Papers I-IV). P-values ≤ 0.05 were considered statistically significant.

The separate TMJ conditions were analyzed in relation to presence/absence of mediotrusive side contacts following lateral excursions in a binary logistic regression model. The right and left sides of each TMJ were classified separately, based on reported symptoms and registered clinical signs.

Before the statistical analyses, dichotomization (0/1) was made for most of the dependent and independent variables as listed below (Papers I-IV). In the analyses, only frequent symptoms were included.
Dependent variable (Paper I)

- (0) Normal TMJ group: those who during the 1-year study period neither had TMJ signs nor reported frequent TMJ symptoms (n = 191).
- (1) 1-year TMJ pain and/or dysfunction: those who at the 1st or 2nd examination reported frequent TMJ clicking, TMJ pain or TMJ locking or had a registered clicking sound, TMJ locking, TMJ pain to palpation, TMJ pain during movements or TMJ pain on joint loading. Those fulfilling criteria of arthralgia according to RDC/TMD criteria were also included (n = 117).

Dependent variables (Paper II)

- (0) Cohort 1: those who had neither signs nor symptoms of myofascial pain during the 1-year period (n = 140).
- (1) Cohort 2: those who reported frequent jaw muscle symptoms or had signs of jaw muscle pain during the 1-year period (n = 168).
- (1) Cohort 3: those who, at baseline or at the follow-up, reported frequent jaw muscle symptoms and had signs of jaw muscle pain simultaneously or fulfilled the criteria for myofascial pain (RDC/TMD) (n = 56).

Dependent variables (Paper III)

- (0) Those without TMD symptoms during the 2-year observation period were used as controls (n = 131).
- (1) Two-year incidence of non-pain TMD symptoms: onset of reported frequent jaw stiffness or tiredness, frequent TMJ sounds, frequent TMJ locking, or frequent difficulties in jaw opening* (cases = 48).

- (0) Those without jaw pain during the 2-year observation period were used as controls (n = 213).
- (1) Two-year incidence of jaw pain: Onset of reported frequent pain in the TMJ and/or jaw muscles* (cases = 49).

- (0) Those without headaches during the 2-year observation period were used as controls (n = 198).
- (1) Two-year incidence of headaches: onset of reported frequent pain in the temples and/or forehead* (cases = 53).

- (0) Those without spinal pain during the 2-year observation period were used as controls (n = 124).
- (1) Two-year incidence of spinal pain: onset of reported frequent pain in the neck, shoulders and/or back* (cases = 63).

- (0) Those without TMD pain during the 2-year observation period were used as controls (n = 229).
- (1) Two-year incidence of TMD pain: onset of TMD pain according to RDC/TMD (myofascial pain and/or arthralgia)* (cases = 33).

*Symptoms reported at the 2nd or 3rd examination, but not at the first.
Dependent variables (Paper IV)

- (0) Those who neither had TMJ signs nor reported TMJ symptoms during the 2-year period were used as controls (n = 128).
  (1) Two-year incidence of TMJ signs or symptoms: onset of TMJ signs OR TMJ symptoms during the 2-year observation period among those who had neither TMJ signs nor TMJ symptoms at the beginning of the study (n = 68).

- (0) Those who neither had TMJ signs nor reported TMJ symptoms during the 2-year period were used as controls (n = 128).
  (1) Two-year incidence of TMJ signs and symptoms: onset of TMJ signs AND TMJ symptoms during the 2-year observation period. The calculations were based on onset of TMJ signs and TMJ symptoms simultaneously among those who had neither TMJ signs nor symptoms at the beginning of the study (cases = 19).

- (0) Those without jaw muscle signs and symptoms during the 2-year observation period were used as controls (n = 99).
  (1) Two-year incidence of jaw muscle signs or symptoms: onset of jaw muscle signs OR jaw muscle symptoms among those without such symptom at baseline (cases = 77).

- (0) Those without jaw muscle signs and symptoms during the 2-year observation period were used as controls (n = 99).
  (1) Two-year incidence of jaw muscle signs and symptoms: onset of jaw muscle signs AND jaw muscle symptoms simultaneously among those without such symptoms at baseline (cases = 32).

- (0) Those who neither had TMJ signs nor reported TMJ symptoms during the 2-year period were used as controls (n = 128).
  (1) Persistent TMJ signs or symptoms: presence of one or more of TMJ signs OR reported TMJ symptoms at all three examinations (cases = 54).

- (0) Those who neither had TMJ signs nor reported TMJ symptoms during the 2-year period were used as controls (n = 128).
  (1) Persistent TMJ signs and symptoms: at least one TMJ sign AND one TMJ symptom registered at the same examination and at all three examinations (cases = 22).

- (0) Those without jaw muscle signs and symptoms during the 2-year observation period were used as controls (n = 99).
  (1) Persistent jaw muscle signs or symptoms: presence of one or more of jaw muscle signs OR symptoms at all three examinations (cases = 78).

- (0) Those without jaw muscle signs and symptoms during the 2-year observation period were used as controls (n = 99).
  (1) Persistent jaw muscle signs and symptoms: at least one jaw muscle sign AND one jaw muscle symptom registered at the same examination and at all three examinations (cases = 13).
• (0) Those without persistent TMJ signs and symptoms or persistent jaw muscle signs
and symptoms were used as controls (n = 247).
(1) Persistent TMJ signs and symptoms or persistent jaw muscle signs and symptoms
at all three examinations (cases = 33).

Independent variables/baseline variables (Papers I, II, IV)

• Age groups: ≤21 years; >21 years
• Gender: males; females
• Bruxism: reported awareness of tooth grinding or clenching (yes; no)
• Perceived tooth contact patterns at jaw closing: bilateral; unilateral or frontal

Morphologic occlusion:
• Sagittal occlusion: neutro-; disto-; mesio- occlusion,
• Vertical occlusion: normal; open bite/edge-to-edge bite; deep bite
• Transversal occlusion: normal bite; crossbite
  (scissors bite dropped in analyses due to few cases)
• Over jet: <5mm; ≥5mm

Functional occlusion:
• Occlusion in ICP: mandibular stability; instability
• Occlusion in RCP: unilateral; bilateral
• Lateral slide in centric: <1mm; ≥1 mm
• Eccentric occlusion:
  mediotrusive side interferences at 3mm: yes; no
  mediotrusive side interferences at 9mm: yes; no
  mediotrusive side interferences (any): yes; no

Independent variables/baseline variables (Paper III)

• Age groups: ≤21 years; >21 years
• Gender: males; females
• Spinal pain: reported frequent pain in the neck, shoulders, or back (yes; no)
• Headache: reported frequent pain in the right/left temple or forehead (yes; no)
• Symptoms of TMD: reported frequent jaw stiffness or tiredness, frequent pain in the
  jaw muscles, frequent TMJ sounds, frequent TMJ locking, frequent TMJ pain, or
  frequent difficulties in jaw opening (yes; no)
• Signs of TMD: one or more of the following variables present at baseline: maximal jaw
  opening capacity ≤39 mm; maximal horizontal movement capacity to the left, right or
  forward ≤6 mm; registered TMJ sounds during jaw opening/closing movements;
  deviation >2 mm when opening wide; TMJ locking; TMJ pain on palpation; TMJ pain
  during movements; jaw muscle pain to palpation at one or more of 16 jaw muscle sites
  (Helkimo, 1974a); no signs of TMD at baseline

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RESULTS

Prevalence, incidence, and course of TMJ pain and dysfunction and contributing factors (Papers I, IV)

Course and gender distribution
At the start of the study 30% of the study population had signs or symptoms of TMJ pain and dysfunction (Table 3). TMJ clicking sounds were the most common symptom (19%) and clinically registered sign (16%).

