# Psychologic Impact of Chronic Orofacial Pain: A Critical Review

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**Aims:** To explore the prevalence of clinically significant anxiety and depression in adult patients with chronic orofacial pain (COFP) conditions. **Methods:** A systematic online search of the Medline (PubMed) and Ovid databases was performed for articles published from 2006 to 2019. Observational studies—including cross-sectional, case-control, and case series—and longitudinal prospective studies were included. A total of 118 articles were selected for inclusion, and the prevalence rates of clinically significant anxiety and depression were summarized. **Results:** Most studies focused on temporomandibular disorder (TMD) pain and less often on neuropathic COFP conditions. Prevalence rates varied widely across studies according to OFP condition and assessment measure; most questionnaire-based assessments yielded rates of clinically significant depression and anxiety in, respectively, 40% to 60% and 40% to 65% of individuals with TMD and in 20% to 50% and 25% to 55% of patients with neuropathic, mixed, or idiopathic/atypical COFP conditions. Rates of anxiety and depression were lower in studies using diagnostic instruments and in TMD studies with nonpatient samples. Most controlled studies showed a higher prevalence of anxiety and depression in individuals with COFP than in those without. Higher COFP pain levels and the presence of comorbid conditions such as migraines or widespread pain increased the likelihood of anxiety and/or depressive symptoms in individuals. **Conclusion:** Clinically significant anxiety and depression were commonly observed in patients with COFP, were present at higher rates than in pain-free participants in controlled studies, and were closely linked to pain severity. More research is needed to evaluate the psychologic impact of multiple COFP conditions in an individual and the prevalence of precondition psychologic morbidity. *J Oral Facial Pain Headache 2022;36:103–140. doi: 10.11607/ofph.3010*

**Keywords:** *anxiety, depression, neuropathic/nonneuropathic pain, orofacial pain, TMD*

Orofacial pain is a noxious, painful experience in the region of the face and/or oral cavity.[1] According to the International Association for the Study of Pain (IASP), *pain* is defined as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."[2] Chronic pain continues after the expected time of recovery.[3] There is evidence that pre-existing psychologic factors can predict the onset of postsurgical chronic pain.[4]

Patients with chronic pain frequently undergo a change in their beliefs and cognitions, and these affective and cognitive pathways contribute to the sensory perception of pain.[5] Over time, individuals with chronic pain may lose the capability to function optimally, and some may retire from work early.[6] Nonorofacial chronic pain conditions can cause a significant degree of disability.[7] In the United States, they are responsible for 21% of visits to accident and emergency departments and for 25% of absenteeism from work annually, significantly increasing the economic burden.[8] Orofacial pain (OFP) is specifically linked to increased workday loss and excessive use of health care systems.[9,10]

The prevalence of OFP ranges from 17% to 26%, with up to 11% considered chronic orofacial pain (COFP).[11] COFP is often associated with psychologic disorders, and there is a strong link between

long-standing OFP and depression and anxiety symptoms, with subsequently impaired psychologic function.[6] Pain management is limited without an acknowledgment of psychologic factors, and the recovery process is often compromised because differences in an individual's psychologic predisposition result in differential responses to pain.[12]

The aim of this review was to investigate studies of psychologic functioning (ie, anxiety and depression) in patients with COFP, with consideration of both neuropathic and nonneuropathic COFP conditions.

## Materials and Methods

The review protocol, including the search strategy, was registered with PROSPERO (International Prospective Register of Systematic Reviews, registration number: CRD42016043703).[13] It was not possible to perform meta-analyses due to the heterogeneity of the included studies. The cumulative evidence from the included studies was assessed, summarized, and narrated.

### Search Strategy and Selection Criteria

The present review included observational studies published between 2006 and 2019. These studies were cross-sectional, case series, and prospective and retrospective cohort studies. The information sources were the Medline (PubMed) and Ovid databases. Gray literature was searched via Google Scholar. Studies in the English language investigating at least one type of COFP condition in adults (aged 18 and older) and exploring psychologic factors such as depression, somatization, posttraumatic stress disorder, and catastrophizing were selected. Studies recruiting individuals under the age of 18 years and studies exploring dental and periodontal inflammatory conditions and their psychosocial impacts or influences were excluded.

### Definitions

Chronic pain is defined as a pain that exceeds a duration of 3 months,[3] and this definition was applied to COFP for the present study.

*Psychology* is defined as the scientific study of an individual's behaviors and their mental processes.[14] According to the World Health Organization (WHO), *depression* is a mental disorder that presents with depressed mood, loss of interest or pleasure, a decreased level of interest and concentration, disturbed sleep, lack of appetite, and feelings of hopelessness and worthlessness.[15] Depression can often be associated with anxiety symptoms.[15] Generalized anxiety disorder (GAD) was defined as 6 months of excessive worry about daily issues and may be associated with autonomic symptoms.[15] State anxiety is a temporary emotional arousal to a perceived threat, and trait anxiety is a personality characteristic and pattern of response (with anxiety) to a threat.[16] Phobias, obsessive-compulsive disorder, and panic disorders were included in anxiety disorders. A *phobia* is a constant and pronounced fear of a situation that can result in either avoidance or panic attacks.[15]

### Search Terms

The keywords used were: psychosocial; psychologic; depression; psychiatric comorbidity; posttraumatic stress disorder (PTSD); and anxiety. These keywords were used with "OR" and "AND" with the following conditions: orofacial pain; temporomandibular joint pain/disorder; trigeminal neuralgia; trigeminal nerve injury; burning mouth syndrome; persistent dento-alveolar pain; atypical facial pain; and atypical odontalgia.

### Outcome Measures

The objective of the present review was to investigate studies on anxiety and depression in patients with COFP and, more specifically, to identify the reported prevalence of anxiety and depression in affected individuals and their relationships with pain chronicity, pain severity, and demographic factors, such as gender and age.

### Data Extraction

The initial search yielded 5,024 articles. Suitable articles were identified (n = 252) during title and abstract screening through the process of selection and filtration. Duplicates were removed. Full-text screening of 134 articles was carried out. Based on the inclusion and exclusion criteria, a total of 118 articles were selected (Fig 1).

Initially, to establish their relevance for the review, one reviewer (A.K.) read the title and abstract of each article. After reading the abstract and ensuring that the article provided the necessary information for the review, the entire article was retrieved and read to further establish whether it fulfilled the eligibility criteria. Any study that was unclear about its inclusion criteria was read by the second (J.S.), third (L.M.), and fourth (T.R.) reviewers. After discussion, consensus was reached for all articles included. The bibliographies of the selected articles were also manually searched for additional studies.

The studies on COFP were categorized according to classification (diagnostic) system: the International Classification of Headache Disorders-3 (ICHD-3),[17] the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD),[18] and the IASP and American Academy of Orofacial Pain (AAOP).[19,20] All studies were assessed on the

following parameters: type of study, type of pain under investigation, sample size, psychologic scale used, psychologic comorbidities under investigation, the reported prevalence of psychologic comorbidities in each study, and the year of publication.

Meta-analyses were not considered appropriate, as there was an insufficient number of studies with a required level of homogeneity in study design, COFP population under study, and depression/anxiety scale or method of assessment used.[21]

### Risk of Bias Assessment

This study used a method previously employed in systematic reviews of oral conditions to assess the risk of bias (RoB).[22–24] Studies were evaluated on the following criteria: *(1)* Study group characteristics (whether consecutive or unselected patient selection was performed); *(2)* presence of an appropriate control group (sex- and age-matched); *(3)* prospective study or data collected purposely for the specific study; and *(4)* whether participants or the investigators were blinded if appropriate according to the study design.

The criteria were assessed as met, unmet, or unclear for each. Three factors were used to assess the study's overall validity: *(1)* There is a low risk of bias because all of the criteria were met according to the study design; *(2)* There is a high risk of bias because at least one criterion was unmet or three criteria were unclear; *(3)* There is a moderate risk of bias because one or two criteria were unclear, or one or two criteria were not applicable according to study design. All four reviewers independently evaluated the RoB, and all studies were distributed equally among the reviewers.

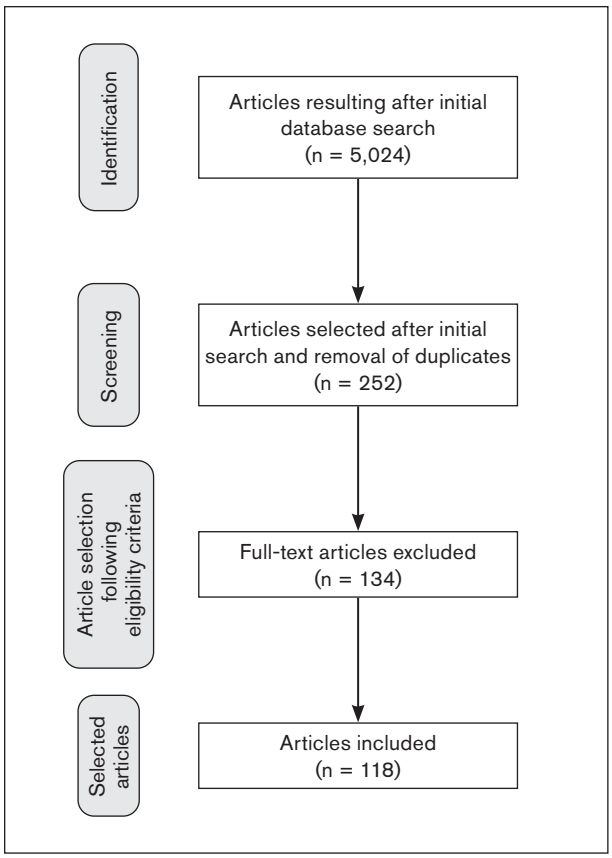



**Fig 1** Flow diagram of study selection.

## Results

The defining characteristics and key findings of the included studies are summarized in Table 1.

### Participant Characteristics

#### *Diagnosis*

The majority of included studies (n = 63) focused exclusively on TMD pain[25–67,69-87,116,121,123] and its impact on psychologic wellbeing (ie, anxiety/depression). Thirty-three studies recruited patients with a single neuropathic pain condition (23 burning mouth syndrome [BMS],[88–103,120,135,136,138,139,164,165] 2 posttraumatic neuropathic pain [PTNP],[104,105] and 8 trigeminal neuralgia [TN]).[106-111,134,137] Eleven studies compared patients with various types of OFP conditi ons[16,112–115,117,119,120,122,124,125]; these included studies comparing BMS to TN; PTNP/TN to TMDs; idiopathic continuous orofacial neuropathic pain to TMDs; TN to TMDs; TMDs to migraine and headaches (ie, neurovascular pain); TN to atypical facial pain, hereby referred to as persistent idiopathic facial pain (PIFP); and BMS to atypical odontalgia (AO), hereby referred to as persistent idiopathic dentoalveolar pain (PDAP). Seven studies focused on COFP in general (where pain types were not specified),[56,126-131] and 2 recruited patients with AO.[132,133] Sample sizes across all studies ranged from 8 to 3,904 participants.

#### *Gender*

With the exception of a clinical trial on PTNP patients, where gender was evenly distributed,[104] mixed-gender studies involving clinical COFP populations employed samples that predominantly comprised women (range: 60% to 97%), with the exception of two studies where women were in the minority (36% and 38%).[61,106] Eight studies included women (TMDs and BMS) only.[36,44,51,52,71,74,93,97] Aside from a community survey of elderly people (77% women),[128] studies recruiting patients from the (general) health care population tended to have a small majority of women (range: 51% to 64%).[31,48,58,131] The age range of the study population across most studies was 18 to 80 years, except for one where the upper limit was 100 years.[118]

### Study Design

A total of 86 studies were cross-sectional in design,[25,27–32,34,36–42,44,47,49,50,53,55–57,59,60,62–65,67–71,73–77,79–81,83–91,94,95,97–100,102,103,105,107,108,110–114,116–124,126–128,133,134] and 11 were longitudinal prospective studies.[33,43,45,46,48,54,109,111,129–131] Ten were designed as case-control,[16,35,51,52,58,61,78,82,96,132] 8 were retrospective,[26,66,92,101,106,110,115,133] 1 was a case series,[93] and 2 were clinical trials.[72,104] An exception was made to include the 2 clinical trials, as these studies measured the postintervention association between the level of pain experienced and the degree of observed anxiety and depression.

### Study Characteristics

A total of 67 studies [16,28,31,35,44,45,47,48,51,52,54,55,57,58,60,64–67,70,71,73,74,77,79–100,102,104–112,114–116,118,119,122,125,126,129,131,133] investigated the association of COFP with anxiety and depression, 9 studies[25,39,42,46,59,61,75,76,103] with anxiety only, 31 studies[26,27,29,30,32,33,36–38,40,41,43,49,50,53,56,62,63,68,69,72,101,113,117,120,121,123,124,127,130,132] with depression only, 1 with psychologic distress, [128] and 1 with hypochondriacal beliefs.[34] Seventy-seven[27–33,36–38,40–49,55,57–62,64–73,76,78–80,82–84,87,89,92,93,96,99–101,105–109,111,112,117–119,122,123,125–130,132,133,135–139] provided prevalence data for anxiety and/or depression, although 3 studies did not report prevalence rates separately for COFP and non-OFP groups.[42,60,129] Most of the research was carried out in Europe (n = 56), followed by Asia (n = 38), Latin America (n = 15), the USA (n = 6), and Australia (n = 1), while 2 spanned across continents. There were 33 (28.0%) low RoB studies and 27 (22.9%) high RoB studies; almost half of the studies (n = 58 [49.2%]) had a moderate risk of bias (Table 2).

### COFP Assessment Criteria

Of the included studies, 97% followed an established diagnostic criteria/classification system for the COFP conditions. These included the RDC/TMD,[25–30,32,34–42,47,49,52–54,56,58,61–64,66,68,70,73,75,76,78,80,81,83,84,86,87,114,115,121,123] the Helkimo Clinical Dysfunction Index for TMD,[31,33,57,59,60,65,77,79] the International Headache Society (IHS) ICHD-3 criteria, [78,89,91,93,94,96,97,99,100,102,108,109,112,115,122–125,129,133] the AAOP criteria,[46,48,50,51,112,114] the IASP criteria,[90,107,114,115,117,120] the Craniomandibular Index (CMI),[43,116] and the European Academy of Craniomandibular Disorders (EACD) criteria.[45] The Liverpool criteria for trigeminal nerve pain were used in one study,[16] while another used the Ma and Zhang classification for TMD pain.[44]

### Psychologic Screening Tools Used

The State-Trait Anxiety Inventory (STAI) was used by 14 studies,[16,39,42,51,52,55,58,76,85,89,90,95,98,164] the Zung Self-Rating Depression Scale (ZSDS) used by 6 studies,[88,100,117,124,133,165] and the Zung Self-Rating Anxiety Scale (ZSAS) used by 3 studies.[59,100,165] A total of 69 studies used a single psychologic tool, while 49 used a combination of psychologic assessment tools. The RDC/TMD Axis II questionnaire [25–27,29,32,36–41,47,49,53,56,58,62,63,66,70,72,83,121,123,132] was used exclusively for TMD pain, the Symptom Checklist-90-Revised (SCL-90-R) [26,28,37,38,40,41,44,47,52,53,63,66,69,70,94,97,113,116,120,121,127] was used to assess psychologic symptoms/distress, and the Hospital Anxiety and Depression Scale (HADS) [31,35,45,54,57,60,61,65,67,71,73–75,78,79,91,92,104,105,107,111,114,115,122,126] was most commonly used to screen for anxiety and/or depression. Five studies used the Structured Clinical Interview for Diagnosis-Diagnostic and Statistical Manual of Mental Disorders (SCID-DSM-4/5) guide.[28,112,119,131,133]

### Prevalence of Anxiety and Depression in Patients with COFP

The prevalence of depression and/or anxiety in COFP, according to COFP group and assessment instrument, are summarized in Figs 2 and 3. With respect to standardized questionnaire assessments, rates were included only for those patients evidencing moderate or severe symptoms (where questionnaires included an umbrella classification of mild to moderate, patients scoring in this range were also considered), or, in the case of HADS, those showing borderline clinical or clinically significant levels. Where studies included assessments at two time points, only the first was included.

