ORAL SURGERY

Oral Surgery ISSN 1752-2471

INVITED REVIEW

Temporomandibular disorders: a review of current concepts in aetiology, diagnosis and management

F.P. Kapos[1,2], F.G. Exposto[3,4], J.F. Oyarzo[5] & J. Durham[6]

[1]Department of Epidemiology, School of Public Health, University of Washington, Seattle, WA, USA
[2]Department of Oral Health Sciences, School of Dentistry, University of Washington, Seattle, WA, USA
[3]Section of Orofacial Pain and Jaw Function, Department of Dentistry, Health, Aarhus University, Aarhus, Denmark
[4]Scandinavian Center for Orofacial Neurosciences (SCON), Aarhus, Denmark
[5]Orofacial Pain and TMD Program, Faculty of Odontology, Universidad Andres Bello, Santiago, Chile
[6]Centre for Oral Health Research & Institute of Health and Society, Newcastle University, Newcastle, UK

Key words:
aetiology, diagnosis, management, orofacial pain, temporomandibular disorders

Correspondence to:
FP Kapos
Department of Epidemiology, School of Public Health
University of Washington
Seattle, WA
USA
Tel.: (206) 543-1065
Email: kapos@uw.edu

Accepted: 18 January 2020

doi:10.1111/ors.12473

Abstract

Temporomandibular disorders (TMD) is a collective term for a group of musculoskeletal conditions involving pain and/or dysfunction in the masticatory muscles, temporomandibular joints (TMJ) and associated structures. It is the most common type of non-odontogenic orofacial pain and patients can present with pain affecting the face/head, TMJ and/or teeth, limitations in jaw movement and sounds in the TMJ during jaw movements. Comorbid painful and non-painful conditions are also common among individuals with TMD. The diagnosis of TMD have significantly improved over time with the recent Diagnostic Criteria for TMD (DC/TMD) being reliable and valid for most common diagnoses, and an efficient way to communicate in multidisciplinary settings. This classification covers 12 most common TMD, including painful (myalgia, arthralgia and headache attributed to TMD) as well as the non-painful (disc displacements, degenerative joint disease and subluxation) TMD diagnoses. Recent studies have demonstrated that the pathophysiology of common painful TMD is biopsychosocial and multifactorial, where no one factor is responsible for its development. Importantly, research has suggested different predisposing, initiating and perpetuating factors, including both peripheral and central mechanisms. This is an active field of investigation and future studies will not only seek to clarify specific causal pathways but translate this knowledge into mechanism-directed diagnosis and treatment. In accordance with this complex aetiology, current evidence supports primarily conservative multidisciplinary treatment including self-management strategies, behavioural therapy, physical therapy and pharmacotherapy. The aim of this review is to present an overview of most recent developments in aetiology, pathophysiology, diagnosis and management of TMD.

Background

Temporomandibular disorders (TMD) is a collective term for a group of musculoskeletal conditions involving pain and/or dysfunction in the masticatory muscles, temporomandibular joints (TMJ) and associated structures[1,2]. Although TMD is defined by pain and dysfunction in the orofacial region, common painful and non-painful comorbidities of common painful TMD include headaches, fibromyalgia, irritable bowel syndrome, tinnitus, chronic fatigue syndrome, depression and sleep disturbances[3–6]. As with many chronic pain conditions, recent research reinforces the biopsychosocial nature of common painful TMD (myalgia and/or arthralgia) and their interconnections with general health[7].

In addition to being the most common type of non-odontogenic orofacial pain, TMD pain is a major driver of treatment seeking[8,9], healthcare costs[10,11] and reduced quality of life[12] among individuals with TMD. Care pathways that support early diagnosis and management are likely to improve prognosis, quality of life and reduced healthcare costs for patients with TMD[10,13,14]. In this study, we present a review of TMD epidemiology, aetiology and pathophysiology in light of recent developments of the field, as well as the current evidence on diagnosis and management, with a focus on common painful TMD. Lastly, we discuss how novel findings may fit in the future direction of TMD research and practice.

Incidence of painful TMD

A large multisite prospective cohort study in the USA (OPPERA study) estimated that each year 4% of TMD-free adults aged 18–44 years develop clinically confirmed first-onset painful TMD, and that annual incidence increases with age (18–25 years = 2.5%; 25–34 years = 3.7% and 35–44 years = 4.5%)[7]. A total of 19% of adults per year reported an initial painful 'TMD symptom episode' (i.e. orofacial pain for at least 5 consecutive days per month for 1 or more months). However, the majority of these episodes were considered preclinical symptoms, as participants did not meet Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) for myalgia and/or arthralgia upon clinical examination[15].

In a large population-based study in adolescents aged 11–14 years, the estimated incidence of clinically confirmed painful TMD was 2% annually, with an additional 10% developing facial pain symptoms not meeting RDC/TMD criteria for painful TMD diagnosis (myalgia and/or arthralgia)[16]. Similarly, another study of adolescents aged 12–19 years reported a 3% annual incidence of painful TMD[17]. In contrast to adults, young adolescent females were at higher risk of new-onset painful TMD (OR = 2.0, 95% CI 1.2–2.3)[16]. In adolescents aged 12–19 years, incidence was also higher in females, especially with increasing age[17].

Prevalence of signs and symptoms of TMD

A large population-based study using the RDC/TMD estimated the prevalence of painful TMD (myalgia and/or arthralgia) is 36% in adults aged 20–49 years[18]. TMJ 'clicking' was reported by 30% of adults, whereas only 8% were diagnosed with a disc displacement (DD)[18]. The estimated prevalence of TMD degenerative joint disease (DJD) diagnosis, also associated with TMJ noises, is 17%. Of note, TMJ DD, the presumed cause of TMJ 'clicking', has been argued to be a normal anatomical variant of TMJ disc position, given its high prevalence in asymptomatic populations[19]. A meta-analysis of non-patient studies estimated the need for TMD treatment in adults is 16%, with higher values for studies of older individuals (≥46 years) and those where need was clinically assessed (vs. perceived by participants)[20].

Estimates of signs and symptoms of TMD in children and adolescents are more variable, as there is not a validated diagnostic protocol for this population[21]. Studies using the RDC/TMD estimated the prevalence of painful TMD ranges from 4 to 13% in children and adolescents aged 6–25 years[8,17,22–24]. A meta-analysis of 11 studies including participants aged 3–18 years estimated the prevalence of clinically identified TMJ noises is 16%[25].

Prognosis from acute to chronic and persistence of TMD

When adults with incident TMD were re-examined after an average of 8 months as initial diagnosis, 51% no longer met criteria for TMD[7]. Longer-term follow-up studies of clinical and community painful TMD cases reported remittance rates of 49% after 5 years[26] and 28% after 8 years[27].