Table 3. Percentage distribution (rounded numbers) of TMJ symptoms, signs, and arthralgia (RDC/TMD) at baseline (n=371).

<table>
<thead>
<tr>
<th></th>
<th>Unilateral</th>
<th>Bilateral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMJ symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>clicking</td>
<td>13</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>pain</td>
<td>12</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>locking</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>TMJ signs</td>
<td>16</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>clicking</td>
<td>12</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>pain</td>
<td>6</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>TMJ symptoms and/or signs</td>
<td>18</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>1</td>
<td>0.5</td>
<td>2</td>
</tr>
</tbody>
</table>

During the first year 62% of the subjects had neither any TMJ signs nor any TMJ symptoms. The prevalence of TMJ signs or symptoms did not differ between baseline and the 1-year follow-up (Paper I). Females had more persistent TMJ signs or symptoms, while incidence and recovery did not differ between males and females (Table 4).

Table 4. Distribution of TMJ pain or dysfunction among 308 individuals during the 1-year study period. Examinations were made at baseline and after one year.

<table>
<thead>
<tr>
<th></th>
<th>Non-symptomatic</th>
<th>Incidence</th>
<th>Recovery</th>
<th>Persistence</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Males (n=112)</td>
<td>81 (72)</td>
<td>9 (8)</td>
<td>7 (6)</td>
<td>15 (13)</td>
<td></td>
</tr>
<tr>
<td>Females (n=196)</td>
<td>110 (56)</td>
<td>17 (9)</td>
<td>17 (9)</td>
<td>52 (27)</td>
<td>0.026*</td>
</tr>
<tr>
<td>Total (n=308)</td>
<td>191 (62)</td>
<td>26 (8)</td>
<td>24 (8)</td>
<td>67 (22)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test
There was a significant relationship ($P<0.001$) between reported and registered TMJ clicking at both examinations and between reported and registered TMJ pain at baseline ($P=0.002$) and at the follow-up ($P<0.001$). The risk of onset of reported TMJ sounds, as well as TMJ pain, increased when TMJ sounds were registered clinically at baseline ($P<0.001$).

The 2-year course of TMJ signs or symptoms among 280 dental students is presented in Figure 1. The first-year incidence was 12% and the second-year onset was 28%. For the 2-year period the prevalence increased significantly ($P<0.001$) and the course demonstrated both onset and recovery of TMJ pain and dysfunction. The main pattern was, however, a maintained state (Paper IV).

<table>
<thead>
<tr>
<th>Course of TMJ signs or symptoms</th>
<th>Baseline</th>
<th>1-year follow-up</th>
<th>2-year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>No TMJ signs or symptoms</td>
<td>196</td>
<td>173</td>
<td>194</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23 (12%)</td>
<td>54 (28%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68 (35%)</td>
<td>15 (17%)</td>
</tr>
<tr>
<td>TMJ signs or symptoms</td>
<td>84 (30%)</td>
<td>63</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21 (25%)</td>
<td>15 (17%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>125 (45%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>280</td>
<td>280</td>
</tr>
</tbody>
</table>

* 2-year cumulative incidence

**Figure 1.** The 2-year course of TMJ pain and dysfunction.

The distribution of 2-year cumulative incidence and persistence of TMJ signs or symptoms among males and females are presented in Table 5. Females were more likely to have persistent TMJ signs or symptoms, while for the onset, there were no gender differences (Paper IV).
Table 5. The 2-year cumulative incidence (C-Inc) and persistence of TMJ signs and/or symptoms.

<table>
<thead>
<tr>
<th>2-year-period observations</th>
<th>Total n=280 (%)</th>
<th>Males n=98 (%)</th>
<th>Females n=182 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMJ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No signs and symptoms</td>
<td>128 (46)</td>
<td>52 (53)</td>
<td>76 (42)</td>
<td>ns</td>
</tr>
<tr>
<td>C-Inc of signs or symptoms</td>
<td>68 (35)¹</td>
<td>27 (34)¹</td>
<td>41 (35)¹</td>
<td>ns</td>
</tr>
<tr>
<td>Persistent signs or symptoms</td>
<td>54 (19)</td>
<td>11 (11)</td>
<td>43 (24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Persistent signs and symptoms</td>
<td>22 (8)</td>
<td>6 (6)</td>
<td>16 (9)</td>
<td>ns</td>
</tr>
</tbody>
</table>

¹ Calculation based on those without TMJ signs and symptoms at baseline (total n = 196, males n = 79 and females n = 117), ns = non-significant

Factors associated with 1-year-period prevalence of TMJ pain and dysfunction

Those with awareness of tooth grinding or clenching, registered crossbite, unilateral contact in RCP, or mandibular instability in ICP at baseline presented a higher risk of TMJ pain and/or dysfunction during the 1-year study period (Paper I). Statistically significant associations are presented in Table 6.

Table 6. Logistic regression analysis of baseline factors and 1-year-period prevalence of TMJ pain and/or dysfunction. The table shows significant associations, percentage distribution, and odds ratio (OR) with 95% confidence interval.

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>Total N in group</th>
<th>% 1-yr TMJ pain and/or dysfunction</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>112</td>
<td>27.7</td>
<td>2.0 (1.2–3.4)</td>
</tr>
<tr>
<td>F</td>
<td>196</td>
<td>43.9</td>
<td></td>
</tr>
<tr>
<td>Bruxism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>158</td>
<td>32.3</td>
<td>1.6 (1.04–2.6)</td>
</tr>
<tr>
<td>Yes</td>
<td>150</td>
<td>44.0</td>
<td></td>
</tr>
<tr>
<td>Morphological occlusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal occlusion</td>
<td>199</td>
<td>33.7</td>
<td>1.7 (1.04–2.7)</td>
</tr>
<tr>
<td>Any deviation</td>
<td>109</td>
<td>45.9</td>
<td></td>
</tr>
<tr>
<td>Transversal occlusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>277</td>
<td>35.7</td>
<td>2.9 (1.3–6.5)</td>
</tr>
<tr>
<td>Cross bite</td>
<td>29</td>
<td>62.1</td>
<td></td>
</tr>
<tr>
<td>Contact in RCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>117</td>
<td>28.2</td>
<td>2.0 (1.2–3.3)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>191</td>
<td>44.0</td>
<td></td>
</tr>
<tr>
<td>Mandibular stability in ICP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stability</td>
<td>274</td>
<td>34.7</td>
<td>3.5 (1.6–7.3)</td>
</tr>
<tr>
<td>Instability</td>
<td>34</td>
<td>64.7</td>
<td></td>
</tr>
</tbody>
</table>
Factors associated with the 2-year incidence of TMJ signs or symptoms

Reported tooth grinding or clenching at baseline significantly increased the risk of onset of TMJ signs or symptoms (Table 7). The positive predictive value of bruxism was 0.47 and the negative predictive value was 0.75, relative to the incidence of TMJ signs or symptoms for the 2-year period.

A registered crossbite at baseline was significantly related to the incidence of TMJ disorders. Among those with no TMJ sign or symptom at baseline, 15 individuals (8%) had unilateral or bilateral crossbite. The positive predictive value of crossbite relative to onset of either a TMJ symptom or a registered TMJ sign was 0.67, and the negative predictive value was 0.68 (Paper IV).