For TMDs, the prevalence of observed depression ranged from 7.0% to 77.4% (Fig 2a). In general, studies using the RDC/TMD or SCL-90-R assessments reported the most consistent prevalence rates, with 14 of 20 (70%) studies observing depression in 41.4% to 56.0% of participants. Studies adopting other standardized questionnaires (eg, HADS/Beck Depression Inventory [BDI]) reported lower rates of depression, although this varied considerably across studies, while diagnostic assessments of depression were consistently around 20% (15.7% to 22.3%). Rates of clinically significant anxiety in TMD also varied widely across studies (7.4% to 78.0%; Fig 2b), although the observed prevalence in studies using the RDC/TMD and SCL-90-R or the HADS assessments were more comparable, with 11 of 14 studies adopting one of the measures and yielding anxiety case rates between 43.9% and 63.0% with either measure. The single study that estimated the prevalence of anxiety using the CID-S[48] reported high rates of anxiety in both TMD MP (78.0%) and TMD JP (64.8%). In contrast, the GAD-7 questionnaire assessments of TMD anxiety[80,84,87] resulted in

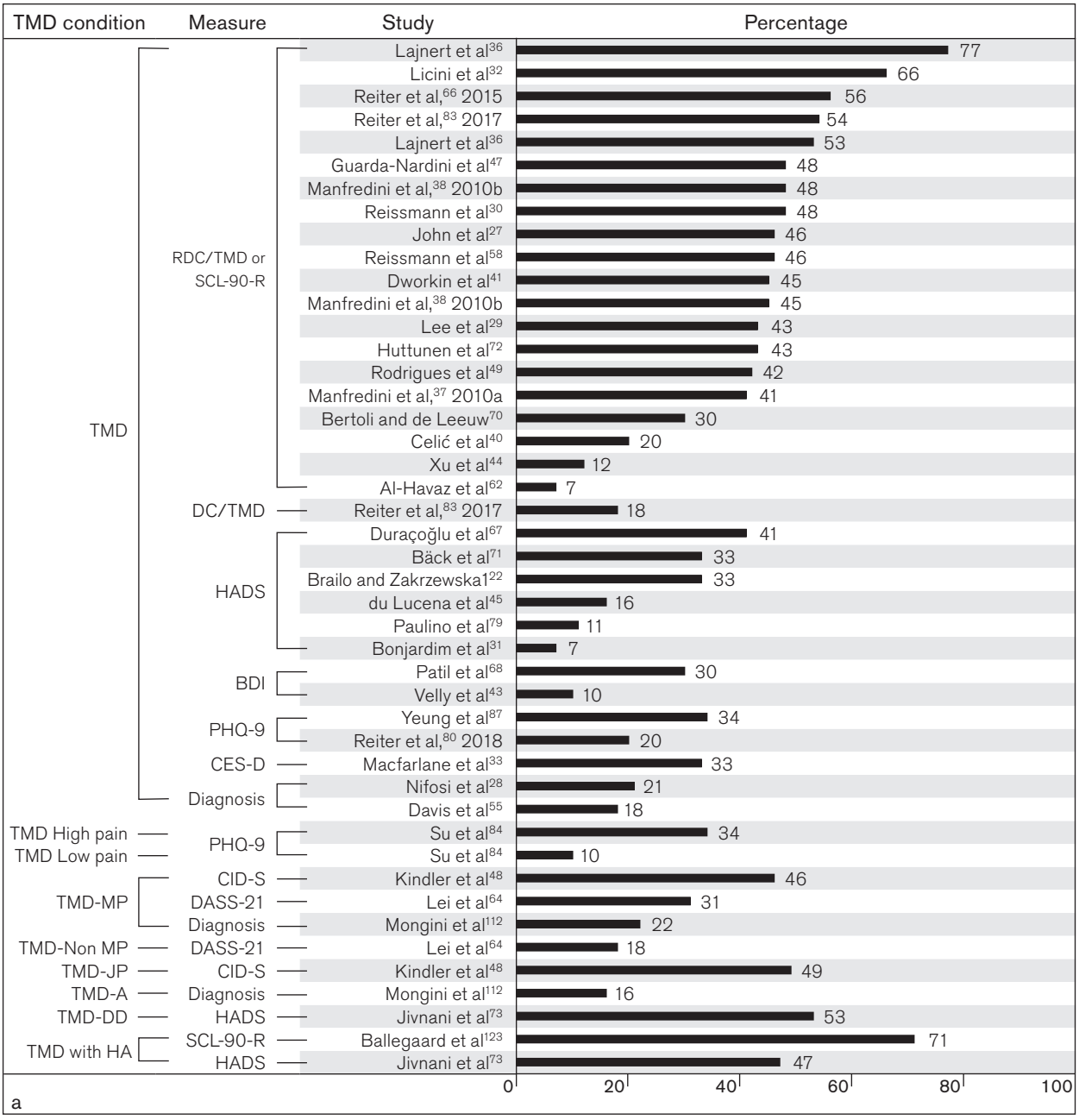
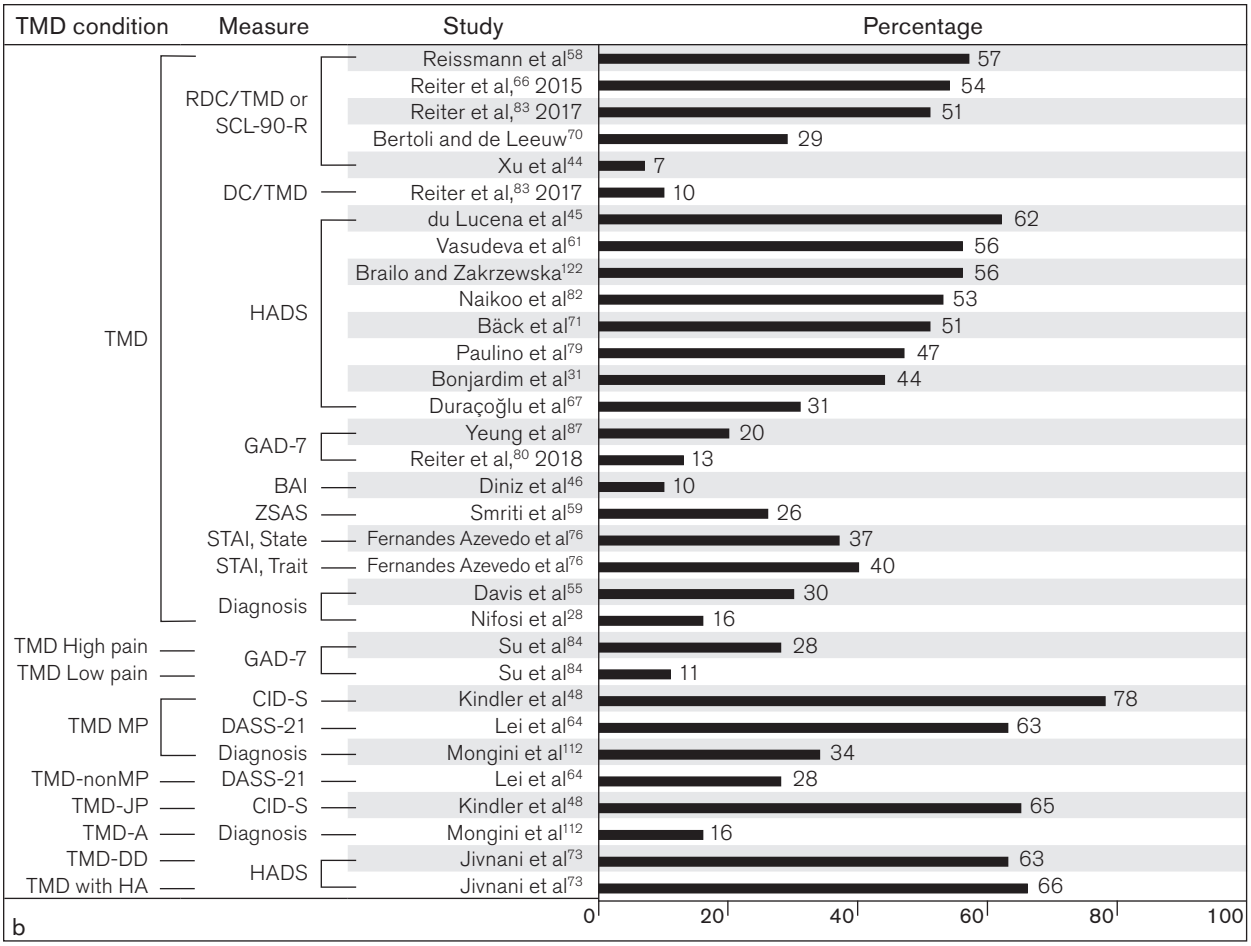



**Fig 2** **(a)** Depression and **(b)** anxiety across TMD studies. Studies are ordered according to TMD condition, depression/anxiety measure, and percentage of depression/anxiety reported. DD = disc displacement; HA = headache. See other abbreviations in Table 1 legend.

lower prevalence rates, ranging from 11.4% to 20.0%. Notably, irrespective of assessment method, studies with a low prevalence of depression and/or anxiety tended to recruit nonclinical samples[31,46,62,79] or TMD samples with low pain disability levels,[44] while higher rates were observed in clinical studies of patients with TMD and headache.[73,123]

The prevalence of depression and anxiety for neuropathic, mixed, and idiopathic/atypical COFP conditions ranged from 2.2% to 100% and from 0% to 80.7%, respectively (Fig 3). Rates of depression and anxiety varied widely in TN samples, with low prevalence rates reported in studies using diagnostic assessments[106,112] and higher rates in TN with associated comorbidities, such as chronic facial pain[118] and MS.[111] Prevalence rates of depression and anxiety in BMS were more consistent. Aside from one small clinical study of 8 patients with treatment-resistant BMS that observed depression in all patients,[93] questionnaire-based assessments yielded moderate to severe symptoms for a quarter to a half of BMS patients across studies. Clinically significant

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levels of anxiety in BMS were highest in studies using the Hamilton Anxiety Rating Scale (HARS) and HADS (39.3% to 80.7%)[92,93,136,139] assessments and lowest in those employing the Beck Anxiety Inventory (BAI; 21.0% to 33.3%).[96,138] Three of the four BMS studies with diagnostic assessments reported anxiety disorders in a third to a half of participating patients.[89,117,119] In one study of PTNP pain, clinically significant anxiety was found in 51.2% of individuals and depression in 30.0% of cases.[105] Depression in AO was reported at 74.0% in one study using the SCL-90-R,[132] but at only 15.4% in a diagnostic assessment study.[133] Similarly, rates of diagnosed anxiety disorders in PDAP samples were uncommon in two studies (10.1% to 10.8%).[117,133]

## Prevalence of Anxiety and Depression in COFP Conditions vs Control Participants

A number of studies comparing prevalence rates in TMD and control participants reported significantly higher rates of anxiety,[31,45,58,59,61,71,73,79,82] depression,[36,58,68,71,73] or anxiety and/or depression[57,65] in individuals with TMD. One TMD study of dental students failed to find significant differences in state and trait anxiety between those with and without TMD,[76] while another three studies of preuniversity/university students reported significantly higher anxiety prevalence rates in TMD cases vs controls, but nonsignificant elevations in depression.[31,45,79] Significantly higher rates of depression were also observed in studies comparing mixed COFP patients to individuals without OFP.[33,127,130]

Although studies comparing mean scores of standardized questionnaires assessing anxiety and depression in neuropathic COFP conditions, such as TN or BMS, against control participants have reported elevated scores in the former (indicative of greater levels of symptoms of anxiety/depression),[91,102,110] fewer controlled studies have compared prevalence rates of clinically relevant anxiety or depression. However, two controlled studies observed significantly elevated rates of both anxiety and depressive

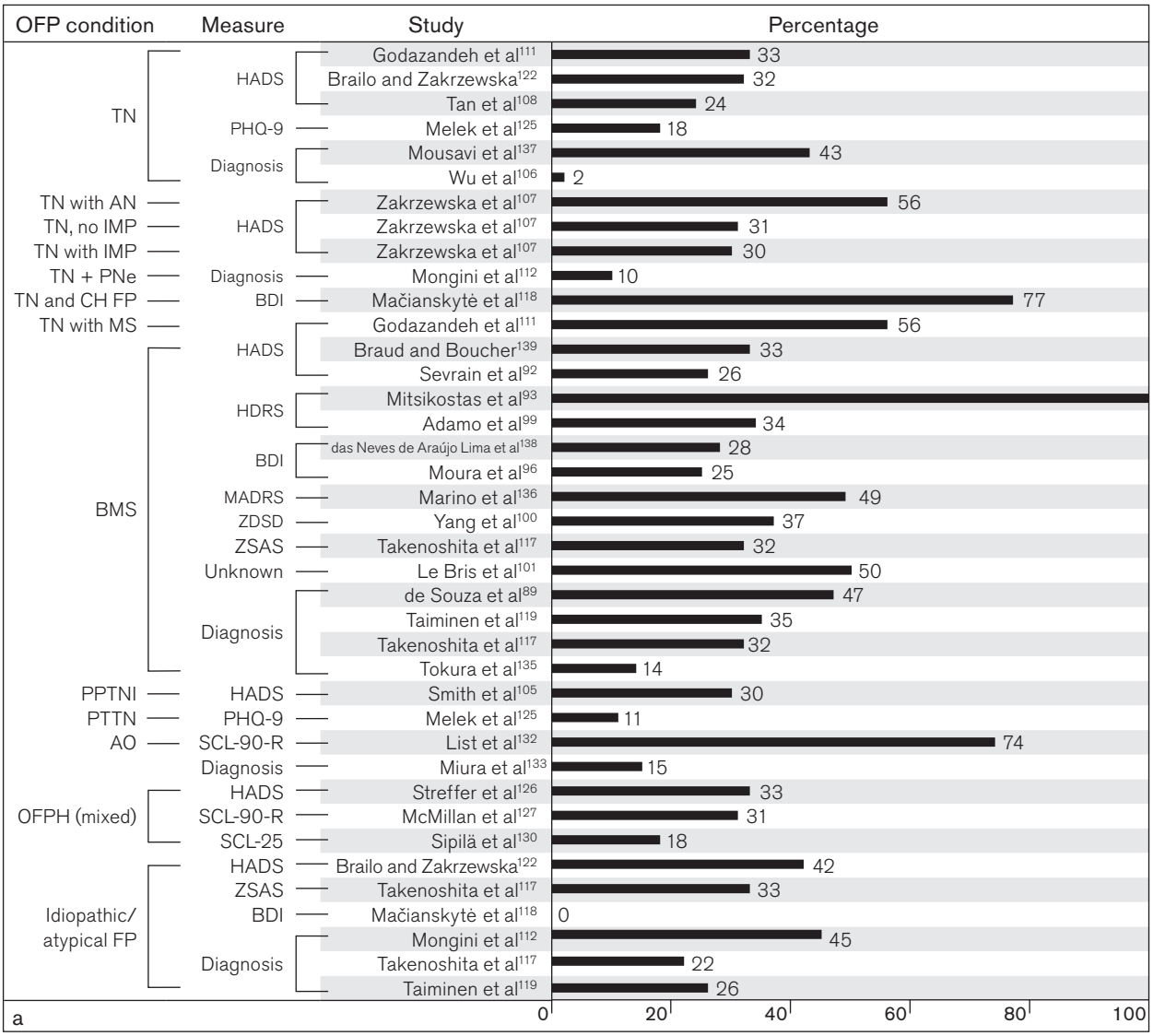


**Fig 3** Rates of **(a)** depression and **(b)** anxiety across neuropathic, mixed, and idiopathic/atypical orofacial pain (OFP) condition studies. Studies are ordered according to OFP condition, depression/anxiety measure, and percentage of depression/anxiety reported. CH = chronic; FP = facial pain. See other abbreviations in Table 1 legend.

disorders in patients with TN[106] and BMS,[89] while another study comparing BMS and secondary oral burning patients reported elevated rates of moderate to severe depression according to the BDI in BMS, but comparable rates of anxiety according to the BAI.[138] Finally, one study comparing PDAP and control participants found significantly more of the PDAP patients showed moderate to severe depression levels.[132]

## Single-Study Comparisons of Different COFP Conditions

Thirteen studies compared two or more types of COFP conditions.[16,112–115,117–122,124,125] In one study, neuropathic pain (TN and trigeminal neuropathy) and TMD pain patients were significantly (but comparably) impaired in domains of anxiety (state and trait anxiety) and depression when compared to controls.[16] Another study reported that TN patients showed numerically higher scores on measures of psychologic impairment than TMD patients, although there were no statistically significant differences between the two groups.[114] When TN and PIFP were investigated, it was observed that TN patients evidenced significantly higher levels of pain perception than PIFP patients and were significantly more likely to exhibit moderate to severe depression levels (76% vs 0%).[118] Another study reported that BMS and PIFP demonstrated comparable levels of depressive symptoms.[119] Komiyama et al compared patients with BMS and TN

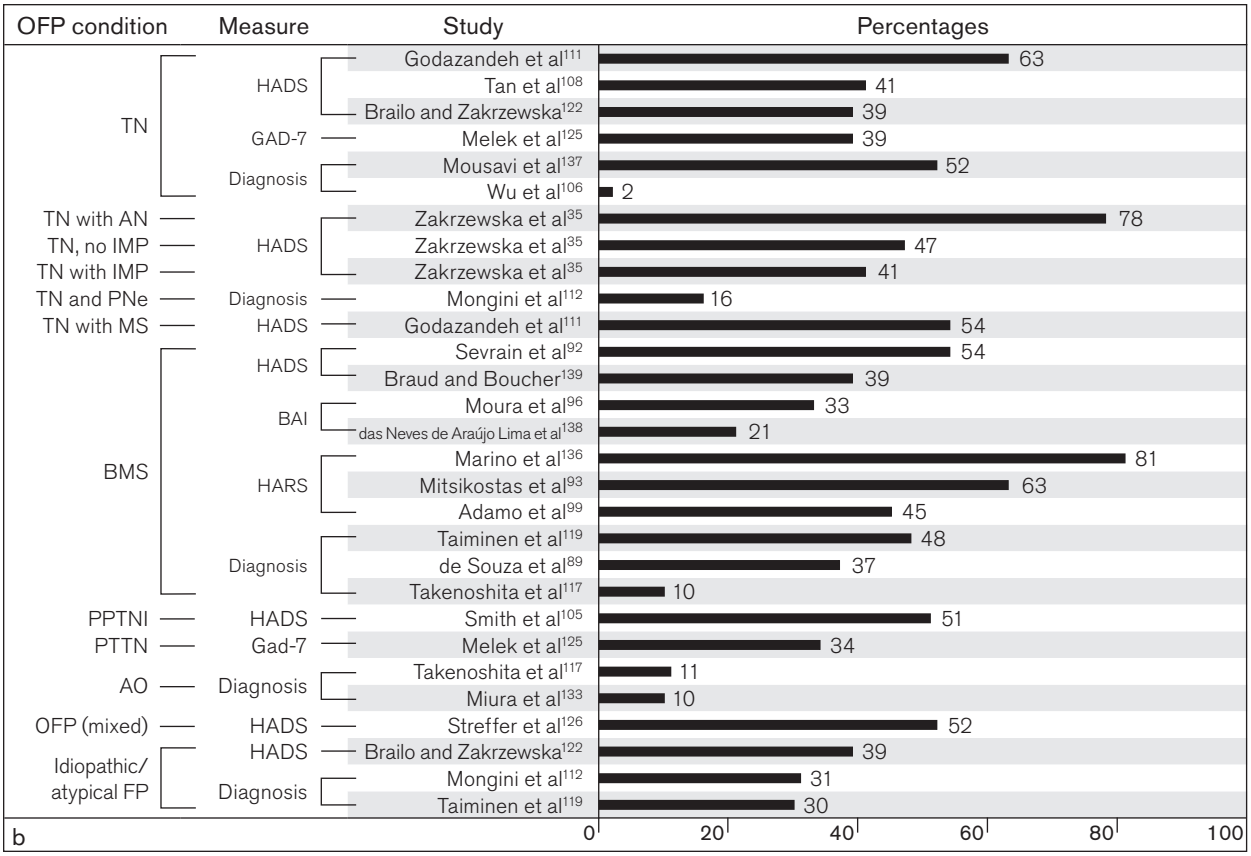


**Fig 3** Rates of **(a)** depression and **(b)** anxiety across neuropathic, mixed, and idiopathic/atypical orofacial pain (OFP) condition studies. Studies are ordered according to OFP condition, depression/anxiety measure, and percentage of depression/anxiety reported. FP = facial pain. See other abbreviations in Table 1 legend.

and reported that pain levels were higher in TN than BMS. However, regression analyses indicated the associated risk of depression in BMS patients was significantly higher than in TN patients.[120] Takenoshita et al investigated mood in COFP patients (BMS and PDAP) using the Zung Self-Rating Depression Scale and observed depressive tendencies in 32.1% of BMS patients and 33.3% of individuals with PDAP.[117] The large-scale study of Gerrits et al on chronic pain suggested the onset of anxiety and/or depression with pain and observed that pain specifically in the orofacial region was associated with depressive symptoms.[131] A study on BMS and PIFP using SCID guides reported high rates of psychiatric disorders, most commonly major depression (30.2%), social phobia (15.9%), specific phobia (11.1%), and panic disorder (7.9%); in these cases, illness runs a chronic course and is difficult to treat.[119] Another study on TMD pain using the same interview technique exhibited frequent presence of psychiatric history in myofascial pain patients.[28] Melek et al compared TN to peripheral painful traumatic trigeminal neuropathy (PPTTN), and depression was reported in 54% of TN and 36% of PPTTN, while anxiety was comparable in both groups (34% and 39%, respectively).[125]

## Association Between Orofacial Pain Severity and Chronicity with Anxiety and Depression

The majority of selected studies (with both neuropathic and nonneuropathic pain samples) demonstrated that an increase in pain intensity and/or pain chronicity (more than 3-month duration)[3] elevated patients' anxiety and depressive symptom levels.