Somewhat surprisingly, the OPPERA cohort study found only a slightly elevated risk of new-onset TMD in women [hazard ratio (HR) = 1.34, 95% CI 1.03–1.75], which was nullified in the fully adjusted multivariable model[6]. Also in contrast to the baseline OPPERA case–control study of chronic TMD[28], pain sensitivity [quantitative sensory testing (QST)] and autonomic function measures did not predict TMD incidence[29]. Authors speculate that given their prominent associations with chronic painful TMD cases; gender and pain sensitivity may be important contributors to TMD prognosis. More details about risk factors for the onset and maintenance of painful TMD are described in the Aetiology and Pathophysiology section.

TMJ noises and intra-articular diagnoses (DD and/or DJD) are poorly correlated with patient-reported jaw pain intensity, jaw function and disability[30]. Furthermore, an 8-year follow-up study demonstrated that structural intra-articular diagnoses remained stable in 71–76% of joints, with similar percentage of progression (14–15%) and reversal (10–14%)[31].

Aetiology and pathophysiology

Painful TMD have been shown to be biopsychosocial and multifactorial disorders, thus a singular cause is highly unlikely to be identified in any given patient[7]. Individuals' psychological profile and a state of pain amplification are two domains hypothesised to play a role in the aetiology of painful TMD[32]. Number of comorbid conditions (e.g. irritable bowel syndrome, insomnia) and non-specific orofacial symptoms (e.g. stiffness, fatigue) were also strong independent predictors of painful TMD onset, which may represent another causal domain related to "general health and global symptoms"[7,33]. Each of these three domains, composed of a variety of specific risk factors, are thought to be regulated by gene expression and influenced by social and environmental factors[32]. To date, there is evidence of a greater contribution of the psychological and global symptoms domains to the first onset of TMD, while pain amplification is associated with prognosis[7,34].

Biological, psychological and social vulnerabilities interact with contextual and environmental stressors to produce painful TMD and comorbid symptoms, with or without identifiable initiating events (e.g. micro-/macro-trauma)[35]. After initial onset, prognostic factors, including pain interference[27], general health, pain sensitivity[34], psychological and social factors, may contribute to perpetuation of symptoms or recovery (Box 1).

Box 1. Summary of painful TMD aetiological and prognostic factors

Predisposing factors

The development of new-onset painful TMD was most strongly predicted by baseline **health status variables and social context,** followed by the **psychological and clinical orofacial domains**. Specifically, four variables emerged as the most important predictors[6]:

- Greater number of comorbid conditions, for example, irritable bowel syndrome, fibromyalgia, insomnia and depression;
- Greater number of non-specific orofacial symptoms, for example, stiffness, cramping, fatigue, pressure and soreness;
- Geographic location/study site – likely a proxy for unmeasured social and contextual factors;
- Higher overall pain interference with normal work

Additional important predictors included[6]:

- Greater number of oral parafunctions;
- Perceived limited mouth opening in the last month;
- Greater number of painful masticatory muscle sites on palpation during clinical exam;
- Greater somatic awareness;
- Older age

Initiating factors

Incident **jaw injury** (e.g. attributed to yawning, prolonged mouth opening, dental treatments, oral intubation, sports injury and motor vehicle accidents) is strongly associated with subsequent TMD incidence (HR = 3.94, 95% CI 2.82–5.50), adjusting for study site, age, race and gender[94].

In addition, baseline **migraine** (HR = 1.67, 95% CI 1.06–2.62), higher baseline headache frequency (0–4 headaches/month) and **worsening headache** during the follow-up period predict TMD incidence[95].

Perpetuating factors

Clinical measures of **pain severity** and **comorbid conditions** at diagnosis were associated with TMD persistence at an average of 8-months follow-up after initial diagnosis of new-onset TMD, including[34]:

- Greater number of comorbid conditions;
- Higher pain intensity, frequency and duration in the previous month;
- Greater number of painful sites (masticatory muscles, TMJs, familiar headache and other body sites) on palpation or jaw movement during clinical exam;
- Pain modified by chewing hard or tough food

Mechanisms

Although the exact pathophysiology remains unclear, several non-mutually exclusive mechanisms have been proposed to explain how biological, psychological and social factors can combine to predispose, perpetuate or initiate painful TMD. Studies of chronic pain and TMD suggest putative neurologic, endocrine and inflammatory pathways outlined below, which can be further studied as potential diagnostic biomarkers or therapeutic targets. Some of these hypothesised mechanisms also highlight possible explanations for the occurrence of painful and non-painful comorbidities.

An evaluation of 3295 single-nucleotide polymorphisms (SNPs) representing 358 genes previously linked to systems involved in pain perception revealed associations between five SNPs and phenotypes that were predictive of TMD incidence[36]. Genes in which these significant SNPs are contained and mechanisms hypothesised to explain their role in TMD pathophysiology are described in Table 1[36].

Reduced Catecholamine-O-methyltransferase (COMT) activity has also been associated with pain and TMD[37]. This enzyme regulates extracellular concentration of epinephrine, norepinephrine and

Table 1 Summary of OPPERA Prospective Cohort genetic findings and potential painful TMD aetiological mechanisms[36]

Gene	Encodes	Function	Phenotype	Implications
SCN1A	Alpha subunit of voltage-gated sodium channel Nav 1.1	Nav 1.1 is involved in the generation and propagation of action potentials in sensory nerves	Non-specific orofacial symptoms†	SCN1A has also been associated with short-term memory performance in other studies and may alter somatic sensitivity
ACE2	Angiotensin I–converting enzyme 2	Angiotensin-related peptides have been suggested to function as neurotransmitters in the periaqueductal grey (PAG) and other brain regions involved in endogenous pain modulation. In addition to angiotensin I, pro and antinociceptive peptides (e.g. bradykinin, substance P and opioids such as dynorphin and enkephalin) are substrates of ACE2	Non-specific orofacial symptoms†	Pharmacologic inhibition of ACE has been associated with increase in nociceptive thresholds and tolerance, and risk of complex regional pain syndrome (CRPS)
PTGS1	Prostaglandin-endoperoxide synthase 1 (COX-1) enzyme	COX-1 catalyses the conversion of arachidonic acid into prostaglandins mediating inflammatory response and regulating neuronal sensitivity to pain	Global psychological symptoms‡	Could alter somatic sensitivity, awareness of autonomic activity and nociception
APP	Amyloid-β precursor protein	APP is expressed by neurons and is involved in synapse formation and neuronal plasticity. May modulate cognitive ability and cognitive aging	Stress and negative affect§	Increased expression of APP may underlie higher perception of stress
MPDZ	Multiple PDZ domain protein (MUPP1)	Scaffolding for G protein–coupled receptors involved in nociception and analgesia (e.g. serotonergic and GABAergic). May also regulate glutamate-related excitatory neurotransmission	Heat pain temporal summation¶	May be associated with temporal summation of pain through neurotransmitter regulation

†Global psychological symptoms is a composite measure built via principal component analysis, characterised by high loadings from SCL-90R Somatization Scale, Pennebaker Inventory of Limbic Languidness (PILL) and the Lifetime Stressor List/PTSD Checklist–Civilian Version PTSD symptom scale.