Factors associated with persistent TMJ signs or symptoms

In the multiple regression analyses of factors associated with 2-year persistent TMJ disorders (Table 7), reported bruxism, crossbite, mandibular instability in ICP, and a lateral slide between RCP and ICP at baseline significantly increased the odds of persistent TMJ disorders (Paper IV).

Table 7. Factors associated with the 2-year incidence and persistence of TMJ signs or symptoms (significant values in bold text). Controls without signs and symptoms n= 128, odds ratio (OR), and 95% confidence interval (CI).

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>Incidence of TMJ signs or symptoms</th>
<th>Persistent TMJ signs or symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases = 68</td>
<td>Cases = 54</td>
</tr>
<tr>
<td>Bruxism</td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Crossbite</td>
<td>2.4 (1.3–4.4)</td>
<td>3.1 (1.5–6.5)</td>
</tr>
<tr>
<td>Lateral slide ≥1mm between RCP* and ICP*</td>
<td>3.5 (1.1–10.9)</td>
<td>5.6 (1.5–21.2)</td>
</tr>
<tr>
<td>Instability in ICP</td>
<td>2.4 (0.7–8.1)</td>
<td>4.0 (1.3–12.1)</td>
</tr>
<tr>
<td></td>
<td>2.0 (0.7–5.9)</td>
<td>4.0 (1.04–15.8)</td>
</tr>
</tbody>
</table>

* RCP, retruded contact position; ICP, intercuspal position
Relationship between mediotrusive side contacts and TMJ signs and symptoms

The distribution of occlusal contact patterns at mandibular lateral excursion is presented in Figure 2. The most common contact pattern at 3 mm lateral excursion was cuspid guidance (36%) while incisal guidance was the most common contact pattern at 9 mm lateral movement (57–58%). Contacts on the mediotrusive side were commonly registered (34–46%). Out of a total of 742 temporomandibular joint sides, 108 (15%) had at least one symptom, and 101 (14%) had signs of pain or dysfunction. Symptoms or signs were registered among 157 (21%).

Presence/absence of TMJ signs or symptoms was analyzed in relation to presence/absence of mediotrusive side contacts on the ipsilateral side. At cross-sectional analysis, no relationship was found between presence of contacts/interferences on the mediotrusive side and the presence of TMJ signs or symptoms on the ipsilateral side at 3mm or 9mm lateral excursion (unpublished data).

![Occlusal contact patterns after lateral excursion](image)

**Figure 2.** Percentage distribution of contact patterns after lateral excursion of the mandible at 3 and 9 mm, to the right and left sides, respectively (n=371).
Prevalence, incidence, and course of myofascial pain in the jaw-face region and contributing factors (Papers II, IV)

Course and gender distribution
At the start of the study 37% of participants had jaw muscle signs or symptoms. Approximately 35% presented with registered jaw muscle pain to palpation and 11% reported frequent jaw muscle pain. Seven percent were classified according to RDC/TMD myofascial pain. The 1-year longitudinal course of jaw muscle signs and symptoms differed significantly between males and females (Table 8).

Table 8. Distribution of jaw muscle signs and/or symptoms during a 1-year period. Examinations were made at baseline and after one year (n = 308).

<table>
<thead>
<tr>
<th></th>
<th>Non-symptomatic n (%)</th>
<th>Incidence n (%)</th>
<th>Recovery n (%)</th>
<th>Persistence n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (n=112)</td>
<td>72 (64)</td>
<td>12 (11)</td>
<td>7 (6)</td>
<td>21 (19)</td>
<td></td>
</tr>
<tr>
<td>Females (n=196)</td>
<td>68 (35)</td>
<td>44 (22)</td>
<td>14 (7)</td>
<td>70 (36)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Total (n=308)</td>
<td>140 (45)</td>
<td>56 (18)</td>
<td>21 (7)</td>
<td>91 (30)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-2 test,

From baseline to the 2nd examination, the prevalence figures increased for the total sample, but were significant only for females. The incidence of myofascial pain (RDC/TMD) was 4% (Paper II).

The 2-year course of jaw muscle signs or symptoms is shown in Figure 3. The cumulative incidence was 44%, and the number of individuals with jaw muscle pain and dysfunction increased significantly during the study period (Paper IV).
Course of jaw muscle signs or symptoms

<table>
<thead>
<tr>
<th>Baseline</th>
<th>1-year follow-up</th>
<th>2-year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No jaw muscle signs or symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>176 (37%)</td>
<td>128 (27%)</td>
<td>148 (28%)</td>
</tr>
<tr>
<td>48 (27%)</td>
<td></td>
<td>39 (28%)</td>
</tr>
<tr>
<td>77 (43%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Jaw muscle signs or symptoms</strong></td>
<td>104 (37%)</td>
<td>84 (26%)</td>
</tr>
<tr>
<td>2-year-period observations</td>
<td>Total n=280 (%)</td>
<td>Males n=98 (%)</td>
</tr>
<tr>
<td><strong>Jaw muscles</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No signs and symptoms</td>
<td>99 (35)</td>
<td>52 (53)</td>
</tr>
<tr>
<td>C-Inc of signs or symptoms</td>
<td>77 (44)¹</td>
<td>21 (29)¹</td>
</tr>
<tr>
<td>C-Inc of signs and symptoms</td>
<td>32 (18)¹</td>
<td>7 (10)¹</td>
</tr>
<tr>
<td>Persistent signs or symptoms</td>
<td>78 (28)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Persistent signs and symptoms</td>
<td>13 (5)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

¹ Calculation is based on those without jaw muscle signs or symptoms at baseline 
(total n = 176, males n = 73, females n = 103)

* 2-year cumulative incidence

**Figure 3.** Two-year course of jaw muscle signs or symptoms

The 2-year cumulative incidence and persistence of jaw muscle signs and/or symptoms, respectively, among males and females are presented in **Table 9.** Females had higher incidence and persistence of myofascial pain (Paper IV).

**Table 9.** Two-year cumulative incidence (C-Inc) and persistence of jaw muscle signs and/or symptoms.

<table>
<thead>
<tr>
<th>2-year-period observations</th>
<th>Total n=280 (%)</th>
<th>Males n=98 (%)</th>
<th>Females n=182 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Jaw muscles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No signs and symptoms</td>
<td>99 (35)</td>
<td>52 (53)</td>
<td>47 (26)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>C-Inc of signs or symptoms</td>
<td>77 (44)¹</td>
<td>21 (29)¹</td>
<td>56 (54)¹</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>C-Inc of signs and symptoms</td>
<td>32 (18)¹</td>
<td>7 (10)¹</td>
<td>25 (24)¹</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Persistent signs or symptoms</td>
<td>78 (28)</td>
<td>15 (15)</td>
<td>63 (35)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Persistent signs and symptoms</td>
<td>13 (5)</td>
<td>3 (3)</td>
<td>10 (5)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

1 Calculation is based on those without jaw muscle signs or symptoms at baseline 
(total n = 176, males n = 73, females n = 103)
Factors associated with the 1-year-period prevalence of myofascial pain

In the regression analyses unilateral contact in RCP and mandibular instability in ICP were associated with an approximately 3-fold risk of having jaw muscle signs and symptoms during the 1-year period. In addition, awareness of bruxism was associated with the 1-year-period prevalence of myofascial pain according to RDC/TMD (Table 10).

Table 10. Regression analyses of baseline factors and (I) 1-year-period prevalence of jaw muscle signs or symptoms, and (II) 1-year-period prevalence of jaw muscle signs and symptoms or myofascial pain (RDC/TMD). The table shows percentage distribution, odds ratios (ORs) and 95% confidence intervals (95% CIs). Significant associations are in bold.