### *Neuropathic Orofacial Pain*

For patients with neuropathic pain, consistent associations of anxiety and depression with pain intensity were identified. For example, patients with severe trigeminal nerve injury pain showed elevated levels of depression on the HADS compared to patients with moderate and mild pain levels in one study.[105] In another study, change in posttraumatic peripheral neuropathic pain levels was significantly associated with change in anxiety and depression levels[104]; every 2-point decrease in level of pain on a 0–10 numeric rating scale was associated with a 1.5-point reduction in anxiety and a 1.2-point reduction in depression

on the HADS.[104] BMS patients also demonstrated a positive association between levels of depression and BMS symptom severity.[88] Additionally, one study found an association between presence of anxiety symptoms and pain severity among elderly individuals with neuropathic pain (BMS).[103]

***TMD Pain***

For TMD pain, cases were divided into acute and chronic by some investigators for comparison. Depression was more prevalent in patients with chronic TMD pain,[36,40,43,66,69] and severity of depression and anxiety increased with higher graded chronic pain scores.[44,47,49,63,66,68,116] Su et al compared TMD patients with high- and low-intensity pain and reported marked differences in prevalence of both moderate to severe anxiety (27.9% vs 11.4%) and moderate to severe depression (33.5% vs 10.2%).[84] Multiple pain sites were also associated with higher levels of depression in another study.[40] A number of investigators also reported significant associations between anxiety levels and chronic TMD pain,[31,39,42,58,61,70] most predominantly for the myofascial subtype of TMD.[25,45,48,64] Patients with TMD pain, especially muscle pain, presented with more psychologic problems compared to patients with TMD joint pain in one study.[28] Moderate-to-severe anxiety and depression in chronic TMD were reported as high as 58.3% and 61.2%, respectively, in another study.[66]

Some studies with TMD patients reported significant associations between the level of physical/psychologic disability and pain intensity using a hierarchical pain grading approach (Graded Chronic Pain Scale [GCPS]), which classifies pain/disability into four broad categories: grade I (low pain intensity/low disability); grade II (high intensity/low disability); grade III (moderately limiting pain/high disability); and grade IV (severely limiting pain/high disability).[140] For example, in one study, psychologic impact tended to be greater in patients with grade III or IV pain, and anxiety was identified in 53.8% of these individuals and depression in 76.9% of these individuals[44]; in another study, severe depression was prevalent in 40.7% of patients with grade III or IV pain.[38]

### Orofacial Pain, Gender/Age, and Anxiety and Depression

Most, but not all, studies considering gender suggested women with OFP may report higher levels of anxiety or depressive symptoms than men. For example, in one study, younger (under the age of 24 years) and middle aged (between 35 and 55 years) women with OFP scored higher on a depression scale compared to men of similar ages.[56] Licini et al[32] reported that moderate to severe depression was evident in 56.1% of women with TMD pain compared to only 10% of men. Women with chronic TMD myofascial pain also scored marginally higher on a depression scale than men in another study,[35] although men with other chronic facial painful conditions (postsurgical pain, posttraumatic, or neuropathic pain) and not specifically TMD pain were more depressed compared to women.[35] In contrast, Giannakopoulos et al did not find any differences in anxiety between men and women with TMD, suggesting poorer psychologic well-being in women is not uniformly observed in studies of OFP.[35]

### Impact of Comorbid Conditions on Anxiety and Depression in Individuals with Orofacial Pain

Both neuropathic and nonneuropathic (ie, TMD) OFP can coexist with other medical conditions, such as degenerative disease, migraine, and widespread pain, and the reviewed studies suggest that their presence can increase the likelihood of significant psychologic disability in affected individuals.[30,71,78,111,113,119,121,123,127,129] For example, a study of acute TMD subtypes showed that individuals with muscle and joint pain, along with a history of degenerative joint disorder, have significantly higher levels of depression compared to those with a single condition.[30] The study by Cioffi et al on TMD pain and migraine found that individuals with a combination of chronic TMD myofascial pain and migraine were experiencing significantly higher levels of depression compared to isolated TMD groups.[121] Ballegaard et al studied depressive symptoms in patients with headache and compared them to patients having headache and comorbid TMD, reporting that 34.1% of headache patients had depressive symptoms compared to more than 70% (70.9%) of those with headache and comorbid TMD pain.[123]

A similar pattern of results emerged from studies on neuropathic OFP. For instance, Lopez-Jornet et al observed a positive association among BMS, poor sleep quality, and comorbid anxiety/depression (as measured using HADS). Regression analyses indicated that for every 1-point increase in HADS depression score, the odds of sleep quality deterioration increased by 1.26 times.[91] McMillan et al found that while patients with OFP were 3.5 times more likely to exhibit moderate to severe depression than control participants, psychologic distress was observed most often in individuals with OFP who had widespread pain symptoms; these patients constituted 13.5% of their OFP sample.[127]

## Discussion

The purpose of this study was to review research describing anxiety and depression in patients with neuropathic and/or nonneuropathic OFP. The results

showed that experience of OFP is associated with both anxiety and depression that can be disabling in nature and markedly influences individuals' emotional well-being. This review of 118 studies identified positive associations between pain intensity, chronicity, and symptom severity and the presence of anxiety and/or depression. The prevalence of clinically significant or moderate to severe anxiety in neuropathic, mixed, and idiopathic/atypical orofacial pain conditions ranged from 0% to 80.7% of cases, while the prevalence of clinically significant or moderate to severe depression ranged from 2.2% to 100% of cases. In nonneuropathic (ie, TMD) pain conditions, the observed ranges were also wide; anxiety ranged from 7.4% to 78.0% of cases, and depression from 7.0% to 77.4% of cases. The large variance in the observed rates across studies likely reflects the differential methods of assessment and/or nature of the recruited samples in the included studies. For TMD conditions, the majority of RDC/TMD or SCL-90-R assessments yielded depression rates of around 40% to 60%, and most RDC/TMD, SCL-90-R, or HADS assessments resulted in an anxiety prevalence of 40% to 65%; diagnostic assessments of depression and anxiety suggested disorder rates of 15% to 20% and 15% to 35%, respectively. Irrespective of assessment method, the lowest observed prevalence rates were in TMD studies employing student samples rather than clinical populations. The majority of questionnaire-based assessment in patients with TN yielded rates of depression and anxiety of around 20% to 35% and 40% to 55%, respectively, with lower rates in studies reporting diagnostic assessments, while questionnaire-based assessments of depression and anxiety in BMS studies showed moderate-severe symptoms in a quarter to a half of patients, with similar rates reported in most diagnostic studies of BMS patients.

The association between pain and depression is complicated due to their common neurobiology, complex environmental influences, and negative cognitions.[141] Neurotransmitters such as serotonin, norepinephrine, glutamate, and gamma-Aminobutyric acid (GABA) are intimately linked with pain processing as well as mood.[141] For instance, serotonin and norepinephrine reduction are associated with an impeded gate control mechanism and mood disorder progression.[142] The present review identified a close association between COFP and psychologic comorbidities. This is in line with available literature, where psychologic factors are now recognized as important comorbid features in the presentation of OFP.[143,144] All types of pain are influenced by psychologic components; however, negative affect appears particularly important in the emergence and maintenance of chronic pain syndromes.[145,146] COFP has a profound influence on the psychologic health of individuals; this includes anxiety, stress, phobias, depressive symptoms, catastrophizing, and emotional disturbances,[12] as well as oral health–related quality of life.[9] Increased pain intensity also negatively impacts quality of life.[10] The American Psychiatric Association (APA) has recognized that mental illnesses such as anxiety disorders, somatoform disorders, and mood disorders are closely related to medical conditions, including hypersensitive pain perception.[145] TMD myofascial pain patients are more likely to have higher levels of psychologic symptoms.[147] This concurs with the findings of a recent systematic review reporting the frequent cooccurrence of psychiatric disorders and masticatory muscle pain.[148]

Pain perception and experience differ considerably across individuals and vary according to gender. The overrepresentation of women in OFP pain samples, especially in studies of TMD pain, was illustrated in this review. Furthermore, gender differences in the few studies directly addressing the role of gender in psychologic correlates of OFP suggested that both anxiety and depression are more often observed in women with TMD pain than in men with TMD pain. There are reports that estrogen may have a role in the pain-regulatory mechanisms of TMD pain subgroups.[149] However, this needs further investigation. The impact of gender on comorbid anxiety and/or depression in individuals with neuropathic OFP is less clear and needs to be addressed in future studies.

The present review also suggests that individuals presenting with multiple pain conditions are more likely to have pronounced psychologic problems.[121,123,131] More specifically, across reviewed studies, individuals with multiple OFP conditions were more likely to have severe negative psychologic impairment, most obviously high levels of depression, compared to those with single conditions. Similar findings have been reported in the OFP literature[150] and are broadly consistent with studies of body pain, where patients with widespread chronic pain (eg, fibromyalgia) often present with marked negative affective and cognitive states.[151]

There was a substantial degree of variability in the designs and associated RoBs of studies included in this review, which contributed to the difficulty in arriving at a consensus. Eleven studies used a longitudinal prospective design, 10 were designed as case-control, and 8 were retrospective. The absence of (pain-free) control groups was a frequent shortcoming of studies included in this review. Nevertheless, the overwhelming majority of studies (46) where a control sample was employed evidenced higher rates of anxiety and/or depression in OFP patients (neuropathic, mixed OFP, and TMD) compared to pain-free controls.[16,132] The only exception to this was a

small number of TMD studies which recruited student (nonpatient) populations in which the individuals diagnosed with TMD were not currently receiving or seeking treatment.[31,45,76,79]

Most studies, particularly those with neuropathic OFP samples, were conducted at tertiary care units through opportunity sampling. Of course, patient recruitment from a tertiary care unit may not be representative of the general population, reducing the generalizability and external validity of the included studies. More specifically, this may have resulted in overpresentation of anxiety and/or depression in individuals with OFP. Most studies (n = 86) were cross-sectional, where the data were collected at a single point in time, rendering it difficult to differentiate between cause and effect through simple association.[152] As such, from this review, a clear association on the etiologic pathway could not be established; specifically, whether pain resulted in psychologic morbidity or vice versa. However, both pain and psychologic morbidity are related to a common etiologic factor (for example, early psychologic or physical trauma could predispose individuals to both pain and psychologic distress in the future), and it is important to consider that a number of studies have suggested that a range of premorbid psychologic variables can predict the development of OFP, particularly TMD.[153,154] However, the available evidence suggests a bidirectional relationship between anxiety and/or depression and pain,[155] supported in part by functional neuroimaging studies suggesting shared underlying neuro mechanisms.[156]

Significant variation in the use of psychologic tools for data collection was found. Various self-report questionnaires were utilized, and the majority of studies did not make a distinction between acute and chronic pain, although most of the patients included in studies had OFP for more than 3 months. This may have affected the validity of the data due to variation in personal characteristics, level of patients' education, their ethnicity, culture, and social beliefs.[157] The majority of studies in the current review employed only a single psychologic scale, and most adopted the questionnaire-specific cut-off points for cases of anxiety or depression, which remain difficult to interpret across measures. For example, comparisons between the State-Trait Anxiety Inventory (STAI)-State[158] can be made with HADS, but a compelling comparison dataset is as yet not available,[35] and STAI-Trait also includes a number of depression items related to depressive symptomatology.[159] Few studies have used the SCID-DSM-IV,[28,112,119,131] which is a formal diagnostic tool, as opposed to questionnaires such as HADS, which better serve as screening instruments (ie, do not allow for definite diagnoses) and provide dimensional rather than categorical representations of mood.[160] More research is needed through employment of a standardized set of questionnaires and screening tools that also address wider psychologic and social aspects of psychologic function in patients with OFP.

Notable differences emerged in the diagnostic procedures of COFP conditions across studies, inasmuch as there were several classification systems used that do not entirely concur with one another; therefore, results across different studies with OFP samples are not completely comparable. Literature on OFP classifications has discussed this issue in detail,[143,161] emphasizing the need for a standardized biopsychosocial classification of OFP, which is highlighted again in the present review.

Limited datasets were considered for this review, and only English-language articles were searched, reducing the scope of reviewed studies. Nevertheless, the review demonstrated substantive evidence for associations of anxiety and depression with both neuropathic and nonneuropathic OFP conditions. Both within and across studies, no meaningful differences in anxiety or depression levels between patients with neuropathic conditions and those with nonneuropathic (ie, TMD) pain were found,[16,121] consistent with broader evidence that the psychologic impact of chronic pain is universal irrespective of neuropathic or nociceptive characteristics of experienced symptoms.[162] Differences in the study designs and psychologic assessment tools employed may have limited the ability to detect differential rates of psychologic comorbidities according to presenting OFP symptoms. Due to the heterogeneity of the studies, meta-analyses were not possible, although this does reduce the strength of the findings. Nevertheless, the present results are consistent with the hypothesis that OFP conditions have an impact on the psychologic well-being of individuals and are meaningful in the context of formulating treatment strategies.

## Conclusions

OFP has a significant impact on patients' psychologic well-being. This critical review, within its limitations, highlighted an association between OFP and psychologic comorbidity. Due to the heterogeneity across studies, it was not possible to conduct meta-analyses in order to substantiate this evidence in a robust manner. Most work to date involves patients with TMD pain (nonneuropathic), and much less concerns other types of pain, such as neurovascular, neuropathic, and idiopathic OFP. OFP requires a biopsychosocial approach for holistic management.[163] Future research should focus on comparing psychologic morbidity in different types of COFP with a

view to develop more tailored treatment strategies for individuals according to presenting symptomatology. There is also a need for studies exploring precondition psychologic morbidity, which may have a significant role in predisposing individuals to developing chronic pain.[4,142]

## Clinical Implications

COFP causes distress and disability, affects life negatively, and often leads to anxiety and/or depression and extensive use of the health care system. Holistic management for OFP requires a biopsychosocial approach.