‡Stress and negative affect is a composite measure built via principal component analysis, characterised by high loadings from State and Trait Anxiety, Perceived Stress Scale (PSS), Profile of Mood States–Bipolar (POMS) Negative Affect scale and Eysenck Personality Questionnaire–Revised (EPQ-R) Neuroticism scale; negative loadings from POMS Positive Affect scale and EPQ-R Extraversion scale.

§Non-specific orofacial symptoms were measured as count of six aversive sensations of the face and jaw not described as pain: stiffness, cramping, fatigue, pressure, soreness and ache.

¶Heat pain temporal summation is a quantitative sensory test measure of endogenous pain facilitation.

dopamine, which are involved with many neurological functions, including pain perception (e.g. through activation of β-adrenergic receptors) and stress reactivity[38]. TMD-free women with 'low COMT activity' haplotypes were 2.3 times (95% CI 1.1–4.8) more likely to develop new-onset painful TMD during a 3-year follow-up[37]. Likewise, adrenal dysregulation of the sympathetic nervous system has been associated with pain in individuals with chronic TMD and fibromyalgia, leading to investigations of the use of β-blockers in this population[39,40]. However, the importance of the environment should be highlighted: the association between COMT haplotypes and pain sensitivity was only detectable in men and women in low and no-stress scenarios[38]. The presence of any stress presumably overwhelms the system with epinephrine, overriding differences between COMT haplotypes, especially in women[38].

In addition, several alterations in pro- and anti-inflammatory cytokines have also been found in individuals with chronic painful TMD relative to TMD controls, including elevated circulating levels pro-inflammatory monocyte chemotactic protein (MCP-1)[41], reduced levels of anti-inflammatory (omentin-1)[42] and reduced transcription of anti-inflammatory transforming growth factor β1 (TGFβ1). Inflammation may play a more substantial role in TMJ arthralgia and DJD, based on associations with several altered markers in the joints or synovial fluid[43]. Specifically, CGRP is a neuropeptide released from trigeminal nerves that activates neurogenic inflammation and has been found to mediate peripheral and central sensitisation to pain in an animal model of TMD[44]. Although its value in TMD treatment remains unknown, CGRP is a promising therapeutic target in novel monoclonal antibody treatments for migraine and other headache disorders that are already commercially available[45,46].

Presentation

Symptoms of painful TMD tend to present as recurrent (recurrent = 65%; persistent episode = 19% and single episode = 12% of incident cases), and the vast majority of incident painful TMD cases have both TMJ arthralgia and myalgia diagnoses (myalgia only = 23%; arthralgia only = 4% and both = 73%)[47]. Interestingly, 23% of incident cases described their TMD pain as 'headache only'[47]. Approximately 14% of painful TMD cases report moderate-to-severe limitation in usual activities due to their symptoms [grades IIb–IV in the Graded Chronic Pain Scale (GCPS)][18,47].

The presence of any RDC/TMD diagnosis in population-based studies of adults is associated with female gender [odds ratio (OR) = 2.2, 95% CI 1.9–2.7][48]. Chronic painful TMD (myalgia and/or arthralgia) is associated with older age (e.g. OR = 2.3, 95% CI 1.5–3.6, comparing individuals aged 35–44 years with 18–24 years)[49]. Children and adolescents with TMD are also more likely to be females, especially with increasing age[8,23]. In addition, female adolescents may present greater TMD pain impact (e.g. jaw functional limitation, school absences and analgesic consumption) compared with males with the same pain intensity[17]. Painful TMD cases in a population-based study of adults aged 20–49 years reported an average duration of symptoms of 6 years[18].

Painful and non-painful comorbid conditions such as headaches, neck and back pain, irritable bowel syndrome, insomnia, depression, anxiety and tinnitus are relatively common among both acute and chronic painful TMD cases in children, adolescents and adults[6,23,50]. Somatic awareness and increased pain sensitivity (including in non-trigeminal areas) are strongly associated with chronic painful TMD (standardised OR> 2.0)[28]. Weaker associations have also been identified between chronic painful TMD and autonomic function,[28] inflammatory markers[42] and endogenous pain modulation[28,51].

Diagnosis

In the past many different forms of TMD assessment have been proposed of which the most used were the Helkimo Index[52] and the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[53]. After many years of validating and revising the RDC/TMD, the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) has been proposed and is an evidence-based set of tools with which to diagnose TMD[54]. The DC/TMD offers a standardised and operationalised method to examine the masticatory structures physically (Axis I) and also to screen the presenting patient for psychosocial and comorbid factors (Axis II). The most important new part of the examination is confirmation that any pain elicited during examination is familiar, meaning that it reproduces or is similar to the pain that the patient experiences in their life and which was reported in the history section of the assessment.

Screening

For assessing the presence of painful TMD in a simple and reliable manner, the DC/TMD recommends the use of a screening questionnaire called the TMD Pain Screener[54,55]. Other validated TMD screeners such as the 3Q/TMD are also available[56,57]. Although these questionnaires do not allow for specific TMD diagnoses to be determined, a quick screening may be appropriate in busy clinical or research settings. Clinicians who are not trained in the DC/TMD examination protocol or do not have time to use it can use one of these brief assessments to inform their decision to refer patients to a colleague with orofacial pain training (Box 2).

Axis I

For more specific TMD diagnoses, the DC/TMD requires a physical examination[54]. This has been described in detail with the commands and procedures being validated in several different languages[58]. The 12 most common TMD diagnoses, most of which have established sensitivity and specificity, are as follows: myalgia (local myalgia, myofascial pain and myofascial pain with referral), arthralgia, four types of disc displacement disorders, degenerative joint disease, subluxation and headache attributed to TMD (Box 3)[54]. It is important to note that an individual may present with multiple simultaneous painful and/or non-painful TMD diagnoses[54]. An expanded version of the DC/TMD including less common TMD is also available[59]. It should be stated that sensitivity and specificity for most of the less common conditions have not yet been established.

Box 2. Examples of TMD screening instruments

TMD Pain Screener (short version)[55]

1. In the last 30 days, on average, how long did you have any pain in your jaw or temple area on either side last?
   a. No Pain
   b. From very brief to more than a week, but it does stop
   c. Continuous
2. In the last 30 days, have you had pain or stiffness in your jaw on awakening?
   a. No
   b. Yes
3. In the last 30 days, did the following activities change any pain (that is, make it better or make it worse) in your jaw or temple area on either side?
   A. Chewing hard or tough food
   a. No
   b. Yes

Scoring: 'a' responses = 0 points; 'b' responses = 1 point; 'c' response = 2 point.