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>n</th>
<th>%</th>
<th>I OR</th>
<th>n</th>
<th>%</th>
<th>II OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>112</td>
<td>35.7</td>
<td></td>
<td>82</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>196</td>
<td>65.3</td>
<td>3.4 (2.1–5.5)</td>
<td>114</td>
<td>40.4</td>
<td>1.9 (2.3–10.4)</td>
</tr>
<tr>
<td>Toothclenching</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>191</td>
<td>52.9</td>
<td></td>
<td>80</td>
<td>22.4</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>117</td>
<td>47.1</td>
<td>1.2 (0.8–1.9)</td>
<td>116</td>
<td>37.5</td>
<td>2.1 (1.1–3.9)</td>
</tr>
<tr>
<td>Tooth grinding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>232</td>
<td>53.0</td>
<td></td>
<td>144</td>
<td>24.3</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>76</td>
<td>47.0</td>
<td>1.3 (0.8–2.2)</td>
<td>52</td>
<td>40.4</td>
<td>2.1 (1.1–4.1)</td>
</tr>
<tr>
<td>Contact in RCP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>117</td>
<td>46.2</td>
<td></td>
<td>77</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>191</td>
<td>53.8</td>
<td>1.7 (1.1–2.7)</td>
<td>119</td>
<td>35.3</td>
<td>2.5 (1.2–4.9)</td>
</tr>
<tr>
<td>Mandibular stability in ICP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stability</td>
<td>274</td>
<td>51.5</td>
<td></td>
<td>181</td>
<td>26.5</td>
<td></td>
</tr>
<tr>
<td>Instability</td>
<td>34</td>
<td>48.5</td>
<td>3.6 (1.5–8.6)</td>
<td>15</td>
<td>53.3</td>
<td>3.2 (1.1–9.2)</td>
</tr>
</tbody>
</table>

Factors associated with the 2-year incidence and persistence of jaw muscle signs and symptoms

Besides female gender, none of the independent baseline variables included in the regression models were associated with an onset of jaw muscle signs and symptoms, except for registered mediotrusive side interferences (Table 11). Female gender, unilateral contact pattern in RCP and mandibular instability in ICP at baseline were related to the persistent jaw muscle signs or symptoms (Paper IV).
Table 11. Multiple regression analyses. Significant associations (in bold) between baseline factors and the 2-year incidence and persistence of jaw muscle signs or symptoms. Controls without signs and symptoms n = 99, odds ratio (OR) and 95% confidence interval (CI).

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>Incidence of jaw muscle signs or symptoms</th>
<th>Persistent jaw muscle signs or symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases = 77, OR (95%CI)</td>
<td>Cases = 78, OR (95%CI)</td>
</tr>
<tr>
<td>Female gender</td>
<td>3.0 (1.6–5.6)</td>
<td>3.8 (1.7–8.1)</td>
</tr>
<tr>
<td>Unilateral contact in RCP*</td>
<td>1.5 (0.8–2.7)</td>
<td>2.9 (1.4–5.8)</td>
</tr>
<tr>
<td>Instability in ICP*</td>
<td>3.7 (0.9–14.5)</td>
<td>4.4 (1.2–16.7)</td>
</tr>
<tr>
<td>Mediotrusive side interferences</td>
<td>2.0 (1.1–3.8)</td>
<td>0.7 (0.3–1.4)</td>
</tr>
</tbody>
</table>

* RCP, retruded contact position; ICP, intercuspal position;

Mandibular instability in ICP and persistent TMD (Paper IV)

Mandibular instability in ICP was at baseline registered among 31 individuals (11%) of the study population observed for 2-years (n = 280). Those with persistent TMJ signs and symptoms or persistent jaw muscle signs and symptoms were merged and formed a specific “persistent TMD group” of totaling 33 individuals (12%) (Paper IV). The positive predictive value of mandibular instability as a risk factor to longstanding TMD was 0.32 and the negative predictive value was 0.91 (OR 4.7 95% CI 2.0–11.1).

Reciprocal influence on the incidence of symptoms in trigeminally and spinally innervated areas (Paper III).

The 2-year cumulative incidence of frequent non-pain TMD symptoms was 27%, frequent jaw pain 19%, frequent headaches 21%, and frequent spinal pain 34%, and the 2-year cumulative incidence of TMD pain (RDC/TMD) was 13% (Paper III). Gender distribution is presented in Table 12.
Table 12. Two-year cumulative incidence (incidence variable) and gender distribution of reported symptoms. Cases represent subjects without a stated symptom at baseline who reported onset of that symptom during a following 2-year period. Controls are those without the symptom in focus during the 2 year period. Excluded are those who presented the indicated symptom at baseline.

<table>
<thead>
<tr>
<th>Incidence variables</th>
<th>Cases</th>
<th>Controls</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>men/women</td>
<td>n</td>
</tr>
<tr>
<td>Non-pain TMD symptoms</td>
<td>48</td>
<td>11/37</td>
<td>131</td>
</tr>
<tr>
<td>Jaw pain</td>
<td>49</td>
<td>10/39</td>
<td>213</td>
</tr>
<tr>
<td>Headaches</td>
<td>53</td>
<td>11/42</td>
<td>198</td>
</tr>
<tr>
<td>Spinal pain</td>
<td>63</td>
<td>17/46</td>
<td>124</td>
</tr>
<tr>
<td>TMD pain</td>
<td>33</td>
<td>3/30</td>
<td>229</td>
</tr>
</tbody>
</table>

Clinically registered signs of TMD at baseline predicted the onset of non-pain TMD symptoms, jaw pain, headaches, and spinal pain. Subjects with spinal pain or signs of TMD were more likely to become incidence cases of headache or jaw pain, compared to those without these conditions at baseline (Table 13).

Table 13. Factors significantly related to the 2-year incidence of respective symptoms. Independent baseline variables included in the model were spinal pain, headaches, symptoms of TMD, and signs of TMD. For the incidence of TMD pain (RDC/TMD) we used only spinal pain in the model, since signs and symptoms of TMD as well as headache are included in this diagnosis. For the incidence of jaw pain, symptoms of TMD were not included in the regression model. Odds ratios (OR) and 95% confidence intervals (95% CI) are presented.

<table>
<thead>
<tr>
<th>2-year incidence</th>
<th>Variables of significance</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-pain TMD symptoms</td>
<td>Signs of TMD</td>
<td>6.3</td>
<td>3.0–13.2</td>
</tr>
<tr>
<td>Jaw pain</td>
<td>Signs of TMD</td>
<td>2.4</td>
<td>1.2–4.7</td>
</tr>
<tr>
<td></td>
<td>Spinal pain</td>
<td>2.4</td>
<td>1.2–4.6</td>
</tr>
<tr>
<td>Headaches</td>
<td>Signs of TMD</td>
<td>2.2</td>
<td>1.1–4.2</td>
</tr>
<tr>
<td></td>
<td>Spinal pain</td>
<td>2.0</td>
<td>1.03–3.9</td>
</tr>
<tr>
<td>Spinal pain</td>
<td>Signs of TMD</td>
<td>2.6</td>
<td>1.4–5.0</td>
</tr>
<tr>
<td>TMD pain</td>
<td>Gender</td>
<td>5.6</td>
<td>1.6–19.7</td>
</tr>
<tr>
<td></td>
<td>Spinal pain</td>
<td>2.9</td>
<td>1.3–6.2</td>
</tr>
</tbody>
</table>
Individuals with an onset of TMD pain according to RDC/TMD significantly more often reported spinal pain at baseline than did controls, and were mainly females. Concurrent presence of registered signs of TMD and reported spinal pain at baseline further increased the risk of onset of headache (Figure 4A) and jaw pain (Figure 4B). Females with spinal pain at baseline had the highest risk of onset of TMD pain during the 2-year study period (Figure 4C).