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## References

1. International Classification of Orofacial Pain, ed 1. Cephalalgia 2020;40:129–221.
2. IASP. Pain terms. In: Merskey H, Bogduk N (eds). Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, ed 2. Seattle: IASP, 1994.
3. Treede RD, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. Pain 2015;156:1003–1007.
4. Macrae WA. Chronic post-surgical pain: 10 years on. Br J Anaesth 2008;101:77–86.
5. Williams DA. The importance of psychological assessment in chronic pain. Curr Opin Urol 2013;23:554–559.
6. Nilsson H, Samuelsson M, Ekdahl S, Halling Y, Oster A, Perseius KI. Experiences by patients and health professionals of a multidisciplinary intervention for long-term orofacial pain. J Multidiscip Healthc 2013;6:365–371.
7. Breivik H, Eisenberg E, O'Brien T; OPENMinds. The individual and societal burden of chronic pain in Europe: The case for strategic prioritisation and action to improve knowledge and availability of appropriate care. BMC Public Health 2013;13:1229.
8. Jamison RN, Edwards RR. Integrating pain management in clinical practice. J Clin Psychol Med Settings 2012;19:49–64.
9. Shueb SS, Nixdorf DR, John MT, Alonso BF, Durham J. What is the impact of acute and chronic orofacial pain on quality of life? J Dent 2015;43:1203–1210.
10. Haviv Y, Zini A, Etzioni Y, et al. The impact of chronic orofacial pain on daily life: The vulnerable patient and disruptive pain. Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:58–66.
11. Macfarlane TV, Blinkhorn AS, Davies RM, Ryan P, Worthington HV, Macfarlane GJ. Orofacial pain: Just another chronic pain? Results from a population-based survey. Pain 2002;99:453–458.
12. Ohrbach R, Durham J. Biopsychosocial aspects of orofacial pain. In: Farah CS, Balasubramaniam R, McCullough MJ (eds). Contemporary Oral Medicine. Heidelberg: Springer, 2018:1–21.
13. Chien PF, Khan KS, Siassakos D. Registration of systematic reviews: PROSPERO. BJOG 2012;119:903–905.
14. American Psychiatric Association. APA Dictionary of Psychology. www.apa.org/research/action/glossary. Accessed 13 April, 2022.
15. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, World Health Organization: 1992.
16. Gustin SM, Wilcox SL, Peck CC, Murray GM, Henderson LA. Similarity of suffering: equivalence of psychological and psychosocial factors in neuropathic and non-neuropathic orofacial pain patients. Pain 2011;152:825–832.
17. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 2013;33:629–808.
18. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications: Recommendations of the international RDC/TMD Consortium network and orofacial pain special interest group. J Oral Facial Pain Headache 2014;28:6–27.
19. Merskey H, Bogduk N (eds). Classification of Chronic Pain, ed 2. Seattle: IASP, 1994.
20. de Leeuw R, Klasser GD. Orofacial Pain: Guidelines for Assessment, Diagnosis, and Management. Chicago: Quintessence, 2018.
21. Higgins JPT, Deeks JJ. Selecting studies and collecting data. In: Higgins JPT, Green S (eds). Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration, 2008:151–185.
22. Galli F, Lodi G, Sardella A, Vegni E. Role of psychological factors in burning mouth syndrome: A systematic review and meta-analysis. Cephalalgia 2016;37:265–277.
23. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: A systematic review with meta-analysis. Oral Dis 2010;16:601–612.
24. Syrjänen S, Lodi G, von Bültzingslöwen I, et al. Human papillomaviruses in oral carcinoma and oral potentially malignant disorders: a systematic review. Oral Dis 2011;17(suppl 1):58–72.
25. GaldÓn MJ, Durá E, Andreu Y, Ferrando M, Poveda R, Bagán JV. Multidimensional approach to the differences between muscular and articular temporomandibular patients: Coping, distress, and pain characteristics. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:40–46.
26. Bertoli E, de Leeuw R, Schmidt JE, Okeson JP, Carlson CR. Prevalence and impact of post-traumatic stress disorder symptoms in patients with masticatory muscle or temporomandibular joint pain: differences and similarities. J Orofac Pain 2007;21:107–119.
27. John MT, Reissmann DR, Schierz O, Wassell RW. Oral health-related quality of life in patients with temporomandibular disorders. J Orofac Pain 2007;21:46–54.
28. Nifosi F, Violato E, Pavan C, et al. Psychopathology and clinical features in an Italian sample of patients with myofascial and temporomandibular joint pain: preliminary data. Int J Psychiatry Med 2007;37:283–300.

29. Lee LT, Yeung RW, Wong MC, McMillan AS. Diagnostic subtypes, psychological distress and psychosocial dysfunction in southern Chinese people with temporomandibular disorders. J Oral Rehabil 2008;35:184–190.
30. Reissmann DR, John MT, Wassell RW, Hinz A. Psychosocial profiles of diagnostic subgroups of temporomandibular disorder patients. Eur J Oral Sci 2008;116:237–244.
31. Bonjardim LR, Lopes-Filho RJ, Amado G, Albuquerque RL Jr, Goncalves SR. Association between symptoms of temporomandibular disorders and gender, morphological occlusion, and psychological factors in a group of university students. Indian J Dent Res 2009;20:190–194.
32. Licini F, Nojelli A, Segù M, Collesano V. Role of psychosocial factors in the etiology of temporomandibular disorders: Relevance of a biaxial diagnosis. Minerva Stomatol 2009;58:557–566.
33. Macfarlane TV, Kenealy P, Kingdon HA, et al. Orofacial pain in young adults and associated childhood and adulthood factors: Results of the population study, Wales, United Kingdom. Community Dent Oral Epidemiol 2009;37:438–450.
34. Stavrianos C, Kafas P, Jerjes W, Upile T, Stavrianous I, Nazaroglou I, Kafas G. Disease phobia in patients with temporomandibular joint pain assessed by the Illness Attitude Scale. Acta Medica (Hradec Kralove) 2009;52:73–75.
35. Giannakopoulos NN, Keller L, Rammelsberg P, Kronmüller KT, Schmitter M. Anxiety and depression in patients with chronic temporomandibular pain and in controls. J Dent 2010;38:369–376.
36. Lajnert V, Frančišković T, Grzic R, et al. Depression, somatization and anxiety in female patients with temporomandibular disorders (TMD). Coll Antropol 2010;34:1415–1419.
37. Manfredini D, Borella L, Favero L, Ferronato G, Guarda-Nardini L. Chronic pain severity and depression/somatization levels in TMD patients. Int J Prosthodont 2010;23:529–534.
38. Manfredini D, Winocur E, Ahlberg J, Guarda-Nardini L, Lobbezoo F. Psychosocial impairment in temporomandibular disorders patients. RDC/TMD axis II findings from a multicentre study. J Dent 2010;38:765–772.
39. Pesqueira AA, Zuim PR, Monteiro DR, Ribeiro Pdo P, Garcia AR. Relationship between psychological factors and symptoms of TMD in university undergraduate students. Acta Odontol Latinoam 2010;23:182–187.
40. Celić R, Braut V, Petricević N. Influence of depression and somatization on acute and chronic orofacial pain in patients with single or multiple TMD diagnoses. Coll Antropol 2011;35:709–713.
41. Dworkin SF. Temporomandibular disorder (TMD) pain-related disability found related to depression, nonspecific physical symptoms, and pain duration at 3 international sites. J Evid Based Dent Pract 2011;11:143–144.
42. Monteiro DR, Zuim PR, Pesqueira AA, Ribeiro Pdo P, Garcia AR. Relationship between anxiety and chronic orofacial pain of temporomandibular disorder in a group of university students. J Prosthodont Res 2011;55:154–158.
43. Velly AM, Look JO, Carlson C, et al. The effect of catastrophizing and depression on chronic pain–a prospective cohort study of temporomandibular muscle and joint pain disorders. Pain 2011;152:2377–2383.
44. Xu WH, Guo CB, Wu RG, Ma XC. Investigation of the psychological status of 162 female TMD patients with different chronic pain severity. Chin J Dent Res 2011;14:53–57.
45. de Lucena IM, Rodrigues LL, Teixeira ML, Pozza DH, Guimaraes AS. Prospective study of a group of pre-university students evaluating anxiety and depression relationships with temporomandibular disorders. J Clin Exp Dent 2012;4:e102–e106.
46. Diniz MR, Sabadin PA, Leite FP, Kamizaki R. Psychological factors related to temporomandibular disorders: an evaluation of students preparing for college entrance examinations. Acta Odontol Latinoam 2012;25:74–81.
47. Guarda-Nardini L, Pavan C, Arveda N, Ferronato G, Manfredini D. Psychometric features of temporomandibular disorders patients in relation to pain diffusion, location, intensity and duration. J Oral Rehabil 2012;39:737–743.
48. Kindler S, Samietz S, Houshmand M, et al. Depressive and anxiety symptoms as risk factors for temporomandibular joint pain: A prospective cohort study in the general population. J Pain 2012;13:1188–1197.
49. Rodrigues JH, Biasotto-Gonzalez DA, Bussadori SK, et al. Signs and symptoms of temporomandibular disorders and their impact on psychosocial status in non-patient university student's population. Physiother Res Int 2012;17:21–28.
50. Schwahn C, Grabe HJ, Meyer zu Schwabedissen H, et al. The effect of catechol-O-methyltransferase polymorphisms on pain is modified by depressive symptoms. Eur J Pain 2012;16:878–889.
51. Castelli L, De Santis F, De Giorgi I, et al. Alexithymia, anger and psychological distress in patients with myofascial pain: A case-control study. Front Psychol 2013;4:490.
52. Chen H, Nackley A, Miller V, Diatchenko L, Maixner W. Multisystem dysregulation in painful temporomandibular disorders. J Pain 2013;14:983–996.
53. Ozdemir-Karatas M, Peker K, Balık A, Uysal O, Tuncer EB. Identifying potential predictors of pain-related disability in Turkish patients with chronic temporomandibular disorder pain. J Headache Pain 2013;14:17.
54. Calixtre LB, Grüninger BL, Chaves TC, Oliveira AB. Is there an association between anxiety/depression and temporomandibular disorders in college students? J Appl Oral Sci 2014;22:15–21.
55. Davis CE, Stockstill JW, Stanley WD, Wu Q. Pain-related worry in patients with chronic orofacial pain. J Am Dent Assoc 2014;145:722–730.
56. Komiyama O, Obara R, Iida T, et al. Age-related associations between psychological characteristics and pain intensity among Japanese patients with temporomandibular disorder. J Oral Sci 2014;56:221–225.
57. Minghelli B, Morgado M, Caro T. Association of temporomandibular disorder symptoms with anxiety and depression in Portuguese college students. J Oral Sci 2014;56:127–133.
58. Reissmann DR, John MT, Seedorf H, Doering S, Schierz O. Temporomandibular disorder pain is related to the general disposition to be anxious. J Oral Facial Pain Headache 2014;28:322–330.
59. Smriti BJ, Patni VM, Mukta M, Gangotri S. Association between symptoms of temporomandibular disorders and gender, morphological occlusion, and psychological factor in dental student's [sic]. Int J Sci Stud 2014;2:55–58.
60. Sood D, Subramaniam AV, Subramaniam T. Association and correlation between temporomandibular disorders and psychological factors in a group of dental undergraduate students. Int J Appl Sci Biotechnology 2014;426–431.
61. Vasudeva S, Iyengar A, Seetaramaiah N. Correlation of anxiety levels between temporomandibular disorder patients and normal subjects. J Oral Dis 2014:579674.
62. Al-Havaz A, Safari S, Mohammadpour N, Kheirkhah F, Motalleb-Nezhad M, Arian M. Relationship between temporomandibular joint dysfunction and psychological distress among students of Babol University of Medical Sciences and Technology, Iran. J Oral Health Oral Epidemiol 2015;94–101.

63. Kotiranta U, Suvinen T, Kauko T, et al. Subtyping patients with temporomandibular disorders in a primary health care setting on the basis of the research diagnostic criteria for temporomandibular disorders axis II pain-related disability: A step toward tailored treatment planning? J Oral Facial Pain Headache 2015;29:126–134.
64. Lei J, Liu MQ, Yap AU, Fu KY. Sleep disturbance and psychologic distress: Prevalence and risk indicators for temporomandibular disorders in a Chinese population. J Oral Facial Pain Headache 2015;29:24–30.
65. Majumder K, Sharma S, Dayashankara Rao JK, Siwach V, Arya V, Gulia S. Prevalence and sex distribution of temporomandibular disorder and their association with anxiety and depression in Indian medical university students. Int J Clin Med 2015;6:570–578.
66. Reiter S, Emodi-Perlman A, Goldsmith C, Friedman-Rubin P, Winocur E. Comorbidity between depression and anxiety in patients with temporomandibular disorders according to the research diagnostic criteria for temporomandibular disorders. J Oral Facial Pain Headache 2015;29:135–143.
67. Dıraçoğlu D, Yıldırım NK, Saral İ, et al. Temporomandibular dysfunction and risk factors for anxiety and depression. J Back Musculoskelet Rehabil 2016;29:487–491.
68. Patil DJ, Dheer DS, Puri G, Konidena A, Dixit A, Gupta R. Psychological appraisal in temporomandibular disorders: A cross-sectional study. Indian J Pain 2016;30:13–18.
69. Visscher CM, Wesemael-Suijkerbuijk EA, Lobbezoo F. Is the experience of pain in patients with temporomandibular disorder associated with the presence of comorbidity? Eur J Oral Sci 2016;124:459–464.
70. Bertoli E, de Leeuw R. Prevalence of suicidal ideation, depression, and anxiety in chronic temporomandibular disorder patients. J Oral Facial Pain Headache 2016;30:296–301.
71. Bäck K, Hakeberg M, Wide U, Hange D, Dahlström L. Orofacial pain and its relationship with oral health-related quality of life and psychological distress in middle-aged women. Acta Odontol Scand 2020;78:74–80.
72. Huttunen J, Qvintus V, Suominen AL, Sipilä K. Role of psychosocial factors on treatment outcome of temporomandibular disorders. Acta Odontol Scand 2019;77:119–125.
73. Jivnani HM, Tripathi S, Shanker R, Singh BP, Agrawal KK, Singhal R. A study to determine the prevalence of temporomandibular disorders in a young adult population and its association with psychological and functional occlusal parameters. J Prosthodont 2019;28:e445–e449.
74. Lira MR, Lemes da Silva RR, Bataglion C, Aguiar ADS, Greghi SM, Chaves TC. Multiple diagnoses, increased kinesiophobia?—Patients with high kinesiophobia levels showed a greater number of temporomandibular disorder diagnoses. Musculoskelet Sci Pract 2019;44:102054.
75. Daher CRdM, Cunha LFd, Ferreira APdL, et al. Pain threshold, sleep quality and anxiety levels in individuals with temporomandibular disorders. Rev CEFAC 2018;20:450–457.
76. Fernandes Azevedo AB, Câmara-Souza MB, Dantas IS, de Resende CMBM, Barbosa GAS. Relationship between anxiety and temporomandibular disorders in dental students. Cranio 2018;36:300–303.
77. Natu VP, Yap AU, Su MH, Irfan Ali NM, Ansari A. Temporomandibular disorder symptoms and their association with quality of life, emotional states and sleep quality in South-East Asian youths. J Oral Rehabil 2018;45:756–763.
78. Nazeri M, Ghahrechahi HR, Pourzare A, et al. Role of anxiety and depression in association with migraine and myofascial pain temporomandibular disorder. Indian J Dent Res 2018;29:583–587.
79. Paulino MR, Moreira VG, Lemos GA, Silva PLPd, Bonan PRF, Batista AUD. Prevalência de sinais e sintomas de disfunção temporomandibular em estudantes pré-vestibulandos: associação de fatores emocionais, hábitos parafuncionais e impacto na qualidade de vida [in Portuguese]. Ciência & Saúde Coletiva 2018;23:173–186.
80. Reiter S, Eli I, Mahameed M, et al. Pain catastrophizing and pain persistence in temporomandibular disorder patients. J Oral Facial Pain Headache 2018;32:309–320.
81. Sruthi S, Jimsha VK, Srinivasan SV, Daniel JM. Prevalence of depression, anxiety and stress in chronic temporomandibular joint disorders patients. J Depress Anxiety 2018;7:4.
82. Naikoo FA, Chalkoo AH, Ahmad MB, Yaqoob G, Tariq S. Prevalence of anxiety levels in patients with temporomandibular disorder among Kashmiri population. Int J Appl Dent Sci 2017;3:101–103.
83. Reiter S, Eli I, Friedman-Rubin P, Emodi-Perlman A, Ziv-Baran T, Winocur E. Comparing axis II scores according to the RDC/TMD and DC/TMD in Israeli patients. J Oral Facial Pain Headache 2017;31:323–330.
84. Su N, Lobbezoo F, van Wijk A, van der Heijden GJ, Visscher CM. Associations of pain intensity and pain-related disability with psychological and socio-demographic factors in patients with temporomandibular disorders: A cross-sectional study at a specialised dental clinic. J Oral Rehabil 2017;44:187–196.
85. Tournavitis A, Tortopidis D, Fountoulakis K, Menexes G, Koidis P. Psychopathologic profiles of TMD patients with different pain locations. Int J Prosthodont 2017;30:251–257.
86. van Selms MK, Muzalev K, Visscher CM, Koutris M, Bulut M, Lobbezoo F. Are pain-related temporomandibular disorders the product of an interaction between psychological factors and self-reported bruxism? J Oral Facial Pain Headache 2017;31:331–338.
87. Yeung E, Abou-Foul A, Matcham F, Poate T, Fan K. Integration of mental health screening in the management of patients with temporomandibular disorders. Br J Oral Maxillofac Surg 2017;55:594–599.
88. Buljan D, Savić I, Karlović D. Correlation between anxiety, depression and burning mouth syndrome. Acta Clin Croat 2008;47:211–216.
89. de Souza FT, Teixeira AL, Amaral TM, et al. Psychiatric disorders in burning mouth syndrome. J Psychosom Res 2012;72:142–146.
90. Schiavone V, Adamo D, Ventrella G, et al. Anxiety, depression, and pain in burning mouth syndrome: First chicken or egg? Headache 2012;52:1019–1025.
91. Lopez-Jornet P, Lucero-Berdugo M, Castillo-Felipe C, Zamora Lavella C, Ferrandez-Pujante A, Pons-Fuster A. Assessment of self-reported sleep disturbance and psychological status in patients with burning mouth syndrome. J Eur Acad Dermatol Venereol 2015;29:1285–1290.
92. Sevrain M, Brenaut E, Le Toux G, Misery L. Primary burning mouth syndrome: A questionnaire study of neuropathic and psychological components. Am J Clin Dermatol 2016;17:171–178.
93. Mitsikostas DD, Ljubisavljevic S, Deligianni CI. Refractory burning mouth syndrome: clinical and paraclinical evaluation, comorbidities, treatment and outcome. J Headache Pain 2017;18:40.
94. Yoo HS, Jin SH, Lee YJ, Song CM, Ji YB, Tae K. The role of psychological factors in the development of burning mouth syndrome. J Oral Maxillofac Surg 2018;47:374–378.
95. Sikora M, Verzak Ž, Matijević M, et al. Anxiety and depression scores in patients with burning mouth syndrome. Psychiatr Danub 2018;30:466–470.