Interpretation: A total sum of ≥ 2 points suggests need of further TMD evaluation.

3Q/TMD[56]

1. Do you have pain in your temple, face, jaw or jaw joint once a week or more?
   a. No
   b. Yes
2. Do you have pain once a week or more when you open your mouth or chew?
   a. No
   b. Yes
3. Does your jaw lock or become stuck once a week or more?
   a. No
   b. Yes

Scoring: Any affirmative answer yields a '3Q-positive' result.

Interpretation: 3Q-positive score suggests need of further TMD evaluation.

Axis II

Studies have shown that TMD patients present with a higher psychosocial burden[60–62] and frequency of comorbid conditions[60] than TMD-free individuals and that these conditions can lead to persistence and aggravation of TMD pain[26,63]. Consequently, it is important to assess these parameters when managing TMD patients, which can be done through validated instruments recommended in the Axis II of the DC/TMD. These instruments assess, among other things, pain behaviour, psychosocial status and functioning[54], which can highlight contributing factors and guide tailored treatment decisions[64]. Table 2 shows the recommended instruments for screening and for a comprehensive assessment. The comprehensive assessment is intended to be used by clinical specialists or researchers to obtain more details about psychosocial status and its possible role in the TMD presentation. The screening instruments may aid in determining the need for a comprehensive assessment or referral to colleagues with training in psychosocial aspects of health.

For example, Visscher *et al*. provide management recommendations for painful TMD patients based on three of the Axis II screening tools: Pain drawing (pain location), GCPS (pain intensity and disability) and PHQ-4 (psychological distress). Patients with localised pain, low GCPS (0-II) and low PHQ-4 (0-5) scores may be treated in primary care including pain education and self-management. Whereas, patients with widespread pain, a high GCPS score (III-IV), or a high PHQ-4 score (6-12), should be treated by an orofacial pain specialist in a multidisciplinary pain team.[64]

'Red flags' requiring special attention

Although common TMD are not life threatening, there are more significant or sinister clinical entities that may mimic common TMD and the clinician should be aware of 'red flags' that may suggest their presence (Table 3). One such example is temporal arteritis (giant cell arteritis) that may cause soreness and fatigue in the temple and jaw when chewing, as well as permanent vision loss; the 'red flags' would be jaw claudication with onset in an individual over 50 years of age, with possible induration of the temporal artery upon palpation and vision changes. If a more ominous reason for the patient's presenting symptoms is suspected, further diagnostic workup and/or referral to appropriate colleagues such as oral (and maxillofacial) surgeons, oral medicine specialists, ENT, neurologists or neurosurgeons is highly recommended.

Management

Given the complex biopsychosocial and multifactorial aetiology of TMD, treatment directed exclusively at local mechanical factors (e.g. jaw position) is not consistent with the current evidence. Instead, management should focus on addressing pain experience, jaw and psychosocial functioning. Given their poor correlation with pain, function, disability and prognosis[30], the presence of TMJ noises and intra-articular diagnoses (DD and/or DJD) should only guide treatment decision making in the presence of pain or clear functional impairment[65] (e.g. inability to open

Box 3. Overview of the most common Temporomandibular Disorders (TMD) diagnoses

Painful TMD

Myalgia† is pain in the masticatory muscles. It can be divided into the following subtypes:

- **Local myalgia** when felt only at the site of palpation.
- **Myofascial pain** when felt at the site of palpation and that in addition spreads beyond the site of palpation but remaining within the boundaries of the muscle.
- **Myofascial pain with referral** when felt at the site of palpation and in addition is felt beyond the boundary of the palpated muscle.

Arthralgia† is pain in the temporomandibular joint(s) (TMJ).

Headache attributed to TMD† is headache located in the temple region as a consequence of TMD-related pain.

†To receive one of the painful TMD diagnoses above, the pain complaint has to be replicated (familiar pain) during clinical examination by provocation tests such as palpation, jaw movement or jaw function.

Non-painful TMD

Disc displacement‡ (DD) is a biomechanical disorder involving the condyle-disc complex. It can occur in the following forms:

- **Disc displacement with reduction:** the disc is positioned anterior to the condyle in the closed mouth position and reduces when the mouth opens and the condyle translates forward. Clicking or popping may occur with disc displacement and/or reduction.
- When the disc positioned anterior to the condyle in the closed mouth position does not reduce with mouth opening, preventing the forward translation movement of the condyle, it can lead to intermittent locking (**Disc displacement with reduction with intermittent locking**) or persistent locking with or without limited mouth opening (**Disc displacement without reduction with or without limited opening**).

Degenerative joint disease‡ (DJD) is characterised by deterioration of articular tissue with concomitant osseous changes in the condyle and/or articular eminence. Crepitus may be detected upon clinical examination by TMJ palpation during mandibular movements.

Subluxation is a hypermobility disorder in which when the mouth is open the condyle-disc complex is positioned anterior to the articular eminence. Clinically, this prevents the patient from closing the mouth without a manipulative manoeuvre.

‡TMJ imaging is required for gold standard diagnoses of DD (magnetic resonance imaging [MRI]) and DJD (cone beam computed tomography [CBCT]), while history and clinical examination provide provisional diagnoses. Importantly, we argue for judicious use of resources and minimising exposure to radiation by weighing the need to rule out a 'red flag' and whether treatment would differ based on imaging findings.

mouth wide due to intermittent or persistent locking).

Education about the benign non-progressive nature of TMD and providing a clear diagnosis to patients, even if provisional, is encouraged at the first point of contact to reduce unnecessary suffering from uncertainty surrounding their symptoms[65]. Reversible conservative therapies are recommended as first line of treatment by international consensus based on the evidence for risks and benefits[66], and a large proportion of incident cases presenting as self-limiting and progress to remission within the first 6–15 months[34]. Multimodal strategies may be included in the treatment plan according to case complexity and contributing factors identified for each patient.

Reversible and conservative treatments

Self-care techniques

A TMD self-management programme may include identification, monitoring and avoidance of oral parafunctions (e.g. daytime clenching, nail biting and gum chewing), advice about sleep hygiene, limited caffeine consumption, pain-free diet, self-massage, therapeutic exercises, thermal therapy and relaxation techniques such as diaphragmatic breathing[67,68]. There are insufficient current data to suggest whether or not specific TMD diagnoses require modifications on self-management protocol[68]. In addition to initial management, these self-care strategies are also of utmost importance to provide patients with some autonomy to control their symptoms in recurrent TMD episodes or flare-ups.