Figure 4. Distribution of subjects at risk for A onset of frequent headaches (n = 251), B onset of frequent jaw pain (n = 262), and C onset of TMD pain according to RDC/TMD (n = 262). Occurrence of the significant baseline variable s in different combinations was compared in relation to the incidence. Filled columns indicate the proportion of cases; unfilled columns indicate the proportion of controls. SP-0 = absence of spinal pain; SP-1 = presence of spinal pain; sTMD-0 = absence of signs of TMD; sTMD-1 = presence of signs of TMD. Statistically significant differences between conditions are denoted in the figure (*P < 0.05; ***P < 0.001).
DISCUSSION

Before this research project started a review on opinions regarding advantages and disadvantages of dental contacts on the mediotrusive side during lateral excursions of the mandible was completed (Marklund and Wänman, 2000). The conclusion was that longitudinal studies based on cohorts with different types of occlusal contacts, estimating the risk of developing TMD, were generally lacking and could provide further knowledge. The overall aim of this thesis was to study the course of TMD, and if biomechanical factors related to dental occlusion and bruxism, pain in the spinal region, and gender predicted the development of TMD.

A sample of dental students was examined on three subsequent occasions during a 2-year period. As a first step the 1-year course of TMJ signs and symptoms and baseline factors related to the 1-year-period prevalence were analyzed (Paper I). The second step was to undertake corresponding analyses related to the course and 1-year period prevalence of jaw muscles signs and symptoms (Paper II). Furthermore, the influence of signs and symptoms in trigeminally innervated and pain in spinally innervated areas on the 2-year cumulative incidence of symptoms in the jaw, head, and spinal regions was evaluated, respectively (Paper III). Finally, risk factors associated with the 2-year incidence and persistence of signs and symptoms of TMD were disclosed (Paper IV).

Altogether, the results in this thesis show high incidence rates for TMD, headaches, and spinal pain among dental students. Crossbite, mandibular instability, reported bruxism, as well as female gender were identified as contributing risk factors. Spinal pain and TMD mutually predicted each other, indicating common pathophysiological mechanisms and individual vulnerability. The findings support a multidisciplinary approach, and it is recommended that the status and function of the jaw system be considered in patients with spinal pain.

Methodological considerations

Study design
The research project used an observational study design to follow the onset and natural course of TMD (Papers I–IV). Longitudinal study designs are necessary when incidence and natural course of a disease is of primary interest, essential when the question is what condition comes first, and useful in the analysis of possible risk factors. A cohort is used to describe a group (population or subgroup) based on some specific common
characteristics. Individuals at risk share the same probability of being affected by a certain condition. The advantage of prospective cohort studies is the possibility to plan and choose beforehand what data to collect, at what time, and with what methods (Persson and Wall, 2003). In addition, it gives the opportunity to test hypotheses and to establish odds ratios of the risk to develop a specific condition. Usually these types of studies require a long follow-up period in order to detect enough cases for reliable estimations. The drawbacks to large prospective population-based observational studies are that they are time-consuming, costly, and subject to high risk of drop-outs which may jeopardize the interpretations. The present research was performed on a selected non-patient sample that was accessible at low cost.

**Study population**
The study population consisted of dental students. The benefit was that these participants were available for examinations at standardized time intervals and allowed the study to be cost-effective, and with a reasonable number of dropouts. They were also a sample of young adults, roughly at the same age, of good general health, and with complete dentitions. As a cohort they were subjected to a similar daily workload, with a homogeneous educational level and fairly common daily social environments as a consequence of following a syllabus. Musculoskeletal pain is known to emerge early in dental careers (Rising et al., 2005) and to increase during the first years of education (Thornton et al., 2008). One plausible reason is that dental students experience exposure to pain-associated risk factors such as stress and bad ergonomics. The study started at the outset of enrolment, when the students were not expected to be familiar with the research field and the topic in focus, and closed before they started the clinical part of their education. The dropouts had all interrupted their studies and, consequently, they could not be examined at the follow-ups. Their reasons for leaving the education can only be speculated on. The most likely is that they had chosen another educational program or a university closer to home. Since the dropouts did not differ from the remaining, except for being proportionally more men, they had hardly any significant effect on the results. An increase of the sample size may have improved the power of the statistics, especially for the smaller incidence groups in Paper III and Paper IV. Yet, research should not be completed on more subjects than what is required to answer the study question (Kingman and Burnside, 2007).

There were no age differences regarding presence of signs or symptoms of TMD or the examined baseline variables in the different age groups. The only discrepancy was a higher number of females in the younger part. Although a wide range of ages was represented at baseline, the median age was 21 years and the majority of subjects (>80%) were between 18 and 24 years old. In that respect, almost all were in approximately the same age group and
accordingly, age differences had no significant influence on the prevalence of signs and symptoms of TMD. Since there were more females than males in the study population and some characteristics of TMD in the general populations vary with age and gender (Magnusson et al., 2005; Wänman, 1996), adjustments were made for age and gender in all analyses.

When observations are based on a selected sample, interpretation and generalization to other populations should be done with ample care. On the other hand, if the demand is that analytic epidemiology always should be based on representative study populations, few studies would pass (Scheutz, 2007). The selection of a study sample should ascertain the presence of variables that enable distinguished scientific hypotheses rather than exclusively focusing on the samples’ representatives of larger populations (Rothman and Greenland, 1998). These criteria were considered reasonably fulfilled in this project.

**Methods of examination**
The questionnaires were always filled out prior to the clinical examinations, and the examiners were blinded to the results to avoid bias. In longitudinal research the use of questionnaires with the same questions and wording makes comparison of the results reasonable. A cut-off value for frequency of symptoms at once a week or more often was used to improve reliability (Wahlund et al., 1998). The validity of questionnaires in relation to presence of TMD was generally reported high (Gerstner et al., 1994; Nilsson et al., 2006). The clinical examination procedure followed a routine of the Department of Clinical Oral Physiology at Umeå University. The reliability of parameters used in the clinical assessments of TMD has been scrutinized in several studies (Anderson et al., 1993; Carlsson et al., 1980; de Wijer et al., 1995; Dworkin et al., 1990; John et al., 2005; Wahlund et al., 1998; Vallon et al., 1989; Visscher et al., 2007) and generally reported acceptable in the range fair to good. In conclusion, training and calibration of observers were advised to improve reliability. Before this project started, the examiners routinely examined the same patients to ensure a high inter-examiner reliability. Any uncertainty could be discussed until consensus was reached. Since intra-examiner consistency has been reported to be higher than the inter-examiner consistency (Carlsson et al., 1980; Vallon et al., 1989), the same examiner examined each subject at baseline and at the follow-ups. To improve reliability of TMJ clicking during examination, only reproducible sounds were registered; this may have reduced the risk of false-positive registrations, but also increased the risk of false-negatives in measuring signs of symptomatic disk displacement. The registration of mandibular stability/instability in the intercuspal position was based on the ability or not to hold a firm grip of an occlusion foil between the molar teeth during moderate clenching. Registered instability was associated with a lack of grip.
of the foil, and a tilting of the mandible during harder clenching, hence the term mandibular instability. The general statistical approach was to compare those with no signs and symptoms of the condition in focus (controls) to those with signs and/or symptoms (cases). Dichotomization was done to make the statistical calculations possible.