96. Moura BS, Ferreira NDR, DosSantos MF, Janini MER. Changes in the vibration sensitivity and pressure pain thresholds in patients with burning mouth syndrome. PLoS One 2018;13:e0197834.
97. Lee YH, Chon S. Burning mouth syndrome in postmenopausal women with self-reported sleep problems. Cranio 2020;38:221–232.
98. Di Stasio D, Candotto V, Serpico R, et al. Depression and distress in burning mouth syndrome: A case control study. J Biol Regul Homeost Agents 2018;32:91–95.
99. Adamo D, Sardella A, Varoni E, et al. The association between burning mouth syndrome and sleep disturbance: A case-control multicentre study. Oral Dis 2018;24:638–649.
100. Yang G, Su S, Jie H, et al. Somatosensory profiling of patients with burning mouth syndrome and correlations with psychologic factors. J Oral Facial Pain Headache 2019;33:278–286.
101. Le Bris V, Chastaing M, Schollhammer M, Brenaut E, Misery L. Usefulness of psychiatric intervention in a joint consultation for the treatment of burning mouth syndrome: A monocentric retrospective study. Acta Derm Venereol 2019;99:813–817.
102. Adamo D, Pecoraro G, Fortuna G, et al. Assessment of oral health-related quality of life, measured by OHIP-14 and GOHAI, and psychological profiling in burning mouth syndrome: A case-control clinical study. J Oral Rehabil 2020;47:42–52.
103. Bakhtiari S, Khalighi HR, Azimi S, Alavi K, Ayoobi Valoogerdi H, Namazi Z. Correlation between burning mouth syndrome and anxiety in the elderly inmates of Sanitaria in Tehran. J Dent Res Dent Clin Dent Prospects 2010;4:37–41.
104. van Seventer R, Serpell M, Bach FW, et al. Relationships between changes in pain severity and other patient-reported outcomes: An analysis in patients with posttraumatic peripheral neuropathic pain. Health Qual Life Outcomes 2011;9:17.
105. Smith JG, Elias LA, Yilmaz Z, et al. The psychosocial and affective burden of posttraumatic neuropathy following injuries to the trigeminal nerve. J Orofac Pain 2013;27:293–303.
106. Wu TH, Hu LY, Lu T, et al. Risk of psychiatric disorders following trigeminal neuralgia: A nationwide population-based retrospective cohort study. J Headache Pain 2015;16:64.
107. Zakrzewska JM, Wu J, Mon-Williams M, Phillips N, Pavitt SH. Evaluating the impact of trigeminal neuralgia. Pain 2017;158:1166–1174.
108. Tan CY, Shahrizaila N, Goh KJ. Clinical characteristics, pain, and quality of life experiences of trigeminal neuralgia in a multi-ethnic Asian cohort. J Oral Facial Pain Headache 2017;31:e15–e20.
109. Heinskou TB, Maarbjerg S, Wolfram F, et al. Favourable prognosis of trigeminal neuralgia when enrolled in a multidisciplinary management program—A two-year prospective real-life study. J Headache Pain 2019;20:23.
110. Chang B, Zhu W, Li S. Effects of depression and anxiety on microvascular decompression outcome for trigeminal neuralgia patients. World Neurosurg 2019;128:e556–e561.
111. Godazandeh K, Martinez Sosa S, Wu J, Zakrzewska JM. Trigeminal neuralgia: Comparison of characteristics and impact in patients with or without multiple sclerosis. Mult Scler Relat Disord 2019;34:41–46.
112. Mongini F, Ciccone G, Ceccarelli M, Baldi I, Ferrero L. Muscle tenderness in different types of facial pain and its relation to anxiety and depression: A cross-sectional study on 649 patients. Pain 2007;131:106–111.
113. Baad-Hansen L, Leijon G, Svensson P, List T. Comparison of clinical findings and psychosocial factors in patients with atypical odontalgia and temporomandibular disorders. J Orofac Pain 2008;22:7–14.
114. Castro AR, Siqueira SR, Perissinotti DM, Siqueira JT. Psychological evaluation and cope with trigeminal neuralgia and temporomandibular disorder. Arq Neuropsiquiatr 2008;66:716–719.
115. Choi SH, Kim KS, Kim ME. Pain disability of orofacial pain patients. J Oral Med Pain 2009;34:217–225.
116. Kim HI, Lee JY, Kim YK, Kho HS. Clinical and psychological characteristics of TMD patients with trauma history. Oral Dis 2010;16:188–192.
117. Takenoshita M, Sato T, Kato Y, et al. Psychiatric diagnoses in patients with burning mouth syndrome and atypical odontalgia referred from psychiatric to dental facilities. Neuropsychiatr Dis Treat 2010;6:699–705.
118. Mačianskytė D, Janužis G, Kubilius R, Adomaitienė V, Ščiupokas A. Associations between chronic pain and depressive symptoms in patients with trigeminal neuralgia. Medicina (Kaunas) 2011;47:386–392.
119. Taiminen T, Kuusalo L, Lehtinen L, et al. Psychiatric (axis I) and personality (axis II) disorders in patients with burning mouth syndrome or atypical facial pain. Scand J Pain 2011;2:155–160.
120. Komiyama O, Obara R, Uchida T, et al. Pain intensity and psychosocial characteristics of patients with burning mouth syndrome and trigeminal neuralgia. J Oral Sci 2012;54:321–327.
121. Cioffi I, Perrotta S, Ammendola L, et al. Social impairment of individuals suffering from different types of chronic orofacial pain. Prog Orthod 2014;15:27.
122. Brailo V, Zakrzewska JM. Grading the intensity of nondental orofacial pain: Identification of cutoff points for mild, moderate, and severe pain. J Pain Res 2015;8:95–104.
123. Ballegaard V, Thede-Schmidt-Hansen P, Svensson P, Jensen R. Are headache and temporomandibular disorders related? A blinded study. Cephalalgia 2008;28:832–841.
124. Tu TTH, Miura A, Shinohara Y, et al. Evaluating burning mouth syndrome as a comorbidity of atypical odontalgia: The impact on pain experiences. Pain Pract 2018;18:580–586.
125. Melek LN, Smith JG, Karamat A, Renton T. Comparison of the neuropathic pain symptoms and psychosocial impacts of trigeminal neuralgia and painful posttraumatic trigeminal neuropathy. J Oral Facial Pain Headache 2019;33:77–88.
126. Streffer ML, Büchi S, Mörgeli H, Galli U, Ettlin D. PRISM (pictorial representation of illness and self measure): A novel visual instrument to assess pain and suffering in orofacial pain patients. J Orofac Pain 2009;23:140–146.
127. McMillan AS, Wong MC, Zheng J, Luo Y, Lam CL. Widespread pain symptoms and psychological distress in southern Chinese with orofacial pain. J Oral Rehabil 2010;37:2–10.
128. Wan KY, McMillan AS, Wong MC. Orofacial pain symptoms and associated disability and psychosocial impact in community-dwelling and institutionalized elderly in Hong Kong. Community Dent Health 2012;29:110–116.
129. Ligthart L, Gerrits MM, Boomsma DI, Penninx BW. Anxiety and depression are associated with migraine and pain in general: An investigation of the interrelationships. J Pain 2013;14:363–370.
130. Sipilä K, Mäki P, Laajala A, Taanila A, Joukamaa M, Veijola J. Association of depressiveness with chronic facial pain: A longitudinal study. Acta Odontol Scand 2013;71:644–649.
131. Gerrits MMJG, van Oppen P, van Marwijk HWJ, Penninx BWJH, van der Horst HE. Pain and the onset of depressive and anxiety disorders. Pain 2014;155:53–59.
132. List T, Leijon G, Helkimo M, Oster A, Dworkin SF, Svensson P. Clinical findings and psychosocial factors in patients with atypical odontalgia: A case-control study. J Orofac Pain 2007;21:89–98.
133. Miura A, Tu TTH, Shinohara Y, et al. Psychiatric comorbidities in patients with Atypical Odontalgia. J Psychosom Res 2018;104:35–40.

134. Tang Y, Ma L, Li N, et al. Percutaneous trigeminal ganglion radiofrequency thermocoagulation alleviates anxiety and depression disorders in patients with classic trigeminal neuralgia: A cohort study. Medicine (Baltimore) 2016;95:e5379.
135. Tokura T, Kimura H, Ito M, et al. Temperament and character profiles of patients with burning mouth syndrome. J Psychosom Res 2015;78:495–498.
136. Marino R, Picci RL, Ferro G, Carezana C, Gandolfo S, Pentenero M. Peculiar alexithymic traits in burning mouth syndrome: Case-control study. Clin Oral Investig 2015;19:1799–1805.
137. Mousavi SH, Sekula RF, Gildengers A, Gardner P, Lunsford LD. Concomitant depression and anxiety negatively affect pain outcomes in surgically managed young patients with trigeminal neuralgia: Long-term clinical outcome. Surg Neurol Int 2016;7:98.
138. das Neves de Araújo Lima E, Barbosa NG, Dos Santos AC, et al. Comparative analysis of psychological, hormonal, and genetic factors between burning mouth syndrome and secondary oral burning. Pain Med 2016;17:1602–1611.
139. Braud A, Boucher Y. The relationship between the clinical features of idiopathic burning mouth syndrome and self-perceived quality of life. J Oral Sci 2016;58:475–481.
140. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. Pain 1992;50:133–149.
141. Goesling J, Clauw DJ, Hassett AL. Pain and depression: An integrative review of neurobiological and psychological factors. Curr Psychiatry Rep 2013;15:421.
142. Dersh J, Polatin PB, Gatchel RJ. Chronic pain and psychopathology: Research findings and theoretical considerations. Psychosom Med 2002;64:773–786.
143. Renton T, Durham J, Aggarwal VR. The classification and differential diagnosis of orofacial pain. Expert Rev Neurother 2012;12:569–576.
144. Haviv Y, Zini A, Etzioni Y, et al. The impact of chronic orofacial pain on daily life: The vulnerable patient and disruptive pain. Oral Surg Oral Med Oral Pathol Oral Radiol 2017;123:58–66.
145. Okeson JP. The classification of orofacial pains. Oral Maxillofac Surg Clin North Am 2008;20:133–144.
146. Vickers ER, Boocock H. Chronic orofacial pain is associated with psychological morbidity and negative personality changes: A comparison to the general population. Aust Dent J 2005;50:21–30.
147. Porto F, de Leeuw R, Evans DR, et al. Differences in psychosocial functioning and sleep quality between idiopathic continuous orofacial neuropathic pain patients and chronic masticatory muscle pain patients. J Orofac Pain 2011;25:117–124.
148. Wieckiewicz M, Zietek M, Smardz J, Zenczak-Wieckiewicz D, Grychowska N. Mental status as a common factor for masticatory muscle pain: A systematic review. Front Psychol 2017;8:646.
149. Berger M, Szalewski L, Bakalczuk M, Bakalczuk G, Bakalczuk S, Szkutnik J. Association between estrogen levels and temporomandibular disorders: A systematic literature review. Prz Menopauzalny 2015;14:260–270.
150. Cole HA, Carlson CR. Mind-Body Considerations in orofacial pain. Dent Clin 2018;62:683–694.
151. Gormsen L, Rosenberg R, Bach FW, Jensen TS. Depression, anxiety, health-related quality of life and pain in patients with chronic fibromyalgia and neuropathic pain. Eur J Pain 2010;14:127.e1–127.e8.
152. Mann CJ. Observational research methods. Research design II: Cohort, cross sectional, and case-control studies. Emerg Med J 2003;20:54.
153. Fillingim RB, Ohrbach R, Greenspan JD, et al. Psychological factors associated with development of TMD: The OPPERA prospective cohort study. J Pain 2013;14(suppl 12):T75–T90.
154. Aggarwal VR, Macfarlane GJ, Farragher TM, McBeth J. Risk factors for onset of chronic oro-facial pain–results of the North Cheshire oro-facial pain prospective population study. Pain 2010;149:354–359.
155. Hooten WM. Chronic pain and mental health disorders: Shared neural mechanisms, epidemiology, and treatment. Mayo Clin Proc 2016;91:955–970.
156. Davidson RJ, Abercrombie H, Nitschke JB, Putnam K. Regional brain function, emotion and disorders of emotion. Curr Opin Neurobiol 1999;9:228–234.
157. Del Boca FK, Noll JA. Truth or consequences: The validity of self-report data in health services research on addictions. Addiction 2000;95:347–360.
158. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press, 1983.
159. Bieling PJ, Antony MM, Swinson RP. The State-Trait Anxiety Inventory, Trait version: Structure and content re-examined. Behav Res Ther 1998;36:777–788.
160. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale–a review of validation data and clinical results. J Psychosom Res 1997;42:17–41.
161. Klasser GD, Goulet JP, De Laat A, Manfredini D. Classification of orofacial pain. In: Farah S, Balasubramaniam R, McCullough MJ (eds). Contemporary Oral Medicine. Cham, Switzerland: Springer, 2018:1–24.
162. Daniel HC, Narewska J, Serpell M, Hoggart B, Johnson R, Rice AS. Comparison of psychological and physical function in neuropathic pain and nociceptive pain: Implications for cognitive behavioral pain management programs. Eur J Pain 2008;12:731–741.
163. Ghurye S, McMillan R. Orofacial pain—An update on diagnosis and management. Br Dent J 2017;223:639–647.
164. Davis CE, Stockstill JW, Stanley WD, Wu Q. Pain-related worry in patients with chronic orofacial pain. J Am Dent Assoc 2014;145:722–730.
165. Gao J, Chen L, Zhou J, Peng J. A case-control study on etiological factors involved in patients with burning mouth syndrome. J Oral Pathol Med 2009;38:24–28.

**Table 1 Study Characteristics**

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 1. Adamo et al, 2020 (Italy) | Cross-sectional | BMS: 52 | 52 (M: 19, F: 81) | HARS<br>HDRS |
| 2. Bäck et al, 2020 (Sweden) | Cross-sectional | TMD with sev pain/TMD with headache cases: 82<br>Controls: 977 | 1,059 (F: 100) | HADS |
| 3. Chang et al, 2019 (China) | Retrospective cross-sectional | TN cases: 45<br>Controls: 61 | 106 (M: 44, F: 56) | HARS<br>HDRS |
| 4. Godazandeh et al, 2019 (UK) | Cross-sectional | TN: 68<br>TN with MS: 26 | 94 (TN M: 21, F: 79; TN with MS M: 23, F: 77) | HADS |
| 5. Heinskou et al, 2019 (Denmark) | Prospective observational | TN after medicine intervention: 103<br>TN after surgical intervention: 50 | 103 (M: 35, F: 65) | Self-report survey |
| 6. Huttunen et al, 2019 (Finland) | Randomized controlled trial | TMD: 80 | 80 (M: 23, F: 77) | RDC/TMD |
| 7. Jivnani et al, 2019 (India) | Cross-sectional | TMD pain and headaches: 15<br>TMD pain with disc displacement:19<br>No TMD: 34 | 68 (M: 49, F: 51) | HADS |
| 8. Le Bris et al, 2019 (France) | Retrospective cohort | BMS: 38 | 38 (M: 16, F: 84) | Self-report questionnaire |
| 9. Lira et al, 2019 (Brazil) | Cross-sectional | TMD cases: 92<br>Controls: 37 | 129 (F: 100) | HADS |
| 10. Melek et al, 2019 (UK) | Cross-sectional | Ne:<br>TN: 40<br>PTTN: 97 | 137 (M: 30, F: 70) | GAD-7<br>PHQ |
| 11. Yang et al, 2019 China | Cross-sectional | BMS cases: 30<br>Controls: 18 | 48 (M: 17, F: 83) | ZSAS<br>ZSDS |
| 12. Adamo et al, 2018 (Italy) | Cross-sectional | BMS: 200<br>Controls: 200 | 400 (M: 17, F: 83) | HARS<br>HDRS |
| 13. Daher et al, 2018 (Brazil) | Cross-sectional | TMD A: 10<br>TMD MP: 15<br>Controls: 10 | 35 (M: 20, F: 80) | HADS |
| 14. Di Stasio et al, 2018 (Italy) | Cross-sectional | BMS cases: 25<br>Controls: 24 | 49 (M: 13, F: 87) | STAI<br>HDRS |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 1. Adamo et al, 2020 (Italy) | Anxiety | – | 102 |
| | Depression | – | |
| 2. Bäck et al, 2020 (Sweden) | Anxiety | Cases: 51.2<br>Controls: 21.2 | 71 |
| | Depression | Cases: 32.9<br>Controls: 7.2 | |
| 3. Chang et al, 2019 (China) | Anxiety | – | 110 |
| | Depression | – | |
| 4. Godazandeh et al, 2019 (UK) | Anxiety (Mild/Sev) | TN: 63.3 (43.3/20.0)<br>TN with MS: 53.9 (23.1/30.8) | 111 |
| | Depression (Mild/Sev) | TN: 33.3 (15.0/18.3)<br>TN with MS: 56.0 (16.0/40.0) | |
| 5. Heinskou et al, 2019 (Denmark) | Anxiety and/or depression | TN after medicine intervention: 14.6<br>TN after surgical intervention: 14.0 | 109 |
| 6. Huttunen et al, 2019 (Finland) | Depression (Mod/Sev) B | 42.5 (27.5/15.0) | 72 |
| 7. Jivnani et al, 2019 (India) | Anxiety (BClin/Clin) | TMD pain and headaches: 47.0 (27.0/20.0)<br>TMD pain with disc displacement: 53.0 (42.0/11.0)<br>No TMD: 6.0 (6.0/0.0) | 73 |
| | Depression (BClin/Clin) | TMD pain and headaches: 66.0 (13.0/53.0)<br>TMD pain with disc displacement: 63.0 (26.0/37.0)<br>No TMD: 24.0 (18.0/6.0) | |
| 8. Le Bris et al, 2019 (France) | Depression symptoms | 50 | 101 |
| 9. Lira et al, 2019 (Brazil) | Anxiety | – | 74 |
| | Depression | – | |
| 10. Melek et al, 2019 (UK) | Anxiety (Clin) | TN: 38.5<br>PTTN: 34.4 | 125 |
| | Depression (Mild-Mod/Mod-Sev to Sev) | TN: 53.6 (35.7/17.9)<br>PTTN: 35.9 (25.0/10.9) | |
| 11. Yang et al, 2019 China | Anxiety (Mild) | BMS: 30 | 100 |
| | Depression (Mild) | BMS: 50 | |
| | Depression (Mod) | BMS: 36.6 | |
| 12. Adamo et al, 2018 (Italy) | Anxiety (Mild-Mod) | BMS: 27 | 99 |
| | Anxiety (Mod-Sev) | BMS: 18 | |
| | Depression (Mild) | BMS: 32 | |
| | Depression (Mod-Sev) | BMS: 34 | |
| 13. Daher et al, 2018 (Brazil) | Anxiety | – | 75 |
| 14. Di Stasio et al, 2018 (Italy) | Anxiety | – | 98 |
| | Depression | – | |