Intraoral appliances

Several systematic reviews of the effects of occlusal appliances on TMD pain support that stabilisation splint (i.e. hard acrylic or soft polyethylene mouthguard providing full coverage of occlusal surfaces) worn on upper or lower teeth at night leads to short-term improvement when compared with no treatment, but evidence is inconclusive when compared with placebo (non-occluding palatal splint)[69]. In addition, stabilisation splints produced a similar improvement in TMD pain compared with physical therapy, behavioural medicine and acupuncture[69]. Partial coverage appliances such as the nociceptive trigeminal inhibition (NTI) and over the counter

Table 2 Summary of DC/TMD Axis II questionnaires for psychosocial assessment[54]

Assessment of	Instrument	Screening	Comprehensive
Pain intensity	Graded Chronic Pain Scale (GCPS)	X	X
Pain locations	Pain drawing	X	X
Physical function	Graded Chronic Pain Scale (GCPS)	X	X
Limitation	Jaw Functional Limitation Scale – short form (JFLS)	X	
	Jaw Functional Limitation Scale – long form (JFLS)		X
Distress	Patient Health Questionnaire – 4 (PHQ-4)	X	
Depression	Patient Health Questionnaire – 9 (PHQ-9)		X
Anxiety	Generalized Anxiety Disorder – 7 (GAD-7)		X
Physical symptoms	Patient Health Questionnaire – 15 (PHQ-15)		X
Parafunction	Oral Behaviors Checklist (OBC)	X	X

Table 3 'Red flags' that require special attention in the assessment of TMD/headache patients[†]

Red flag	Differential diagnoses to consider
History of malignancy	Malignancy recurrence
Presence of lymphadenopathy or neck masses	Neoplastic, infective or autoimmune cause
Sensory or motor function changes (specifically focusing on cranial nerves V, VII and VIII)	Intracranial causes or malignancy affecting the nerve's peripheral branches
Recurrent epistaxis, purulent nasal drainage or anosmia	Nasopharyngeal carcinoma or chronic sinusitis
Trismus	Oral malignancy
Unexplained fever, fatigue and weight loss	Malignant tumours, immunosuppression and infective causes
Facial asymmetry or masses	Neoplastic, infective or inflammatory causes
Occlusal changes	Growth disturbance of condyle, neoplasia, rheumatoid arthritis and traumatic causes
Ipsilateral objective change in hearing	Acoustic neuroma or other ear disease
Neurological symptoms (confusion, aphasia and dysarthria)	Artery dissection and intracranial haemorrhage
History of recent head and neck trauma	Arterial dissection and intracranial haemorrhage
Sudden onset headache	Subarachnoid haemorrhage
Postural or positional aggravation	Increased/decreased intracranial pressure (idiopathic intracranial hypertension and meningitis)
Onset> 50 years of age + jaw claudication	Temporal arteritis
Persisting or worsening symptoms despite treatment	Misdiagnosis or more complex case

[†]Adapted from Durham et al. 2015[65] and Cady 2014[44].

mouth-guards can be associated with adverse complications such as unwanted occlusal changes[69–71].

Pharmacotherapy

A systematic review with network meta-analysis of chronic orofacial pain supports the short-term (3 weeks) effectiveness of the muscle relaxant cyclobenzaprine for reducing TMD muscle pain. The review also indicated possible effects of topical Ping-On ointment and melatonin based on one study each[72]. In chronic TMD joint pain, there is evidence for non-steroidal anti-inflammatories (NSAIDs)[72].

Off-label use of neuromodulatory drugs such as tricyclic antidepressants, serotonin–noradrenaline reuptake inhibitors, benzodiazepines, gabapentin and pregabalin as well as lidocaine patches have been reported[73,74], especially for the management of more complex cases with persistent pain, comorbid conditions and/or with central sensitisation. However, the available evidence is mostly based on their use in other chronic pain conditions and potential mechanisms of action specific to TMD are not well understood[72,75]. Comorbid headaches, sleep disturbance and anxiety symptoms should also be considered in treatment selection[74]. Thorough evaluation of medical history should help prevent serious interactions with current medications or other known allergic reactions and complications.

Psychological and multimodal therapies

A systematic review and meta-analysis of the effect of cognitive behavioural therapy (CBT) suggest long-term (>3 months) improvements in TMD pain, depression and interference with activities compared with 'usual care' (education, counselling and an stabilisation splint), for CBT alone or in combination with biofeedback[76]. Patients with TMD pain and major psychological symptoms may obtain more improvement with multimodal treatment than patients with TMD disc displacement and pain without major psychological symptoms[69]. Biofeedback was found to be superior to active control and similar to relaxation training for reducing TMD pain[69], but did not add a significant benefit compared with CBT alone[76].

Physical therapy

Although clinical protocols for interventions and control groups vary, randomised clinical trials (RCTs) of jaw mobilisation or stretching exercises for TMD muscle pain suggest improvements in pain and jaw mobility compared with education and trans-cranial direct current stimulation, as well as improvements in pain compared with stabilisation splint[77]. RCTs of postural exercises suggest improvements in TMD muscle pain and jaw mobility compared with education and CBT[77].

For TMD joint pain, RCTs of jaw mobilisation or stretching exercises suggest improvements in pain and jaw mobility compared with no treatment and stabilisation splint[77]. Combinations of jaw strengthening and coordination exercises, and mobilisation and postural exercises improved joint pain and jaw mobility compared with education and stabilisation splint[77].

Acupuncture, dry needling and substance injection for TMD myalgia

A systematic review including four small RCTs of acupuncture (traditional, trigger point and laser) provides evidence for short-term improvement in TMD muscle pain compared with placebo acupuncture, as well as similar results to stabilisation splint[78]. Another systematic review and meta-analysis including 13 studies of TMD found improvements in TMD muscle pain for acupuncture compared with placebo (sham) acupuncture[79].

Although a meta-analysis could not be performed due to heterogeneity of studies, a systematic review found support for short-term improvements in TMD muscle pain for dry needling superior to false needling and to a combination of methocarbamol/paracetamol, but similar to local anaesthetic injections[80].

A systematic review with network meta-analysis revealed equivocal evidence for the effects of intramuscular botulinum toxin injections for TMD muscle pain compared with placebo injection[72]. Further studies are needed to determine its efficacy, safety and cost–benefit.

Irreversible and invasive treatments

In light of the biopsychosocial aetiology of TMD, its natural course and the success rates of reversible and conservative therapy, only a small minority of cases of chronic TMD pain **with** severe functional impairment may benefit from minimally invasive and invasive procedures. There are insufficient predictive tools for TMD prognosis and treatment efficacy[81], and failure of reversible and conservative treatments alone is **not** an indication to progress to irreversible and invasive approaches. In addition, as chronic TMD generally requires long-term symptom management of recurrent episodes, appropriate expectation setting is warranted.