**Course of TMD**

The prevalence and course of TMD during the 2-year observation period showed a complex pattern of onset, recovery, or persistence, corresponding to a substantial fluctuation (*Papers I, II, IV*). A similar fluctuating pattern has been reported in other prospective studies (Könönen and Nyström, 1993; Könönen et al., 1996; Magnusson et al., 2000; Nilsson et al., 2007; Wänman, 1987). Prevalence figures of TMD differ between these studies and the incidence rates in the present study were generally higher than previously reported (LeResche et al., 2007; Magnusson et al., 2005; Nilsson et al., 2007; Wänman, 1996). Reasons for these discrepancies may be differences in study populations and the investigated variables, as well as variation among examiners.

**TMJ signs and symptoms**

The main TMJ disorder was clicking sounds, reported or registered (*Papers I, IV*). Disk displacement is considered the most common underlying cause of clicking (Stegenga and de Bont, 2006). According to magnetic resonance imaging, TMJ clicking may appear in subjects with a normal disc position, and about one-third of those without TMJ clicking have a displaced disk (Davant et al., 1993; Kircos et al., 1987). Reproducible clicking sounds may be a fairly reliable clinical sign of symptomatic displacement of the TMJ disk but a negative finding does not ensure a neutral disk position.

In the present study, both prevalence and incidence of TMJ dysfunction was high (*Papers I, IV*). A 1-year incidence rate of reported TMJ clicking sounds between 6–9% and clinically registered sounds between 8–15% has been reported previously (Könönen and Nyström, 1993; Wänman and Agerberg, 1990). Compared with the present results, the incidence of reported sounds was similar, while incidence of registered sounds was somewhat higher in the former studies. The difference is most likely related to the more strict criterion of reproducible sounds used in this study. During the observation period no one passed into a locking state with impaired jaw opening. This was in line with results from other cohort studies (Könönen et al., 1996; Sato et al., 2003). In clinical decision making, one important question is whether or not a condition is self-limiting and another is: who may be at risk for longstanding, persistent symptoms and in need of
treatment? Based on the results from an experimental animal study, TMJ disk displacement at early ages has been suggested to retard mandibular growth (Bryndahl et al., 2006). Reported TMJ clicking at baseline has been shown to predict other TMD symptoms 20 years later (Magnusson et al., 2005). In the present study, clinically registered or reported TMJ sounds at baseline increased the risk of developing TMJ pain the following year. This result contradicts another recent study (Reissmann and John, 2007), which found no associations between clinical TMJ clicking and pain in the affected TMJ. The different outcomes may be related to different study samples (referred patients vs. university students) and study designs (cross-sectional vs. prospective analysis). Even though TMJ signs and symptoms developed and disappeared during the observation period the main pattern was a maintained status (Papers I,II,IV), in accordance with previous studies (Kamisaka et al., 2000; Sato et al., 2003). Altogether, the study results support a regular follow-up routine of these conditions in the clinician’s daily practice, reassurance, and in general, a wait-and-see policy. When the disorder calls for treatment, a conservative and reversible treatment approach should be considered before invasive therapy is applied.

Jaw muscle signs and symptoms
The prevalence of myofascial pain (signs or symptoms) was high (Papers II, IV). The main finding was muscles pain to palpation, similar to other population-based studies on TMD (Könnön and Nyström, 1993; Magnusson et al., 2000; Wänman and Agerberg, 1986c). It was difficult to find comparable studies presenting temporal variability of jaw muscle pain as these signs and symptoms most commonly have been merged and described in indices (Könnön and Nyström, 1993; Magnusson et al., 2000). When myofascial pain was defined according to RDC/TMD, the prevalence, as well as incidence, was significantly reduced. Annual incidence rates of TMD pain or jaw pain at 2–3% among adolescents have been reported (Kitai et al., 1997; LeResche et al., 2007; Nilsson et al., 2007). In a 5-year prospective study based on both patients and community cases the calculated annual incidence rate was approximately 8% (Rammelsberg et al., 2003). The incidence of myofascial pain in the present study, was thus within the range of these studies.

A general reflection refers to the significance of jaw muscle pain to palpation. The negative predictive value was high, but the positive predictive value was low (Paper II). These signs or reaction patterns are probably composed of physiological as well as pathophysiological mechanisms, not completely understood. The interpretation should thus be done with caution in the clinical setting and not extrapolated as signs of muscle injury in all cases.
Differences between males and females

Females presented with persistent TMJ signs or symptoms more often than males, but there were no gender differences for onset or recovery (Papers I, IV). Incidence and maintenance of jaw muscle pain (Papers II, IV), onset of TMD pain according to RDC/TMD (Paper III), and onset of spinal pain, as well as headaches (Paper III), were predominantly found among females. These results correspond with previous findings of women reporting a higher prevalence of headache and facial pain (Von Korff et al., 1988) and more multiple pains in more body regions (Berkley, 1997). Incidence of TMD pain showed an almost exponential effect between gender and presence of spinal pain (Paper III). The reason for these gender differences is not fully explained. Some theories advocate that this is a consequence of a greater sensitivity among females to develop and maintain musculoskeletal pain due to lower pain thresholds (Rollman and Lautenbacher, 2001), mechanisms related to sex hormones (Cairns, 2007), and genetics (Diatchenko et al., 2005). In addition differences in coping strategies (Fillingim, 2000) and stress behavior may contribute to the fact that females are more likely than males to experience a variety of recurrent pains, more frequent pain, and pain of longer duration (Unruh, 1996). When gender differences are a general pattern, these differences may be a consequence of the evolution that may have favored females with higher perception and vigilance on sensory information.

Risk factors for TMD

Dental occlusion

Approximately one-third of the study population had any deviation from neutral morphological occlusion, and presence of occlusal interferences was very common (Paper I). These results are in line with other studies (Magnusson et al., 2005; Wänman and Agerberg, 1987). Some morphological malocclusions were related to TMJ signs or symptoms, but in most cases the results were inconsistent. Crossbite, however, presented as a more consistent risk factor for TMJ pain and dysfunction (Papers I, IV). There are conflicting opinions in the literature, some reported no relation between crossbite and TMJ disorders (Farella et al., 2007; Gesch et al., 2005) while others found indications of a connection between the two states (Mohlin and Thilander, 1984; Pullinger et al., 1993; Pullinger and Seligman, 2000). In a Swedish population-based 20-year prospective study, crossbite was found to be a predisposing factor to TMJ pain, and TMJ clicking was three times more common among those with unilateral crossbite at the examination 10 years earlier (Magnusson et al., 2005). In the present study population the positive and negative predictive values, respectively, indicated that approximately 67% of those with a non-symptomatic TMJ, but with registered crossbite at baseline had onset of TMJ pain or dysfunction, and 68% of those with a neutral transversal occlusion remained non-
symptomatic in the TMJ. Crossbite was not only related to onset, but also to persistent TMJ disorders. Crossbite is established already in childhood, with exception of the third molar eruption, and is also reported to be related to condylar asymmetry (Kilic et al., 2008). As the majority of the TMJ signs and symptoms in the present study were represented by joint sounds, the result may thus be linked to biomechanical properties related to occlusion and the TMJ and this finding warrants further studies.