**Table 1 Study Characteristics**

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 15. Fernandes Azevedo et al, 2018 (Brazil) | Cross-sectional | TMD cases: 38<br>Controls: 67 | 105 | STAI |
| 16. Lee and Chon, 2020 (Korea) | Cross-sectional | BMS with sleep problems: 15<br>BMS without sleep problems: 10 | 25 (F: 100) | SCL-90-R |
| 17. Miura et al, 2018 (Japan) | Retrospective cross-sectional | AO: 383 | 383 (M: 15, F: 85) | DSM-V<br>ZSDS |
| 18. Moura et al, 2018 (Brazil) | Case-control | BMS cases: 15<br>Controls: 15 | 30 (M: 20, F: 80) | BAI<br>BDI |
| 19. Natu et al, 2018 (Singapore) | Cross-sectional | No TMD: 142<br>Mild TMD: 79<br>Mod TMD: 23 | 244 (M: 16, F: 84) | DASS-21 |
| 20. Nazeri et al, 2018 (Iran) | Case-control | TMD MP and migraines: 50<br>TMD MP: 25<br>Migraines: 15<br>Controls: 38 | 128 (M: 24, F: 76) | HADS |
| 21. Paulino et al, 2018 (Brazil) | Cross-sectional | TMD cases: 171<br>Controls: 132 | 303 (M: 31, F: 69) | HADS |
| 22. Reiter et al, 2018 (Israel) | Cross-sectional | TMD | 163 (M: 25, F: 75) | GAD-7<br>PHQ-9 |
| 23. Sikora et al, 2018 (Croatia) | Cross-sectional | BMS cases: 43<br>Controls: 50 | 93 (M: 18, F: 82) | STAI<br>BDI |
| 24. Sruthi et al, 2018 (India) | Cross-sectional | TMD MP: 27<br>TMD JP: 26<br>TMD mixed: 23<br>Controls: 24 | 100 (M: 46, F: 54) | DASS-42 |
| 25. Tu et al, 2018 (Japan) | Cross-sectional | AO: 272<br>AO and BMS: 83 | 355 (M: 12, F: 88) | ZSDS |
| 26. Yoo et al, 2018 (Korea) | Cross-sectional | BMS cases: 50<br>Controls: 50 | 100 (M: 42, F: 58) | SCL-90-R |
| 27. Mitsikostas et al, 2017 (Greece) | Case series | BMS: 8 | 8 (F: 100%) | HARS<br>HDRS |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 15. Fernandes Azevedo et al, 2018 (Brazil) | St Anxiety (Mod) | TMD: 39.5<br>No TMD: 29.9 | 76 |
| | Tr Anxiety (Mod) | TMD: 36.8<br>No TMD: 46.3 | |
| 16. Lee and Chon, 2020 (Korea) | Anxiety | – | 97 |
| | Depression | – | |
| 17. Miura et al, 2018 (Japan) | Anxiety | 10.1 | 133 |
| | Depression | 15.4 | |
| 18. Moura et al, 2018 (Brazil) | Anxiety (Mild/Mod) | BMS: 16.6/33.3 | 96 |
| | Anxiety (Mod) | Controls: 13.3 | |
| | Depression BMS (Mod/Sev) | BMS: 16.7/8.3<br>Controls: 0.0/0.0 | |
| 19. Natu et al, 2018 (Singapore) | Anxiety | – | 77 |
| | Depression | – | |
| 20. Nazeri et al, 2018 (Iran) | Anxiety and/or depression | TMD MP and migraines: 90.0<br>TMD MP: 24.0<br>Migraines: 66.7<br>Controls: 31.6 | 78 |
| 21. Paulino et al, 2018 (Brazil) | Anxiety | TMD: 46.8<br>No TMD: 26.5 | 79 |
| | Depression | TMD: 10.5<br>No TMD: 9.1 | |
| 22. Reiter et al, 2018 (Israel) | Anxiety (Mild/Mod/Sev) | 19.6/8.0/4.9 | 80 |
| | Depression (Mild/Mod/Sev) | 26.4/12.3/8.0 | |
| 23. Sikora et al, 2018 (Croatia) | Anxiety | – | 95 |
| | Depression | – | |
| 24. Sruthi et al, 2018 (India) | Anxiety | – | 81 |
| | Depression | – | |
| 25. Tu et al, 2018 (Japan) | Depression | – | 124 |
| 26. Yoo et al, 2018 (Korea) | Anxiety | – | 94 |
| | Depression | – | |
| 27. Mitsikostas et al, 2017 (Greece) | Anxiety (Mild-Mod) | 50.0 | 93 |
| | Anxiety (Mod-Sev) | 12.5 | |
| | Dep (Mod-Sev) | 100 | |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 28. Naikoo et al, 2017 (India) | Case-control | TMD cases: 100<br>Controls: 100 | 220 (M: 36, F: 64) | HADS |
| 29. Reiter et al, 2017 (Israel) | Cross-sectional | TMD:<br>RDC: 142<br>DC: 157 | 299 (M: 24, F: 76) | RDC/TMD<br>DC/TMD (GAD-7, PHQ-9) |
| 30. Su et al, 2017 (China) | Cross-sectional | TMD low pain intensity n = 156<br>TMD high pain intensity n = 164 | 320 (M: 22, F: 78) | GAD-7<br>PHQ-9 |
| 31. Tan et al, 2017 (Malaysia) | Cross-sectional | TN: 75 | 75 (M: 31, F: 69) | HADS |
| 32. Tournavitis et al, 2017 (Greece) | Cross-sectional | TMD: 75 | 75 (M: 48, F: 52) | STAI<br>CES-D |
| 33. van Selms et al, 2017 (Netherlands) | Cross-sectional | TMD cases: 268<br>Controls: 254 | 522 (M: 14, F: 86) | GAD-7<br>PHQ-15 |
| 34. Yeung et al, 2017 (UK) | Cross-sectional | TMD: 162 | 162 (M: 20, F: 80) | GAD-7<br>PHQ-9 |
| 35. Zakrzewska et al, 2017 (UK) | Cross-sectional | TN no IMP: 155<br>TN with IMP: 32<br>TN with AN: 38 | 225 (M: 37, F: 63) | HADS |
| 36. Bertoli and de Leeuw, 2016 (USA) | Cross-sectional | TMD: 1,241 | 1,241 (M: 12, F: 88) | SCL-90-R |
| 37. Braud and Boucher, 2016 (France) | Cross-sectional | BMS: 18 | 18 (M: 6, F: 94) | HADS |
| 38. das Neves de Araújo Lima et al, 2016 (Brazil) | Cross-sectional | BMS: 64<br>SOB: 99 | 163 (M: 19, F: 81) | BAI<br>BDI |
| 39. Davies et al, 2016 (UK) | Cross-sectional | BMS: 30<br>Other oral conditions: 11 | 41 (M: 12, F: 88) | Customized questionnaire and clinical interviews |
| 40. Duraçoğlu et al, 2016 (Turkey) | Cross-sectional | TMD: 273 | 273 (M: 22, F: 78) | HADS |
| 41. Mousavi et al, 2016 (USA) | Cross-sectional | TN: 21 | 21 (M: 14, F: 86) | DSM-IV |
| 42. Patil et al, 2016 (India) | Cross-sectional | Chronic TMD cases: 60<br>Controls: 60 | 120 (M: 25, F: 75) | BDI |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 28. Naikoo et al, 2017 (India) | Anxiety | TMD: 53.0<br>No TMD: 21.0 | 82 |
| | Depression | – | |
| 29. Reiter et al, 2017 (Israel) | RDC Anxiety (Mod/Sev) | 51.4 (27.9/23.5) | 83 |
| | RDC Depression (Mod/Sev) | 54.2 (29.6/24.6) | |
| | DC Anxiety (Mod/Sev) | 10.2 (7.6/2.6) | |
| | DC Depression (Mod/Sev) | 17.8 (9.6/8.2) | |
| 30. Su et al, 2017 (China) | Anxiety (Mild/Mod/Sev) | Low pain: 23/8.9/2.5<br>High pain: 9.5/16.4/11.5 | 84 |
| | Depression (Mild/Mod/Sev) | Low pain: 31.4/7.0/3.2<br>High pain: 26.8/15.8/17.7 | |
| 31. Tan et al, 2017 (Malaysia) | Anxiety | 41.3 | 108 |
| | Depression | 24.0 | |
| 32. Tournavitis et al, 2017 (Greece) | Anxiety | – | 85 |
| | Depression | – | |
| 33. van Selms et al, 2017 (Netherlands) | Anxiety | – | 86 |
| | Depression | – | |
| 34. Yeung et al, 2017 (UK) | Anxiety (Mild/Mod/Sev) | 27/12/8 | 87 |
| | Depression (Mild/Mod/Sev) | 27/20/14 | |
| 35. Zakrzewska et al, 2017 (UK) | Anxiety (BClin/Clin) | TN no IMP: 46.4 (21.5/25.2)<br>TN with IMP: 40.7 (11.1/29.6)<br>TN with AN: 77.8 (50.0/27.8) | 107 |
| | Depression (BClin/Clin) | TN no IMP: 30.6 (15.3/15.3)<br>TN with IMP: 29.6 (18.5/11.1)<br>TN with AN: 55.5 (22.2/33.3) | |
| 36. Bertoli and de Leeuw, 2016 (USA) | Anxiety | 28.9 | 70 |
| | Depression | 30.4 | |
| 37. Braud and Boucher, 2016 (France) | Anxiety | 38.8 | 139 |
| | Depression | 33.3 | |
| 38. das Neves de Araújo Lima et al, 2016 (Brazil) | Anxiety (Mild/Mod/Sev) | BMS: 30.0/6.7/13.3<br>SOB: 20.0/10.0/0 | 138 |
| | Depression (Mild-Mod/Mod-Sev) | BMS: 53.1/28.1<br>SOB: 16.1/6.0 | |
| 39. Davies et al, 2016 (UK) | Anxiety | – | 164 |
| | Depression | – | |
| 40. Duraçoğlu et al, 2016 (Turkey) | Anxiety | 31.1 | 67 |
| | Depression | 40.7 | |
| | Anxiety and/or depression | 49.8 | |
| 41. Mousavi et al, 2016 (USA) | Anxiety (Diag) | 52.3 | 137 |
| | Depression (Diag) | 42.8 | |
| 42. Patil et al, 2016 (India) | Depression (BClin/Mod/Sev) | Cases: 30.0 (13.3/13.3/3.3)<br>Controls: 10.0 (6.7/3.3/0.0) | 68 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 43. Sevrain et al, 2016 (France) | Retrospective | BMS: 35 | 35 (M: 9, F: 91) | HADS |
| 44. Tang et al, 2016 (China) | Cross-sectional | TN: 167 | 167 (M: 40.7, F: 59.3) | BAI<br>BDI |
| 45. Visscher et al, 2016 (Netherlands) | Retrospective | TMD: 112 | 112 (M: 13, F: 87) | SCL-90 |
| 46. Al-Havaz et al, 2015 (Iran) | Cross-sectional | TMD: 171 | 171 (M: 43, F: 57) | RDC/TMD |
| 47. Brailo and Zakrzewska, 2015 (UK) | Cross-sectional | TN: 48<br>TMD: 112<br>CIFP: 85 | 245 (M: 24, F: 76) | HADS |
| 48. Kotiranta et al, 2015 (Finland) | Cross-sectional | TMD: 399 | 399 (M: 17, F: 83) | RDC/TMD (SCL-90-R) |
| 49. Lei et al, 2015 (China) | Cross-sectional | TMD:<br>MFP: 128<br>No MFP: 382 | 510 (M: 24, F: 76) | DASS-21 |
| 50. Lopez-Jornet et al, 2015 (Spain) | Cross-sectional | BMS cases: 70<br>Controls: 70 | 140 (M: 9, F: 91) | HADS |
| 51. Majumder et al, 2015 (India) | Cross-sectional | TMD cases: 311<br>Controls: 689 | 1,000 (M: 45, F: 55) | HADS |
| 52. Marino et al, 2015 Italy | Case-control | BMS cases: 58<br>Controls: 58 | 116 (M: 21, F: 79) | HARS<br>MADRS |
| 53. Reiter et al, 2015 (Israel) | Retrospective observational | Acute TMD: 49<br>Chronic TMD: 139 | 207 (M: 24, F: 76) | RDC/TMD (SCL-90-R) |
| 54. Tokura et al, 2015 (Japan) | Cross-sectional | BMS cases: 65<br>Controls: 116 | 181 (M: 19, F: 82) | BDI |
| 55. Wu et al, 2015 (Korea) | Retrospective cohort | TN cases: 3,273<br>Controls: 13,092 | 16,365 (M: 62, F: 38) | ICD-9 CM |
| 56. Calixtre et al, 2014 (Brazil) | Longitudinal | TMD: 19 | 19 (M: 5, F: 94) | HADS |
| 57. Cioffi et al, 2014 (Italy) | Cross-sectional | TMD/migraine:<br>TMD MP: 676<br>Migraine: 39<br>TMD MP + migraine: 66 | 781 (M: 22, F: 78) | RDC/TMD (SCL-90) |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 43. Sevrain et al, 2016 (France) | Anxiety | 54.3 | 92 |
| | Depression | 25.7 | |
| 44. Tang et al, 2016 (China) | Anxiety | 20.4 | 134 |
| | Depression | 72.5 | |
| 45. Visscher et al, 2016 (Netherlands) | Depression | 25.8 | 69 |
| 46. Al-Havaz et al, 2015 (Iran) | Depression (Mod-Sev) | TMD: 7.0 | 62 |
| 47. Brailo and Zakrzewska, 2015 (UK) | Anxiety (BClin/Clin) | TN: 39.3 (17.9/21.4)<br>TMD: 55.7 (26.2/29.5)<br>CIFP: 38.5 (15.4/23.1) | 122 |
| | Depression (BClin/Clin) | TN: 32.1 (25.0/7.1)<br>TMD: 32.8 (19.7/13.1)<br>CIFP: 42.3 (11.5/30.8) | |
| 48. Kotiranta et al, 2015 (Finland) | Anxiety | – | 63 |
| | Depression | – | |
| 49. Lei et al, 2015 (China) | Anxiety | TMD: 36.5<br>MFP: 62.5<br>No MFP: 27.7 | 64 |
| | Depression | TMD: 17.6<br>MFP: 31.3<br>No MFP: 13.1 | |
| 50. Lopez-Jornet et al, 2015 (Spain) | Anxiety | – | 91 |
| | Depression | – | |
| 51. Majumder et al, 2015 (India) | Anxiety and/or Depression | TMD: 66.2<br>No TMD: 31.1 | 65 |
| 52. Marino et al, 2015 Italy | Anxiety (Mild-Mod/Mod-Sev) | BMS: 80.7 (31.6/49.1) | 136 |
| | Depression (Mild/Mod/Sev) | BMS: 49.1 (47.3/1.8/0) | |
| 53. Reiter et al, 2015 (Israel) | Anxiety (Mod/Sev) | TMD: 54.1 (29.5/24.6)<br>Acute: 44.9 (28.6/16.3)<br>Chronic: 58.3 (30.2/28.1) | 66 |
| | Depression (Mod/Sev) | TMD: 56.0 (33.3/22.7)<br>Acute: 40.8 (26.5/14.3<br>Chronic: 61.2 (36.0/25.2) | |
| 54. Tokura et al, 2015 (Japan) | Depression (Diag MDD) | BMS: 14 | 135 |
| 55. Wu et al, 2015 (Korea) | Anxiety (Diag) | TN: Cases: 1.8<br>Controls: 0.60 | 106 |
| | Depression (Diag) | TN: Cases: 2.2<br>Controls: 0.79 | |
| 56. Calixtre et al, 2014 (Brazil) | Anxiety | – | 54 |
| | Depression | – | |
| 57. Cioffi et al, 2014 (Italy) | Depression | – | 121 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 58. Davis et al, 2014 (USA) | Cross-sectional | TMD: 50 | 50 (M: 8, F: 92) | Psych Diag-(MR)<br><br>STAI |
| 59. Gerrits et al, 2014 (Netherlands) | Longitudinal cohort | OFP: 13 | 614 (M: 39, F: 61) | DSM-IV<br><br>CIDI version 2.1 |
| 60. Komiyama et al, 2014 (Japan) | Cross-sectional | TMD: 1,437 | 1,437 (M: 29, F: 71) | RDC/TMD |
| 61. Minghelli et al, 2014 (Portugal) | Cross-sectional | TMD cases: 633<br><br>Controls: 860 | 1,493 (M: 32, F: 68) | HADS |
| 62. Reissmann et al, 2014 (Germany) | Case-control | TMD cases: 320<br><br>Controls: 888 | 1,208 (M: 36, F: 64) | STAI<br><br>RDC/TMD |
| 63. Smriti et al, 2014 (India) | Cross-sectional | TMD cases: 27<br><br>Controls: 123 | 150 (M: 31, F: 69) | ZSAS |
| 64. Sood et al, 2014 (India) | Cross-sectional | TMD cases: 104<br><br>Controls: 396 | 400 (M: 25, F: 75) | HADS |
| 65. Vasudeva et al, 2014 (India) | Case-control | TMD cases: 255<br><br>Controls: 250 | 505 (M: 64, F: 36) | HADS |
| 66. Castelli et al, 2013 (Italy) | Case-control | TMD (chronic MP) cases: 45<br><br>Controls: 45 | 90 (F: 100) | BDI<br><br>STAI-Y1 |
| 67. Chen et al, 2013 (USA) | Case-control, secondary analysis | TMD:<br><br>TMD cases, no pain: 14<br><br>TMD cases with chronic pain: 145<br><br>Controls: 131 | 290 (F: 100) | STAI<br><br>SCL-90-R |
| 68. Ligthart et al, 2013 (Netherlands) | Longitudinal cohort | OFP:<br><br>Facial pain: 401 (at 2-y follow-up) | 2,981 (total);<br>(M: 34, F: 66) | BAI<br><br>IDS-SR |
| 69. Ozdemir-Karatas et al, 2013 (Turkey) | Cross-sectional | TMD: 104 | 104 (M: 38, F: 62) | RDC/TMD (SCL-90-R) |
| 70. Sipilä et al, 2013 (Finland) | Longitudinal cohort | Chronic OFP:<br><br>Cases: 162<br><br>Controls: 200<br><br>Follow-up: 63<br><br>Follow-up controls: 85 | Baseline: 362<br><br>Follow-up: 148 | SCL-25 |
| 71. Smith et al, 2013 (UK) | Cross-sectional | Ne: PPTN: 89 | 89 (M: 32, F: 68) | HADS |