Surgical treatments for TMJ intra-articular disorders (e.g. disc displacements and degenerative joint disease) and TMD arthralgia

One systematic review reported similar effects for arthrocentesis, arthroscopy and physical therapy on pain intensity, jaw mobility and function in patients with DD without reduction, while another systematic review reported similar effects for arthrocentesis, arthroscopy and discectomy[69]. Although some of these studies presented important methodological limitations, a more recent high-quality RCT corroborates these findings; Schiffman and colleagues found no additional effect of surgical interventions (arthroscopy and arthroplasty) on outcomes of DD without reduction with limited mouth opening compared with medical management or non-surgical rehabilitation[82]. There were no differences in TMJ pain intensity and frequency, mandibular range of motion, TMJ sounds or impairment of chewing at 3, 6, 12, 18, 24 and 60-month follow-ups[82].

One systematic review reported improvements in TMD joint pain for intra-articular injections of hyaluronic acid (HA) and corticosteroid compared with placebo injection[72], but there was no comparison to conservative management. There was no evidence for differences between HA or plasma rich in growth factors (PRGF), between low- or medium-weight HA, between one- or two-needle HA injection technique[72] or between arthrocentesis with or without HA[83].

Orthodontics and occlusal adjustments

There is no evidence for the efficacy of occlusal adjustment compared with placebo in TMD treatment or prevention, including therapeutic occlusal position or equilibration by orthopaedic, orthodontics or prosthodontics means[84]. Although occlusion is of evident functional importance to mastication and should be managed with care in dental practice[84], current evidence does not support a causal role in the pathophysiology of TMD[85].

Future directions

Prior to the early 2010s, most of what was known about TMD was based on cross-sectional, case-control or follow-up studies of prevalent TMD cases (i.e. including participants with TMD at study enrolment, regardless of duration as first onset). However, studies of prevalent cases tend to oversample individuals with longer TMD duration (i.e. chronic) resulting in length-biased sampling[86]. That is, the longer duration of chronic TMD cases makes them 'more available' for being observed at any one point in time, obscuring the early events of the disorder and potentially missing cases with more rapid resolution of symptoms. Accumulating evidence from studies of painful TMD incidence and follow-up of incident cases allow us to glean aetiological mechanisms and risk factors for the transition from acute to chronic painful TMD.

Future TMD aetiological research is bound to include more detailed evaluation of life stressors, rare genetic variants and genome-wide association studies (GWAS)[7]. Despite substantial progress in the understanding of biological and psychological determinants of painful TMD, the investigation of multilevel social and contextual factors has been lacking[6]. Evidence from the broader pain literature indicates that neighbourhood disadvantage is associated with the onset of chronic musculoskeletal pain after motor vehicle collision[87] and onset of disabling pain in older adults[88]. In addition, individual and neighbourhood social capital are associated with dental pain[89], psychosomatic symptoms, musculoskeletal pain and depression[90].

The International Classification of Orofacial Pain (ICOP), the first classification system for all orofacial pain disorders, including TMD, has been recently published.[91] Despite being a new classification, when it comes to TMD most of the criteria and the examination suggested in the ICOP are the same as for the validated DC/TMD.

Furthermore, as there has been some improvement in the understanding of the pathophysiology behind TMD and other pain disorders, future taxonomy will most likely begin to include a more mechanistic classification. This means that not only would the classification be divided into what type of pain disorder is present based on signs and symptoms, myalgia for example, but it will also include: the type of mechanism responsible for the myalgia such as peripheral and/or central sensitisation; the molecular target that is responsible for this specific mechanism, for example, CGRP or nerve growth factor[92]. Such improvements in diagnosis could clarify the substantial heterogeneity of prognosis and response to treatment within diagnostic categories observed in the current system. Upcoming research developments will likely support more precise risk prediction, treatment development and administration, allowing for different causal pathways to be addressed[93].

Conclusions

A new generation of painful TMD research is helping to clarify its natural history and prognosis, with clear indications that it goes beyond a localised 'jaw' disorder. Moreover, a stronger grasp of the complex multifactorial aetiology of painful TMD may lead to better prevention, diagnosis and treatment strategies directed at causal contributing factors and mechanisms. Current evidence supports the need for a biopsychosocial assessment including validated DC/TMD diagnostic instruments and primarily conservative multidisciplinary management strategies.

Acknowledgements

Research reported in this publication was supported by the National Institute of Dental and Craniofacial Research (NIDCR) of the National Institutes of Health under award number R90DE023059. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author contributions

JD contributed with overall study conceptualisation and design; FPK, FGE and JFOS reviewed the substantive literature and contributed to manuscript drafting; In addition, all authors provided critical review for intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. American Academy of Orofacial Pain. Guidelines for Assessment, Diagnosis, and Management, 6th edition (de Leeuw R, Klasser G, editors). Hanover Park, IL: Quintessence Publishing Co, Inc, 2018.
2. List T, Jensen RH. Temporomandibular disorders: old ideas and new concepts. Cephalalgia 2017;37:692–704.