Mediotrusive side contacts or interferences have since the 1950s been thought to disturb mandibular function. The benefit or detriment of mediotrusive side contacts related to TMD has been reviewed, and no scientific evidence to support a balanced occlusion in favor of a mutually protected occlusion or vice versa was found (Marklund and Wänman, 2000). The prevalence of mediotrusive side interferences was high, especially in the more extreme lateral positions (Paper I). These contacts were presented in a higher frequency than the median value of 16% (0–77%) calculated from 17 different studies on dental occlusion, although well within the range (Marklund and Wänman, 2000). No significant relationships were found between presence of mediotrusive side interferences and presence or incidence of TMJ signs and/or symptoms (Papers I, IV). In experimental settings, a balanced occlusion was found to cause the smallest upward displacement of the TMJ during clenching in lateral positions (Baba et al., 2001; Okano et al., 2002) and it has also been proposed that mediotrusive side contacts may be protective of the ipsilateral TMJ (Minagi et al., 1999; Minagi et al., 2000). Others (Christensen et al., 1996) have, in line with the present study, not found evidence for such associations. The hypothesis that mediotrusive side contacts have a protective effect on the ipsilateral TMJ was thus not supported. Nor was there any indication of any detrimental effects of such contacts or interferences on the TMJ during the observation period. This contradicts some studies (Molin et al., 1976; Nishigawa et al., 1991), but is in line with others (Egermark-Eriksson et al., 1987; Gesch et al., 2005; Uhac et al., 2002). A weak correlation was found between mediotrusive side interferences and incidence of jaw muscle signs or symptoms (Paper IV). In an experimental short-term study, incorporation of mediotrusive side interferences induced temporary symptoms (predominantly headache) and signs (mainly jaw muscle pain to palpation) in otherwise healthy females (Magnusson and Enbom, 1984). Mediotrusive side interferences were found to be significantly related to myofascial pain in a cross-sectional case-control study (Landi et al., 2004), but the explanatory value was low. Despite expectations of the present longitudinal study to illuminate the question of whether mediotrusive side contacts or interferences may be detrimental or protective to the function of the jaw system, the outcome was ambiguous. The risk of persistent TMD showed a trend to be lower among those with mediotrusive side interferences. The result was not consistent for incidence
of myofascial pain, since the risk was increased only for those with signs or symptoms and not for those with both signs and symptoms.

A notable result in this thesis was the association between mandibular instability and 1-year-period prevalence of signs and symptoms of TMD (Papers I, II) and 2-year persistent TMD (Paper IV). From a biomechanical point of view, the mandible is raised by the elevator muscles, until contact is established between the teeth. The related force is distributed to the skeleton at mainly three areas: the right and left sides of the TMJ and the teeth in the upper and lower jaw. If contacts are established only on one side in the intercuspal position (ICP), the force from the muscles tends to pivot the mandible, resulting in a levering action on the mandible. In this situation the contralateral TMJ is subjected to an increased force or loading (Korioth and Hannam, 1990; Okeson, 2008b; Rassouli and Christensen, 1995). University students with TMD has been reported to have greater bilateral asymmetry in number of contacts compared to others without TMD (Ciancaglini et al., 2002), and clenching on a bite-force transducer diminished the TMJ space dimension (Kuboki et al., 1996; Takenami et al., 1999). These studies may capture a similar phenomenon, but with different techniques. The direction of the association cannot, however, be assessed, since mandibular instability did not affect the onset of TMD (Paper IV).

Why mandibular instability occurred in the natural dental occlusion is not known, but obviously, the establishment of a stable contact pattern between the lower and upper jaw has failed for some reason. Since this finding was fairly prevalent and identified as a risk factor for signs and symptoms of long-standing TMD, dentists are advised to pay attention to this phenomenon.

Bruxism
Approximately half of the study population was aware of tooth grinding or clenching (Paper I). This figure was higher, as compared to previous reports (Barbosa Tde et al., 2008; Johansson et al., 2003; Lavigne et al., 2003). Approximately half of those with awareness of bruxism at the beginning of the study had an onset of TMJ dysfunction during the observation period (Paper IV). Bruxism, reported at baseline, was also related to presence (Paper I) and persistence (Paper IV) of TMJ disorders, thus supporting the hypothesis that TMJ disorders can be a consequence of an overload of the structures involved. However, reported bruxism was not associated with incidence of jaw muscle signs and/or symptoms and was only weakly related to presence and persistence of myofascial pain (Papers II, IV). The negative predictive value of bruxism was high, but the positive predictive value low, indicating that myofascial symptoms will not develop in all subjects with reported bruxism. These results concur with previously reported predictive values of bruxism in relation to demand for TMD.
treatment (Magnusson et al., 2005). A significant relationship between tooth grinding and clenching and signs and symptoms of TMD has been reported (Johansson et al., 2003; Magnusson et al., 2000; 2005). Bruxism has, furthermore, been related to both social and general health factors (Johansson et al., 2004) and identified as a predictor of the demand for TMD treatment (Carlsson et al., 2004). Patients without TMJ dysfunction, but with awareness of bruxism, should be given appropriate information and advice to avoid these habits as a preventive step.

Spinal pain
In the present study, spinal pain at baseline predicted the onset of jaw pain, headaches, and TMD pain according to RDC/TMD. In addition, signs of TMD at baseline predicted the onset of headaches and spinal pain (Paper III). These results indicate a mutual influence between these pain conditions. This finding supports the suggestion that TMD and neck pain may share common etiology or that one is the cause of the other (Kirveskari et al., 1988). Furthermore, in a 5-year prospective study on patients suffering from chronic cervicobrachial pain and/or headache, establishment of a stable dental occlusion improved the patients’ response to physical therapy (Karppinen et al., 1999). In a case-control study, TMJ dysfunction was reported to be associated with asymptomatic cervical spine dysfunction (Stiesch-Scholz et al., 2003), and a specific examination of the cervical area was recommended when signs and symptoms of internal derangement of the TMJ are present. It has convincingly been shown that neck injury can impair the jaw function (Eriksson et al., 2007). Based on the integrative jaw-neck motor control found in healthy subjects and the disturbed jaw-neck behavior in patients with whiplash-associated disorders (WAD), the authors proposed a new integrated approach for rehabilitation of jaw-neck dysfunction and pain in WAD. The results from these clinical studies are in accord with the findings of the present research. In experimental studies, induced pain in jaw muscles and the TMJ in cats influenced the fusimotor system in neck muscles (Hellström et al., 2000; Hellström et al., 2002), and induced jaw muscle pain was found to change the mechanical thresholds in the hind paws in rats (Ambalavanar et al., 2006). In experimental studies in humans, glutamate injections into the masseter muscle affected the neck muscles (Svensson et al., 2004; Wang et al., 2004). Conversely, spread of pain to the jaw-face region and impaired jaw motor function followed experimentally induced nociception in the trapezius muscle (Komiyama et al., 2005). These results, indicating reciprocity between the trigeminal and spinal sensory-motor systems, thus concur with the outcome of the present study.

In the subgroup analyses simultaneous presence of signs of TMD and spinal pain increased the risk for onset of headaches and jaw pain (Paper III). This pattern may be an effect of spatial summations (Graven-Nielsen et al.,
1997; Staud et al., 2007) and additive effects between sensory input from trigeminal and spinal nerves. Pain conditions have previously been found to predict onset of pain at other locations (LeResche et al., 2007; Von Korff et al., 1993), and local conditions such as TMD pain have been suggested to be involved in the spread of pain (Vierck, 2006). Pain research during the last decade has pointed to sensitization of higher-order neurons in the nociceptive pathways as a possible pathophysiological mechanism underlying pain in the jaw-face region (Sessle, 1999; Svensson and Graven-Nielsen, 2001). One possible mechanism behind the result in the present thesis may thus be an effect of central sensitization with altered pain thresholds and a higher vulnerability. Since other mechanisms also may be involved, this research area warrants further studies.