| 72. de Lucena et al, 2012 (Brazil) | Longitudinal population-based prospective | TMD (two time periods; T1 and T2):<br><br>Cases: 99<br><br>Controls: 54 | 153 (M: 46, F: 54) | HADS |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 58. Davis et al, 2014 (USA) | Anxiety (Diag) | 30.0 | 55 |
| | Depression (Diag) | 18.0 | |
| 59. Gerrits et al, 2014 (Netherlands) | Anxiety | – | 131 |
| | Depression | – | |
| 60. Komiyama et al, 2014 (Japan) | Depression | – | 56 |
| 61. Minghelli et al, 2014 (Portugal) | Anxiety or depression | Cases: 61.4<br>Controls: 38.6 | 57 |
| 62. Reissmann et al, 2014 (Germany) | State Anxiety (Mod/Sev) | Cases: 56.6 (25.3/31.3)<br>Controls: 32.2 (22.2/10) | 58 |
| | Depression (Mod/Sev) | Cases: 45.9 (20.6/25.3)<br>Controls: 38.5 (16.9/21.6) | |
| 63. Smriti et al, 2014 (India) | Anxiety (Mild-Mod) | TMD: 25.9<br>No TMD: 6.5 | 59 |
| 64. Sood et al, 2014 (India) | Anxiety | – | 60 |
| | Depression | – | |
| 65. Vasudeva et al, 2014 (India) | Anxiety (BClin/Clin) | TMD 55.9 (45.0/10.9)<br>No TMD: 20.4 (19.2/0.8) | 61 |
| 66. Castelli et al, 2013 (Italy) | Anxiety | – | 51 |
| | Depression | – | |
| 67. Chen et al, 2013 (USA) | Anxiety | – | 52 |
| | Depression | – | |
| 68. Ligthart et al, 2013 (Netherlands) | Anxiety | – | 129 |
| | Depression | – | |
| 69. Ozdemir-Karatas et al, 2013 (Turkey) | Depression | – | 53 |
| 70. Sipilä et al, 2013 (Finland) | Depression symptoms | Baseline cases: 17.5<br>Controls: 7.0 | 130 |
| | Depression (Diag) | Follow-up cases: 6.3<br>Controls: 1.2 | |
| 71. Smith et al, 2013 (UK) | Anxiety (BClin/Clin) | 51.2 (17.5/33.7) | 105 |
| | Depression (BClin/Clin) | 29.8 (14.3/15.5) | |
| 72. de Lucena et al, 2012 (Brazil) | Anxiety | Cases: T1 = 61.6/T2 = 60.6<br>Controls: T1 = 22.2/T2 = 37.0 | 45 |
| | Depression | Cases: T1 = 16.2/T2 = 26.3<br>Controls: T1 = 5.6/T2 = 14.8 | |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 73. de Souza et al, 2012 (Brazil) | Cross-sectional | BMS cases: 30<br>Controls: 31 | 61 (M: 3, F: 97) | MINI-Plus<br>HDRS<br>BDI<br>STAI |
| 74. Diniz et al, 2012 (Brazil) | Longitudinal cohort | Baseline TMD: 20<br>Controls: 35<br>Follow-up TMD: 28<br>Follow-up controls: 27 | 55 | BAI |
| 75. Guarda-Nardini et al, 2012 (Italy) | Cross-sectional | Acute TMD: 51<br>Chronic TMD: 59 | 110 (M: 19, F: 81) | HARS<br>HDRS<br>SCL-90-R |
| 76. Kindler et al, 2012 (Germany) | Prospective cohort | TMD:<br>TMD JP: 122<br>No TMD JP: 2,884<br>TMD MP: 50<br>No TMD MP: 2,984 | 6,040 (M: 49, F: 51) | CID-S |
| 77. Komiyama et al, 2012 (Japan) | Cross-sectional | Ne:<br>BMS: 282 (acute: 169, chronic: 113)<br>TN n = 83 (acute: 43, chronic: 40) | 365 (M: 20, F: 80) | RDC/TMD (SCL-90-R) |
| 78. Rodrigues et al, 2012 (Brazil) | Cross-sectional | TMD:<br>TMD pain: 54<br>TMD no pain: 129 | 183 (M: 42, F: 58) | RDC/TMD |
| 79. Schiavone et al, 2012 (Italy) | Cross-sectional | BMS:<br>Chronic BMS: 53<br>Controls: 51 | 104 (M: 30, F: 70) | HDRS<br>STAI-Y1/Y2 |
| 80. Schwahn et al, 2012 (Germany) | Cross-sectional | TMD: 3,904 | 3,904 (M: 50, F: 50) | CID-S |
| 81. Wan et al, 2012 (Hong Kong) | Cross-sectional | OFP:<br>CD: 200<br>IE: 200 | 400 | GHQ-12 |
| 82. Celić et al, 2011 (Croatia) | Cross-sectional | Acute TMD: 126<br>Chronic TMD: 28 | 154 (M: 24, F: 76) | RDC/TMD (SCL-90-R) |
| 83. Dworkin, 2011 (Italy, Israel, Amsterdam) | Cross-sectional | TMD: 1,149 | 1,149 (M: 20, F: 80) | SCL-90-R |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 73. de Souza et al, 2012 (Brazil) | Anxiety (Diag)<br><br>Depression (Diag) | Cases: 36.7<br>Controls: 9.7<br><br>Cases: 46.7<br>Controls: 12.9 | 89 |
| 74. Diniz et al, 2012 (Brazil) | Anxiety (Mild/Mod-Sev) | Baseline TMD: 65.0 (55.0/10)<br>Follow-up TMD: 64.3 (18.6/39.3) | 46 |
| 75. Guarda-Nardini et al, 2012 (Italy) | Anxiety<br><br>Depression (Mod-Sev) | –<br><br>TMD (acute and chronic): 48.0 (30–18) | 47 |
| 76. Kindler et al, 2012 (Germany) | Anxiety symptoms<br><br>Depression symptoms | JP: 64.8<br>No JP: 47.1<br>MP: 78.0<br>No MP: 47.3<br><br>JP: 49.2<br>No JP: 28.3<br>MP: 46.0<br>No MP: 29.0 | 48 |
| 77. Komiyama et al, 2012 (Japan) | Depression | – | 120 |
| 78. Rodrigues et al, 2012 (Brazil) | Depression (Mod/Sev) | TMD: 41.5 (30.2/11.3) | 49 |
| 79. Schiavone et al, 2012 (Italy) | Anxiety<br><br>Depression | –<br><br>– | 90 |
| 80. Schwahn et al, 2012 (Germany) | Depression | – | 50 |
| 81. Wan et al, 2012 (Hong Kong) | Psychologic distress | CD: 4<br>IE: 11.0 | 128 |
| 82. Celić et al, 2011 (Croatia) | Depression (Sev) | TMD (acute and chronic): 19.5 | 40 |
| 83. Dworkin, 2011 (Italy, Israel, Amsterdam) | Depression (Mod-Sev) | 45.4 | 41 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 84. Gustin et al, 2011 (Australia) | Case-control | Ne/TMD:<br>TNP: 24<br>TMD: 21<br>Controls: 38 | 83 (M: 24, F: 76) | STAI<br>BDI |
| 85. Mačianskytė et al, 2011 (Lithuania) | Cross-sectional | Ne/IP:<br>TN + Chronic facial pain: 30<br>ATFP: 30 | 60 (M: 15, F: 85) | CAS<br>BDI |
| 86. Monteiro et al, 2011 (Brazil) | Cross-sectional | Chronic TMD: 49<br>Controls: 101 | 150 (M: 78, F: 22) | STAI |
| 87. Taiminen et al, 2011 (Finland) | Cross-sectional | Ne/IP:<br>BMS: 40<br>ATFP: 23 | 63 (M: 10, F: 90) | SCID-I |
| 88. van Seventer et al, 2011 (UK, Netherlands, Canada) | Secondary analysis of a randomized controlled trial | Ne (posttraumatic peripheral neuropathic pain):<br>TN: unknown | 254 (M: 49, F: 51) | HADS |
| 89. Velly et al, 2011 (USA) | Prospective cohort | TMD chronic pain onset (GCPS I): 261<br>Pain prognosis (GCPS II-IV): 309 | Baseline: 570 (M: 15, F: 85)<br>– | BDI |
| 90. Xu et al, 2011 (China) | Cross-sectional | TMD: 162 | 162 (F: 100) | SCL-90-R |
| 91. Bakhtiari et al, 2010 (Iran) | Cross-sectional | BMS:<br>BMS: 50<br>Controls: 50 | 100 (M: 17, F: 83) | CAS |
| 92. Giannakopoulos et al, 2010 (Germany) | Case-control | TMD:<br>MP: 88<br>JP: 43<br>NonTMD facial pain: 45<br>Controls n = 46 | 222 (M: 27, F: 73) | HADS |
| 93. Kim et al, 2010 (Korea) | Cross-sectional | TMD:<br>TMD trauma: 34<br>TMD no trauma: 340 | 374 (M: 29, F: 71) | SCL-90-R |
| 94. Lajnert et al, 2010 (Croatia) | Cross-sectional | Acute TMD: 30<br>Chronic TMD: 30<br>Controls: 30 | 90 (F: 100) | RDC/TMD |
| 95. Manfredini et al, 2010a (Italy) | Cross-sectional | TMD: 11 | 111 (M: 19, F: 81) | RDC/TMD (SCL-90-R) |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 84. Gustin et al, 2011 (Australia) | Anxiety | – | 16 |
| | Depression | – | |
| 85. Mačianskytė et al, 2011 (Lithuania) | Anxiety | – | 118 |
| | Depression (Mod/Sev) | TN: 76.7 (46.7/30.0)<br>ATFP: 0 | |
| 86. Monteiro et al, 2011 (Brazil) | State anxiety | – | 42 |
| | Trait anxiety | – | |
| 87. Taiminen et al, 2011 (Finland) | Anxiety (Diag) | BMS: 47.5<br>ATFP: 30.4 | 119 |
| | Depression (Diag) | BMS: 35<br>ATFP: 26 | |
| 88. van Seventer et al, 2011 (UK, Netherlands, Canada) | Anxiety | – | 104 |
| | Depression | – | |
| 89. Velly et al, 2011 (USA) | Depression (Mod/Sev), baseline | TMD: 10.3<br>GCPS I: 7.0<br>GCPS II-IV: 14.0 | 43 |
| 90. Xu et al, 2011 (China) | Anxiety | 7.4 | 44 |
| | Depression | 11.7 | |
| 91. Bakhtiari et al, 2010 (Iran) | State anxiety | – | 103 |
| | Trait anxiety | – | |
| 92. Giannakopoulos et al, 2010 (Germany) | Anxiety | – | 35 |
| | Depression | – | |
| 93. Kim et al, 2010 (Korea) | Anxiety | – | 116 |
| | Depression | – | |
| 94. Lajnert et al, 2010 (Croatia) | Depression (Mod/Sev) | Acute: 52.7 (28.0/24.7)<br>Chronic: 77.4 (30.0/6.0)<br>Controls: 36.0 (30.0/6.0) | 36 |
| 95. Manfredini et al, 2010a (Italy) | Depression (Mod/Sev) | 41.4 (1.8/39.6) | 37 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 96. Manfredini et al, 2010b (Italy, Israel, Netherlands) | Cross-sectional | Acute TMD: 293<br>Chronic TMD: 856 | 1,149 (M: 20, F: 80) | RDC/TMD (SCL-90) |
| 97. McMillan et al, 2010 (Hong Kong) | Cross-sectional, case-control | OFP cases: 200<br>Controls: 200 | 400 (M: 36, F: 64) | SCL-90 |
| 98. Pesqueira et al, 2010 (Brazil) | Cross-sectional, case-control | TMD cases: 61<br>Controls: 89 | 150 | STAI<br>RDC/TMD |
| 99. Takenoshita et al, 2010 (Japan) | Cross-sectional<br>IASP | Ne/IP:<br>BMS: 125<br>AO: 37 | 162 (M: 13, F: 87) | SDS<br>Psych Diag<br>MR |
| 100. Bonjardim et al, 2009 (Brazil) | Cross-sectional | TMD cases: 98<br>Controls: 98 | 196 (M: 49, F: 51) | HADS |
| 101. Choi et al, 2009 (Korea) | Retrospective | Ne/PIFP/TMD:<br>TN: 8<br>Ne: 9<br>PIFP: 8<br>TMD: 138 (TMD MP: 73, TMD JP: 24, TMD MP + JP: 41) | 163 (M: 40, F: 60) | HADS |
| 102. Gao et al, 2009 (China) | Case-control | BMS cases: 87<br>Controls: 82 | 169 (M: 24, F: 76) | SAS<br>SDS |
| 103. Licini et al, 2009 (Italy) | Cross-sectional | TMD: 308 | 308 (M: 25, F: 75) | RDC/TMD |
| 104. Macfarlane et al, 2009 (UK) | Prospective cohort | TMD:<br>OFP in young adults: 78 | 337 (M: 43, F: 57) | CES-D<br>PSS |
| 105. Stavrianos et al, 2009 (UK) | Prospective cohort | TMD: 22 | 22 (M: 36, F: 64) | IAS |
| 106. Streffer et al, 2009 (Switzerland) | Cross-sectional | OF: 102 | 102 (M: 22, F: 78) | HADS |
| 107. Baad-Hansen et al, 2008 (Denmark) | Cross-sectional | TMD: 41<br>AO: 46 | 87 (M: 17, F: 83) | SCL-90-R |
| 108. Ballegaard et al, 2008 (Denmark) | Cross-sectional | TMD/headache:<br>TMD with headache: 55<br>Headache without TMD: 44 | 99 (M: 23, F: 76) | RDC/TMD |
| 109. Buljan et al, 2008 (Croatia) | Cross-sectional | BMS cases: 42<br>Controls: 78 | 120 (M: 39, F: 61) | BAI<br>SDS |
| 110. Castro et al, 2008 (Brazil) | Cross-sectional | TN: 15<br>TMD: 15 | 30 (M 27, F: 73) | HADS |
| 111. Lee et al, 2008 (China) | Cross-sectional | TMD: 87 | 87 (M: 12, F: 88) | RDC/TMD |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 96. Manfredini et al, 2010b (Italy, Israel, Netherlands) | Depression (Mod/Sev) | Acute: 45.0 (23.1/21.9)<br>Chronic: 47.7 (25.1/22.6) | 38 |
| 97. McMillan et al, 2010 (Hong Kong) | Depression | Cases: 31.0<br>Controls: 11.0 | 127 |
| 98. Pesqueira et al, 2010 (Brazil) | State anxiety | – | 39 |
| | Trait anxiety | – | |
| 99. Takenoshita et al, 2010 (Japan) | Depressive tendencies | BMS: 32.1<br>AO: 33.3 | 117 |
| | Depression (Diag) | BMS: 32.0<br>AO: 21.6 | |
| | Anxiety (Diag) | BMS: 9.6<br>AO: 10.8 | |
| 100. Bonjardim et al, 2009 (Brazil) | Anxiety (BClin/Clin) | TMD: 43.9 (26.5/17.3)<br>No TMD: 24.5 (21.4/3.1) | 31 |
| | Depression (BClin) | TMD: 6.6<br>No TMD: 3.1 | |
| 101. Choi et al, 2009 (Korea) | Anxiety | – | 115 |
| | Depression | – | |
| 102. Gao et al, 2009 (China) | Anxiety | – | 165 |
| | Depression | – | |
| 103. Licini et al, 2009 (Italy) | Depression (Mod/Sev) | 65.7 (13.3/52.6) | 32 |
| 104. Macfarlane et al, 2009 (UK) | Depression | OFP: 33.3<br>No OFP: 18.9 | 33 |
| 105. Stavrianos et al, 2009 (UK) | Heart phobia | – | 34 |
| | Cancer phobia | – | |
| 106. Streffer et al, 2009 (Switzerland) | Anxiety (BClin/Clin) | 51.7 (33/18.7) | 126 |
| | Depression (BClin/Clin) | 32.6 (16.9/15.7) | |
| 107. Baad-Hansen et al, 2008 (Denmark) | Depression | – | 113 |
| 108. Ballegaard et al, 2008 (Denmark) | Depression (Mod-Sev) | TMD with headache: 70.9<br>Headache without TMD: 34.1 | 123 |
| 109 Buljan et al, 2008 (Croatia) | Anxiety | – | 88 |
| | Depression | – | |
| 110. Castro et al, 2008 (Brazil) | Anxiety | – | 114 |
| | Depression | – | |
| 111. Lee et al, 2008 (China) | Depression (Mod/Sev) | 42.5 (26.4/16.1) | 29 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) | Study type | Orofacial pain group types and sample sizes, n | No. of patients (% gender distribution) | Psychosocial scales |
|---|---|---|---|---|
| 112. Reissmann et al, 2008 (Germany) | Cross-sectional | TMD: 225 | 225 (M: 14, F: 86) | RDC/TMD |
| 113. Bertoli et al, 2007 (USA) | Retrospective | TMD: 445 | 445 (M: 9, F: 91) | SCL-90-R |
| 114. John et al, 2007 (Germany) | Cross-sectional | Chronic TMD: 416 | 416 (M: 21, F: 79) | RDC/TMD Axis II |
| 115. List et al, 2007 (Sweden) | Case-control | AO cases: 46<br>Controls: 35 | 81 (M: 22, F: 78) | SCL-90-R |
| 116. Mongini et al, 2007 (Italy) | Cross-sectional | TMD/OFP:<br>TMD MP: 462<br>TMD A: 70,<br>Ne (TN + PNe): 68<br>FPD: 49 | 649 (M: 22, F: 78) | SCID-DSM-IV |
| 117. Nifosi et al, 2007 (Italy) | Cross-sectional | TMD MFP: 19<br>TMD JP: 26<br>TMD MFP + JP: 18 | 63 (M: 25, F: 75) | SCID-DSM-IV<br>HARS<br>HDRS<br>SCL-90-R |
| 118. GaldÓn et al, 2006 (Spain) | Cross-sectional | TMD MP: 58<br>TMD A: 56 | 114 (M: 11, F: 89) | BSI-18 |