3. Hoffmann RG, Kotchen JM, Kotchen TA, Cowley T, Dasgupta M, Cowley AW Jr. Temporomandibular disorders and associated clinical comorbidities. Clin J Pain 2011;27:268–74.
4. Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. Arch Intern Med 2000;160:221–7.
5. Maixner W, Fillingim RB, Williams DA, Smith SB, Slade GD. Overlapping Chronic pain conditions: implications for diagnosis and classification. J. Pain 2016;17:T93–107.
6. Bair E, Ohrbach R, Fillingim RB, Greenspan JD, Dubner R, Diatchenko L *et al*. Multivariable modeling of phenotypic risk factors for first-onset TMD: the OPPERA prospective cohort study. J Pain 2013;14: T102–15.
7. Slade GD, Fillingim RB, Sanders AE, Bair E, Greenspan JD, Ohrbach R *et al*. Summary of findings from the OPPERA prospective cohort study of incidence of first-onset temporomandibular disorder: implications and future directions. J Pain 2013;14:T116–24.
8. List T, Wahlund K, Wenneberg B, Dworkin SF. TMD in children and adolescents: prevalence of pain, gender differences, and perceived treatment need. J Orofac Pain 1999;13:9–20.
9. De Kanter RJAM, Truin GJ, Burgersdijk RCW, Van't Hop MA, Battistuzzi PGFCM, Kalsbeek H *et al*. Prevalence in the Dutch adult population and a meta-analysis of signs and symptoms of temporomandibular disorder. J Dent Res 1993;72:1509–18.
10. Durham J, Shen J, Breckons M, Steele JG, Araujo-Soares V, Exley C *et al*. Healthcare cost and impact of persistent orofacial pain. J Dent Res 2016;95:1147–54.
11. White BA, Williams LA, Leben JR. Health care utilization and cost among health maintenance organization members with temporomandibular disorders. J Orofac Pain 2001;15:158–69.
12. Dahlstrom L, Carlsson GE. Temporomandibular disorders and oral health-related quality of life. A systematic review. Acta Odontol Scand 2010;68:80–5.
13. Durham J, Breckons M, Araujo-Soares V, Exley C, Steele J, Vale L. Developing effective and efficient care pathways in chronic pain: DEEP study protocol. BMC Oral Health 2014;14:1–9.
14. Durham J, Steele JG, Wassell RW, Exley C. Living with uncertainty: temporomandibular disorders. J Dent Res 2010;89:827–30.
15. Slade GD, Sanders AE, Bair E, Brownstein N, Dampier D, Knott C *et al*. Preclinical episodes of orofacial pain symptoms and their association with health care behaviors in the OPPERA prospective cohort study. Pain 2013;154:750–60.
16. LeResche L, Mancl LA, Drangsholt MT, Huang G, Von Korff M. Predictors of onset of facial pain and temporomandibular disorders in early adolescence. Pain 2007;129:269–78.
17. Nilsson I-M. Reliability, validity, incidence and impact of temporormandibular pain disorders in adolescents. Swedish Dent J 2007;183:7–86.
18. Progiante PS, Pattussi MP, Lawrence HP, Goya S, Grossi PK, Grossi ML. Prevalence of temporomandibular disorders in an adult Brazilian community population using the research diagnostic criteria (Axes I and II) for temporomandibular disorders (The Maringá Study). Int J Prosthodont 2015;28: 600–9.
19. Türp JC, Schlenker A, Schröder J, Essig M, Schmitter M. Disk displacement, eccentric condylar position, osteoarthrosis - misnomers for variations of normality? Results and interpretations from an MRI study in two age cohorts. BMC Oral Health 2016;16:1–10.
20. Al-Jundi MA, John MT, Setz JM, Szentpétery A, Kuss O. Meta-analysis of treatment need for temporomandibular disorders in adult nonpatients. Heal Serv Needs Demand 2008;22:97–107.
21. de Sena MF, de Mesquita KSF, Santos FRR, Silva FWGP, Serrano KVD. Prevalence of temporomandibular dysfunction in children and adolescents. Rev Paul Pediatr 2014;31:538–45.
22. Vierola A, Suominen AL, Eloranta AM, Lintu N, Ikävalko T, Närhi M *et al*. Determinants for craniofacial pains in children 6–8 years of age: the PANIC study. Acta Odontol Scand 2017;75:453–60.
23. Casanova-Rosado JF, Medina-Solís CE, Vallejos-Sánchez AA, Casanova-Rosado AJ, Hernández-Prado B, Avila-Burgos L. Prevalence and associated factors for temporomandibular disorders in a group of Mexican adolescents and youth adults. Clin Oral Investig 2006;10:42–9.
24. Moyaho-Bernal A, Lara-Muñoz MDC, Espinosa-De Santillana I, Etchegoyen G. Prevalence of signs and symptoms of temporomandibular disorders in children in the State of Puebla, Mexico, evaluated with the research diagnostic criteria for temporomandibular disorders (RDC/TMD). Acta Odontol Latinoam 2010;23:228–33.
25. da Silva CG, Pachêco-Pereira C, Porporatti AL, Savi MG, Peres MA, Flores-Mir C *et al*. Prevalence of clinical signs of intra-articular temporomandibular disorders in children and adolescents. A systematic review and meta-analysis. J Am Dent Assoc 2016;147:10–8.e8.
26. Ohrbach R, Dworkin SF. Five-year outcomes in TMD: relationship of changes in pain to changes in physical and psychological variables. Pain 1998;74: 315–26.
27. Kapos FP, Look JO, Zhang L, Hodges JS, Schiffman EL. Predictors of long-term temporomandibular disorder pain intensity: An 8-year cohort study. J Oral Facial Pain Headache 2018;32:113–22.

28. Fillingim RB, Slade GD, Diatchenko L, Dubner R, Greenspan JD, Knott C *et al*. Summary of findings from the OPPERA baseline case-control study: implications and future directions. J Pain 2011;12:T102–7.
29. Greenspan JD, Slade GD, Bair E, Dubner R, Fillingim RB, Ohrbach R *et al*. Pain sensitivity and autonomic factors associated with development of TMD: the OPPERA prospective cohort study. J Pain 2013;14: T63–74.
30. Chantaracherd P, John MT, Hodges JS, Schiffman EL. Temporomandibular joint disorders' impact on pain, function, and disability. J Dent Res 2015; 94:79S–86S.
31. Schiffman EL, Ahmad M, Hollender L, Kartha K, Ohrbach R, Truelove EL *et al*. Longitudinal stability of common TMJ structural disorders. J Dent Res 2017;96:270–6.
32. Maixner W, Diatchenko L, Dubner R, Fillingim RB, Greenspan JD, Knott C *et al*. Orofacial pain prospective evaluation and risk assessment study – the OPPERA study. J Pain 2012;12: T4–11.e2.
33. Bair E, Gaynor S, Slade GD, Ohrbach R, Fillingim RB, Greenspan JD *et al*. Identification of clusters of individuals relevant to temporomandibular disorders and other chronic pain conditions: the OPPERA study. Pain 2016;157:1266–78.
34. Meloto CB, Slade GD, Lichtenwalter RN, Bair E, Rathnayaka N, Diatchenko L *et al*. Clinical predictors of persistent temporomandibular disorder in people with first-onset temporomandibular disorder: a prospective case-control study. J Am Dent Assoc 2019;150:572–81.e10.
35. Suvinen TI, Reade PC, Kemppainen P, Könönen M, Dworkin SF. Review of aetiological concepts of temporomandibular pain disorders: Towards a biopsychosocial model for integration of physical disorder factors with psychological and psychosocial illness impact factors. Eur J Pain 2005;9:613–33.
36. Smith SB, Mir E, Bair E, Slade GD, Dubner R, Fillingim RB *et al*. Genetic variants associated with development of TMD and its intermediate phenotypes: The genetic architecture of TMD in the OPPERA prospective cohort study. J. Pain 2013;14: T91–101.e3.
37. Diatchenko L, Slade GD, Nackley AG, Bhalang K, Sigurdsson A, Belfer I *et al*. Genetic basis for individual variations in pain perception and the development of a chronic pain condition. Hum Mol Genet 2005;14:135–43.
38. Meloto CB, Bortsov AV, Bair E, Helgeson E, Ostrom C, Smith SB *et al*. Modification of COMT-dependent pain sensitivity by psychological stress and sex. Pain 2016;157:858–67.
39. Light KC, Bragdon EE, Grewen KM, Brownley KA, Girdler SS, Maixner W. Adrenergic dysregulation and pain with and without acute beta- blockade in women with fibromyalgia and temporomandibular disorder. J Pain 2009;10:542–52.
40. Tchivileva IE, Lim PF, Smith SB, Slade GD, Diatchenko L, McLean SA *et al*. Effect of catechol-O-methyltransferase polymorphism on response to propranolol therapy in chronic musculoskeletal pain: a randomized, double-blind, placebo-controlled, crossover pilot study. Pharmacogenet Genomics 2010;20: 239–48.
41. Slade GD, Conrad MS, Diatchenko L, Rashid NU, Zhong S, Smith S *et al*. Cytokine biomarkers and chronic pain: association of genes, transcription, and circulating proteins with temporomandibular disorders and widespread palpation tenderness. Pain 2011;152:2802–12.
42. Harmon J, Sanders A, Wilder R, Essick G, Slade G, Hartung J *et al*. Circulating omentin-1 and chronic painful temporomandibular disorders. J Oral Facial Pain Headache 2016;30:203–9.
43. Kopp S. Neuroendocrine, immune, and local responses related to temporomandibular disorders. J Orofac Pain 2001;15:9–28.
44. Cady RJ, Glenn JR, Smith KM, Durham PL. Calcitonin gene-related peptide promotes cellular changes in trigeminal neurons and glia implicated in peripheral and central sensitization. Mol Pain 2011;7:94.
45. Tepper SJ. CGRP and headache: a brief review. Neurol Sci 2019;40:99–105.
46. Han L, Liu Y, Xiong H, Hong P. CGRP monoclonal antibody for preventive treatment of chronic migraine: an update of meta-analysis. Brain Behav 2019;9: 1–6.
47. Slade GD, Bair E, Greenspan JD, Dubner R, Fillingim RB, Diatchenko L *et al*. Signs and symptoms of first-onset TMD and sociodemographic predictors of its development: the OPPERA prospective cohort study. J. Pain 2013;14:T20–32.e3.
48. Bueno CH, Pereira DD, Pattussi MP, Grossi PK, Grossi ML. Gender differences in temporomandibular disorders in adult populational studies: a systematic review and meta-analysis. J Oral Rehabil 2018;45:720–9.
49. Slade GD, Bair E, By K, Mulkey F, Baraian C, Rothwell R *et al*. Study methods, recruitment, sociodemographic findings, and demographic representativeness in the OPPERA study. J Pain 2011;12: T12–26.
50. Vierola A, Suominen AL, Ikavalko T, Lintu N, Lindi V, Lakka HM *et al*. Clinical signs of temporomandibular disorders and various pain conditions among children 6 to 8 years of age: the PANIC study. J Orofac Pain 2012;26:17–25.
51. Moana-Filho EJ, Herrero Babiloni A, Theis-Mahon NR. Endogenous pain modulation in chronic orofacial pain. Pain 2018;159:1441–55.