Concluding remarks

In the individual case, development and course of TMD is related to different contributing factors that alone or in combinations can affect the jaw-system. In research, systematic patterns in groups are important to disclose. Over the years efforts have been made to discover and understand the underlying mechanisms of pain and dysfunction in the jaw-system. Opinions of these conditions have varied, as have the interpretation of both symptoms and clinical signs. A shift in perspective from dysfunction to pain seems to have occurred during the past 20 years. The construction of a condition is crucial. If TMD is viewed from the myofascial pain perspective only, the conclusion from the present research implies that the common denominator will most likely be related to female gender. If the definition of the disorder is related to mandibular mobility, dental occlusion, or function of the TMJ, then other risk factors will emerge. Probably, there are individual differences in vulnerability, not only to pain conditions, but to also to biomechanical properties. Accordingly, it recently was suggested that the etiological role of occlusal interferences in TMD has not been correctly addressed in previous studies (Le Bell et al., 2006). One main reflection is that the choice of construct of a condition (i.e., pain or dysfunction, locus of interest focused on muscles or joint, temporal duration of the condition, etc.) influences the outcome of analyses and thus the understanding and comprehension of the construct itself. Accordingly, caution should be paid in any interpretation of study outcomes as they relate to best practice and management of a patient’s specific situation. TMD is not a single entity, but composed of different diseases affecting the jaw system. One shortcoming of many studies is the focus on TMD as a whole.

In this thesis, the attempt was to analyze factors associated with onset and persistence of TMJ and jaw muscle signs and/or symptoms separately. The results indicate that the relative importance of risk factors related to TMJ
and jaw muscle disorders differ, and thus support a distinction of different conditions affecting the jaw system in the search for risk factors.

**Clinical implications**

Prevention of disease onset and progress is a major goal in health care. Signs and symptoms of TMD are common in the population, and dentists are thus expected to meet patients with TMD of varying severity in their daily practice. Signs and symptoms related to the temporomandibular joint, mostly represented by clicking, can both be neglected and constitute a severe disturbance to a patient. With reference to the high incidence and fluctuating pattern, dentists are recommended at first hand to give advice and reassure that these conditions fluctuate and rarely progress to locking or painful status. When treatment is demanded, a reversible approach should be considered before invasive therapy is applied. For individuals with crossbite the relative risk of developing TMJ disorders should be included in the clinical decision process. If mandibular instability indicates an increased load on the TMJ, the instability should be adjusted. Variations in dental occlusion do not have the significant importance they were previously ascribed, but there is a potential risk that a too simplistic view of the dental occlusion may be harmful to the individual patient with long-standing TMD. Patients who are aware of bruxism should be given advice to reduce these habits, since these are related to both onset and persistence of TMJ pain and dysfunction. From the perspective of pain as a common condition in the population, with impairment of function, sick leaves, use of health care services, and related costs (Statens beredning för medicinsk utvärdering, 2006), prevention of progress of pain should be a priority. Dentists, and particularly TMD specialists, should take part in teams working with pain patients, since these may benefit from a multidisciplinary approach. The financial systems for health care and dentistry should, accordingly, be uniform for these patients. Studies have shown a relationship between sick leaves and TMD (Alanen and Kirveskari, 1983; Kuttila et al., 1997), and a significant reduction of sick leave after treatment of TMD (Kirveskari and Alanen, 1984; Wedel and Carlsson, 1987). Altogether, these studies suggest a multidisciplinary treatment approach for pain patients. The state and function of the jaw system should be considered in patients with spinal pain, and dentists may significantly contribute to the preventive, as well as the rehabilitative process.
SUMMARY OF RESULTS

- Incidence of TMJ pain and dysfunction was high and similar for males and females. The course was composed of onset, recovery, and maintenance, resulting in a fluctuating pattern over time. Females were more likely to have persistent TMJ pain and dysfunction.

- Incidence and persistence of jaw muscle pain was high, especially among females. A fluctuating pattern similar to that of TMJ pain and dysfunction was found.

- Crossbite was associated with onset and persistent TMJ pain and dysfunction.

- Mandibular instability was associated with persistent TMJ pain and dysfunction, as well as persistent jaw muscle pain.

- Reported bruxism was associated with incidence and persistence of TMJ pain and dysfunction.

- Signs of TMD predicted the onset of non-pain TMD symptoms, jaw pain, headache, and spinal pain.

- Spinal pain predicted the onset of jaw pain, headache, and TMD pain.

- Females with spinal pain had an increased risk of TMD pain onset.

- Simultaneous presence of TMD signs and spinal pain additionally increased the risk of jaw pain and headache onset.
CONCLUSIONS

- The findings of a high incidence and a fluctuating pattern of TMJ pain and dysfunction and jaw muscle pain, support a regular follow-up routine and reassurance for these conditions in the daily practice, and, in general, a wait-and-see policy.

- Females have higher risk for longstanding TMD, which should be taken into account, and may partly explain the higher prevalence of females seeking care for TMD.

- The increased risk among individuals with crossbite of developing and maintaining TMJ disorders should be considered in the decision process for treatment planning among these patients.

- A stable dental occlusion in centric position reduced the risk for longstanding TMD. Dental occlusion was, therefore, not rejected as a contributing risk factor for TMD.

- Patients without TMJ dysfunction, but with awareness of bruxism, should be given appropriate information and advice to avoid tooth grinding and clenching as a preventive measure.

- Pain and dysfunction in trigeminally as well as pain in spinally innervated areas mutually predicted the onset of new symptoms, indicating common pathophysiological mechanisms and individual vulnerability.

- The results indicate that spinal pain and TMD affect each other. Hence, identifying multiple pain conditions at different locations should be included in risk assessment and treatment planning. These findings further support a multidisciplinary approach and warrant more research.

- It is recommended that the status and function of the jaw system be considered in patients with spinal pain.
POPULÄRVETENSKAPLIG SAMMANFATTNING

För att förebygga och behandla sjukdom krävs kunskap om riskfaktorer och sjukdomsförlopp. Käkfunktionsstörning (eng. temporomandibular disorders, TMD), är en term som används för att beskriva tillstånd med smärta och nedsatt funktion i käkled och käkmuskulatur. I avhandlingen studerades uppkomst (incidens) och förlopp av käkfunktionsstörning i förhållande till kön, tandgnissling och tandpressning (bruxism), olika bettförhållanden samt huvudvärk, nackvärk och ryggvärk som möjliga riskfaktorer i en 2-årig observationsstudie.


Studien visar att kvinnor har en högre risk för långvariga symtom på käkfunktionsstörning, vilket delvis kan förklara den högre andelen kvinnor som söker vård för dessa tillstånd. För personer med korsbett och tandpressning eller tandgnissling, bör den ökade risken att utveckla käkledsbesvär tas med i bedömningen, i samband med behandlingsplanering. Stabila kontaktförhållanden vid sammanbitning minskar risken för långvarig TMD. Studien indikerar att nack- och ryggvärk och käkfunktionsstörning ömsesidigt påverkar varandras förlopp, vilket stödjer behovet av ett multidisciplinärt omhändertagande av patienter med flera smärtområden. En bedömning av käksystemet bör därför ingå vid utredning och behandling av patienter med smärta i nacke och rygg.
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