**Table 1 Study Characteristics *(continued)***

| Study, y (country) *continued from prev. page* | Psychologic comorbidity | Prevalence, % | Reference no. |
|---|---|---|---|
| 112. Reissmann et al, 2008 (Germany) | Depression | 47.6 (21.8–25.7) | 30 |
| 113. Bertoli et al, 2007 (USA) | Depression | – | 26 |
| 114. John et al, 2007 (Germany) | Depression (Mod/Sev) | 46.2 (19.7/26.5) | 27 |
| 115. List et al, 2007 (Sweden) | Depression (Mod/Sev) | Cases: 74 (26.0/48.0)<br>Controls: 54 (37.0/17.0) | 132 |
| 116. Mongini et al, 2007 (Italy) | Anxiety (Diag) | TMD MP: 33.5<br>TMD A: 15.7<br>Ne: 16.2<br>FPD: 30.6 | 112 |
| | Depression (Diag) | TMD MP: 22.3<br>TMD A: 15.7<br>Ne: 10.3<br>FPD: 44.9 | |
| 117. Nifosi et al, 2007 (Italy) | Anxiety (Diag) | TMD: 15.9 | 28 |
| | Depression (Diag) | TMD: 20.6 | |
| | Anxiety and depression symptoms | – | |
| 118. GaldÓn et al, 2006 (Spain) | Anxiety | – | 25 |
| | General distress | – | |

Note: Only percentages of psychologic functioning impact of orofacial pain conditions were included (at the decimal point level presented in study papers).

AN = autonomic symptoms; AO = atypical odontalgia; ATFP = atypical facial pain; BAI = Beck Anxiety Inventory (BAI); BClin = borderline clinically significant; BDI = Beck Depression Inventory; BMS = Burning Mouth Syndrome; BSI-18 = Brief Symptom Inventory-18; CAS = Covi Anxiety Scale; CD = community dwellers; CES-D = Centre for Epidemiological studies Scale; CIDI = Composite International Diagnostic Interview; CID-S = Composite International Diagnostic-Screener; CIFP = chronic idiopathic facial pain; Clin = clinically significant (Clin); DASS-21 = Depression, Anxiety and Stress Scale; DC/TMD = Diagnostic Criteria for Temporomandibular Disorders; Diag = diagnosis; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders; FPD = facial pain disorder; GAD-7 = Generalized Anxiety Disorder questionnaire; GCPS = Graded Chronic Pain Scale (grades I to IV); GHQ = General Health Questionnaire; HADS = Hospital Anxiety and Depression Scale; HARS = Hamilton Anxiety Rating Scale; HDRS = Hamilton Depression Rating Scale; IAS = Illness Attitude Scale (IAS); ICD-9 = International Classification of Diseases, 9th Revision; IDS-SR = Inventory of Depressive Symptomatology; IE = institutionalized elderly; IMP = intermittent pain; IP = idiopathic pain; JP = TMD joint pain; MADRS = Montgomery-Åsberg Depression Rating Scale; MDD = major depressive disorder; MFP/MP = myofascial pain/TMD muscle pain; MINI-Plus = International Neuropsychiatric Interview; MR = medical record; MS = multiple sclerosis; Ne = neuropathic pain; OFP = orofacial pain; PHQ = Patient Health Questionnaire; PIFP = persistent idiopathic facial pain; PNe = persistent neuropathic pain; PPTNI = painful posttraumatic nerve injury; PSS = Perceived Stress Scale; Psych Diag = psychiatric diagnosis; RDC/TMD = Research Diagnostic Criteria/Temporomandibular Disorders Axis II questionnaire; SAS/SDS = self-rating anxiety/depression scale; SCID = Structured Clinical Interview for DSM-IV; STAI (Y1/Y2) = State-Trait Anxiety Inventory (Form 1/Form 2); SCL-25 = Symptom Checklist-25; SCL-90-R = Symptom Checklist-90-Revised; SOB = secondary oral burning; TMD A = arthrogenous TMD; TNP = trigeminal neuropathic pain; TN = trigeminal neuralgia; ZSAS = Zung Self Rating Anxiety Scale; ZSDS = Zung Self-Rating Depression Scale.

**Table 2 Risk of Bias of Individual Studies**

| Study | Study design | Study group | Control group | Prospective design | Blinded | Cumulative risk of bias | Reference no. |
|---|---|---|---|---|---|---|---|
| 1. Adamo et al, 2020 | Cross-sectional | Met | Met | Met | N/A | Low | 102 |
| 2. Bäck et al, 2020 | Cross-sectional | Unmet | Met | Met | N/A | High | 71 |
| 3. Chang et al, 2019 | Retrospective cross-sectional | Met | Met | Unmet | N/A | High | 110 |
| 4. Godazandeh et al, 2019 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 111 |
| 5. Heinskou et al, 2019 | Prospective observational | Met | N/A | Met | N/A | Moderate | 109 |
| 6. Huttunen et al, 2019 | Randomized controlled trial | Met | Met | Met | N/A | Low | 72 |
| 7. Jivnani et al, 2019 | Cross-sectional | Met | Met | Met | N/A | Low | 73 |
| 8. Le Bris et al, 2019 | Retrospective cohort | Met | N/A | Unclear | N/A | Moderate | 101 |
| 9. Lira et al, 2019 | Cross-sectional | Unclear | Unmet | Met | N/A | High | 74 |
| 10. Melek et al, 2019 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 125 |
| 11. Yang et al, 2019 | Cross-sectional | Met | Unclear | Met | N/A | Moderate | 100 |
| 12. Adamo et al, 2018 | Cross-sectional | Met | Met | Met | N/A | Low | 99 |
| 13. Daher et al, 2018 | Cross-sectional | Unmet | Unclear | Met | N/A | High | 75 |
| 14. Di Stasio et al, 2018 | Cross-sectional | Met | Met | Met | N/A | Low | 98 |
| 15. Fernandes Azevedo et al, 2018 | Cross-sectional | Met | Unclear | Met | N/A | Moderate | 76 |
| 16. Lee and Chon, 2020 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 97 |
| 17. Miura et al, 2018 | Retrospective cross-sectional | Met | N/A | Unmet | N/A | High | 133 |
| 18. Moura et al, 2018 | Case-control | Met | Met | Met | N/A | Low | 96 |
| 19. Natu et al, 2018 | Cross-sectional | Unmet | Met | Met | N/A | High | 77 |
| 20. Nazeri et al, 2018 | Case-control | Met | Met | Met | N/A | Low | 78 |
| 21. Paulino et al, 2018 | Cross-sectional | Met | Unmet | Met | N/A | High | 79 |
| 22. Reiter et al, 2018 | Cross-sectional | Met | Unmet | Unmet | N/A | High | 80 |
| 23. Sikora et al, 2018 | Cross-sectional | Met | Met | Met | N/A | Low | 95 |
| 24. Sruthi et al, 2018 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 81 |
| 25. Tu et al, 2018 | Cross-sectional | Met | Met | Unmet | N/A | High | 124 |
| 26. Yoo et al, 2018 | Cross-sectional | Met | Met | Met | N/A | Low | 94 |
| 27. Mitsikostas et al, 2017 | Case series | Met | N/A | Met | N/A | Moderate | 93 |
| 28. Naikoo et al, 2017 | Case-control | Met | Met | Met | N/A | Low | 82 |
| 29. Reiter et al, 2017 | Cross-sectional | Met | Met | Met | N/A | Low | 83 |
| 30. Su et al, 2017 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 84 |
| 31. Tan et al, 2017 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 108 |
| 32. Tournavitis et al, 2017 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 85 |
| 33. van Selms et al, 2017 | Cross-sectional | Met | Met | Met | N/A | Low | 86 |
| 34. Yeung et al, 2017 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 87 |
| 35. Zakrzewska et al, 2017 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 107 |
| 36. Bertoli and de Leeuw, 2016 | Cross-sectional | Met | N/A | Unmet | N/A | High | 70 |
| 37. Braud and Boucher, 2016 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 139 |
| 38. das Neves de Araújo Lima et al, 2016 | Cross-sectional | Met | Unclear | Met | N/A | Moderate | 138 |
| 39. Davies et al, 2016 | Cross-sectional | Met | Unclear | Met | N/A | Moderate | 164 |
| 40. Duraçoğlu et al, 2016 | Cross-sectional | Met | Unmet | Met | N/A | High | 67 |
| 41. Mousavi et al, 2016 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 137 |
| 42. Patil et al, 2016 | Cross-sectional | Met | Met | Met | N/A | Low | 68 |
| 43. Sevrain et al, 2016 | Retrospective study | Unmet | NA | Met | NA | High | 92 |
| 44. Tang et al, 2016 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 134 |
| 45. Visscher et al, 2016 | Retrospective study | Unmet | N/A | Unmet | N/A | High | 69 |

**Table 2 Risk of Bias of Individual Studies *(continued)***

| Study | Study design | Study group | Control group | Prospective design | Blinded | Cumulative risk of bias | Reference no. |
|---|---|---|---|---|---|---|---|
| 46. Al-Havaz et al, 2015 | Cross-sectional | Unmet | N/A | Met | N/A | High | 62 |
| 47. Brailo and Zakrzewska, 2015 | Cross-sectional | Unclear | N/A | Met | N/A | Moderate | 122 |
| 48. Kotiranta et al, 2015 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 63 |
| 49. Lei et al, 2015 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 64 |
| 50. Lopez-Jornet et al, 2015 | Cross-sectional | Met | Met | Met | N/A | Low | 91 |
| 51. Majumder et al, 2015 | Cross-sectional | Unmet | N/A | Met | N/A | High | 65 |
| 52. Marino et al, 2015 | Case-control | Met | Met | Met | N/A | Low | 136 |
| 53. Reiter et al, 2015 | Retrospective observational | Met | N/A | Unmet | N/A | High | 66 |
| 54. Tokura et al, 2015 | Cross-sectional | Met | Met | Met | N/A | Low | 135 |
| 55. Wu et al, 2015 | Retrospective cohort | Unmet | Met | Met | N/A | High | 106 |
| 56. Calixtre et al, 2014 | Longitudinal study | Unmet | NA | Met | NA | High | 54 |
| 57. Cioffi et al, 2014 | Cross-sectional | Unmet | N/A | Met | N/A | High | 121 |
| 58. Davis et al, 2014 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 55 |
| 59. Gerrits et al, 2014 | Longitudinal cohort | Unmet | N/A | Met | N/A | High | 131 |
| 60. Komiyama et al, 2014 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 56 |
| 61. Minghelli et al, 2014 | Cross-sectional | Unmet | N/A | Met | N/A | High | 57 |
| 62. Reissmann et al, 2014 | Case-control | Met | Unclear | Met | N/A | Moderate | 58 |
| 63. Smriti et al, 2014 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 59 |
| 64. Sood et al, 2014 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 60 |
| 65. Vasudeva et al, 2014 | Case-control | Met | Met | Met | N/A | Low | 61 |
| 66. Castelli et al, 2013 | Case-control | Met | Met | Met | N/A | Low | 51 |
| 67. Chen et al, 2013 | Case-control | Met | Met | Met | N/A | Low | 52 |
| 68. Ligthart et al, 2013 | Longitudinal cohort | Met | N/A | Met | N/A | Low | 129 |
| 69. Ozdemir-Karatas et al, 2013 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 53 |
| 70. Sipilä et al, 2013 | Longitudinal cohort | Met | Met | Met | N/A | Low | 130 |
| 71. Smith et al, 2013 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 105 |
| 72. de Lucena et al, 2012 | Longitudinal prospective | Met | Unclear | Met | N/A | Moderate | 45 |
| 73. de Souza et al, 2012 | Cross-sectional | Met | Met | Met | N/A | Low | 89 |
| 74. Diniz et al, 2012 | Longitudinal cohort | Met | N/A | Met | N/A | Moderate | 46 |
| 75. Guarda-Nardini et al, 2012 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 47 |
| 76. Kindler et al, 2012 | Prospective cohort | Met | N/A | Met | N/A | Moderate | 48 |
| 77. Komiyama et al, 2012 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 120 |
| 78. Rodrigues et al, 2012 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 49 |
| 79. Schiavone et al, 2012 | Cross-sectional | Met | Met | Met | N/A | Low | 90 |
| 80. Schwahn et al, 2012 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 50 |
| 81. Wan et al, 2012 | Cross-sectional | Unclear | N/A | Met | N/A | Moderate | 128 |
| 82. Celić et al, 2011 | Cross-sectional | Unclear | N/A | Met | N/A | Moderate | 40 |
| 83. Dworkin, 2011 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 41 |
| 84. Gustin et al, 2011 | Case-control | Met | Met | Met | N/A | Low | 16 |

**Table 2 Risk of Bias of Individual Studies *(continued)***

| Study | Study design | Study group | Control group | Prospective design | Blinded | Cumulative risk of bias | Reference no. |
|---|---|---|---|---|---|---|---|
| 85. Mačianskytė et al, 2011 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 118 |
| 86. Monteiro et al, 2011 | Cross-sectional | Unmet | N/A | Met | N/A | High | 42 |
| 87. Taiminen et al, 2011 | Cross-sectional | Unclear | N/A | Met | N/A | Moderate | 119 |
| 88. van Seventer et al, 2011 | Secondary analysis of a randomized clinical trial | Met | Met | Met | Met | Low | 104 |
| 89. Velly et al, 2011 | Prospective cohort | Met | N/A | Met | N/A | Moderate | 43 |
| 90. Xu et al, 2011 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 44 |
| 91. Bakhtiari et al, 2010 | Cross-sectional | Met | Met | Met | N/A | Low | 103 |
| 92. Giannakopoulos et al, 2010 | Case-control | Met | Unclear | Met | N/A | Moderate | 35 |
| 93. Kim et al, 2010 | Cross-sectional | Met | Unclear | Met | N/A | Moderate | 116 |
| 94. Lajnert et al, 2010 | Cross-sectional | Met | Met | Met | N/A | Low | 36 |
| 95. Manfredini et al, 2010a | Cross-sectional | Met | N/A | Met | N/A | Moderate | 37 |
| 96. Manfredini et al, 2010b | Cross-sectional | Met | N/A | Met | N/A | Moderate | 38 |
| 97. McMillan et al, 2010 | Cross-sectional | Met | Met | Met | N/A | Low | 127 |
| 98. Pesqueira et al, 2010 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 39 |
| 99. Takenoshita et al, 2010 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 117 |
| 100. Bonjardim et al, 2009 | Cross-sectional | Unmet | N/A | Met | N/A | High | 31 |
| 101. Choi et al, 2009 | Retrospective | Unclear | N/A | Unmet | N/A | High | 115 |
| 102. Gao et al, 2009 | Case-control | Met | Met | Met | N/A | Low | 165 |
| 103. Licini et al, 2009 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 32 |
| 104. Macfarlane et al, 2009 | Prospective cohort | Unmet | N/A | Met | N/A | High | 33 |
| 105. Stavrianos et al, 2009 | Prospective cohort | Met | N/A | Met | N/A | Moderate | 34 |
| 106. Streffer et al, 2009 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 126 |
| 107. Baad-Hansen et al, 2008 | Cross-sectional | Met | Met | Met | N/A | Low | 113 |
| 108. Ballegaard et al, 2008 | Cross-sectional | Met | N/A | Met | Met | Low | 123 |
| 109. Buljan et al, 2008 | Cross-sectional | Unmet | N/A | Unclear | N/A | High | 88 |
| 110. Castro et al, 2008 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 114 |
| 111. Lee et al, 2008 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 29 |
| 112. Reissmann et al, 2008 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 30 |
| 113. Bertoli et al, 2007 | Retrospective | Unmet | N/A | Unmet | N/A | High | 26 |
| 114. John et al, 2007 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 27 |
| 115. List et al, 2007 | Case-control | Met | Met | Met | N/A | Low | 132 |
| 116. Mongini et al, 2007 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 112 |
| 117. Nifosi et al, 2007 | Cross-sectional | Met | N/A | Met | Met | Low | 28 |
| 118. GaldÓn et al, 2006 | Cross-sectional | Met | N/A | Met | N/A | Moderate | 25 |