52. Helkimo M. Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. Sven Tandlak Tidskr 1974;67:101–21.
53. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: review, criteria, examinations and specifications, critique. J Craniomandib Disord 1992;6:301–55.
54. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet J-P *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.
55. Gonzalez YM, Schiffman E, Gordon SM, Seago B, Truelove EL, Slade G *et al*. Development of a brief and effective temporomandibular disorder pain screening questionnaire: reliability and validity. J Am Dent Assoc 2011;142:1183–91.
56. Lövgren A, Visscher CM, Häggman-Henrikson B, Lobbezoo F, Marklund S, Wänman A. Validity of three screening questions (3Q/TMD) in relation to the DC/TMD. J Oral Rehabil 2016;43:729–36.
57. Lövgren A, Parvaneh H, Lobbezoo F, Häggman-Henrikson B, Wänman A, Visscher CM. Diagnostic accuracy of three screening questions (3Q/TMD) in relation to the DC/TMD in a specialized orofacial pain clinic. Acta Odontol Scand 2018;76:380–6.
58. Ohrbach R, Gonzalez Y, List T, Michelotti A, Schiffman E. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) Clinical Examination Protocol: Version January 6, 2014 [accessed 19 November 2017].
59. Peck CC, Goulet J-P, Lobbezoo F, Schiffman El, Alstergren P, Anderson GC *et al*. Expanding the taxonomy of the diagnostic criteria for temporomandibular disorders. J Oral Rehabil 2014;41:2–23.
60. Macfarlane TV, Gray RJM, Kincey J, Worthington HV. Factors associated with the temporomandibular disorder, pain dysfunction syndrome (PDS): Manchester case-control study. Oral Dis 2001;7(6):321–30.
61. Carlson CR, Okeson JP, Falace DA, Nitz AJ, Curran SL, Anderson D. Comparison of psychologic and physiologic functioning between patients with masticatory muscle pain and matched controls. J Orofac Pain 1993;7:15–22.
62. 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;38:765–72.
63. Garofalo JP, Gatchel RJ, Wesley AL, Ellis E 3rd. Predicting chronicity in acute temporomandibular joint disorders using the research diagnostic criteria. J Am Dent Assoc 1998;129:438–47.
64. Visscher CM, Baad-Hansen L, Durham J, Goulet JP, Michelotti A, Roldán BC. Benefits of implementing pain-related disability and psychological assessment in dental practice for patients with temporomandibular pain and other oral health conditions. J Am Dent Assoc 2018;149:422–31.
65. Durham J, Newton-John TRO, Zakrzewska J. Temporomandibular disorders. BMJ 2015;1154:1–9.
66. Greene CS. Managing the care of patients with temporomandibular disorders: a new guideline for care. J Am Dent Assoc 2010;141:1086–8.
67. Durham J, Aggarwal V, Davies SJ, Harrison SD, Jagger RG, Leeson R *et al*. Temporomandibular Disorders (TMDs): An Update and Management Guidance for Primary Care from the UK Specialist Interest Group in Orofacial Pain and TMDs (USOT). London, UK: Royal College of Surgeons, 2013.
68. Durham J, Al-Baghdadi M, Baad-Hansen L, Breckons M, Goulet JP, Lobbezoo F *et al*. Self-management programmes in temporomandibular disorders: results from an international Delphi process. J Oral Rehabil 2016;43:929–36.
69. List T, Axelsson S. Management of TMD: evidence from systematic reviews and meta-analyses. J Oral Rehabil. 2010;37:430–51.
70. Fricton J. Current evidence providing clarity in management of temporomandibular disorders: summary of a systematic review of randomized clinical trials for intra-oral appliances and occlusal therapies. J Evid Based Dent Pr. 2006;6:48–52.
71. Wassell RW, Verhees L, Lawrence K, Davies S, Lobbezoo F. Over-the-counter (OTC) bruxism splints available on the Internet. Br Dent J 2014;216:E24.
72. Häggman-Henrikson B, Alstergren P, Davidson T, Högestätt ED, Östlund P, Tranaeus S *et al*. Pharmacological treatment of oro-facial pain - health technology assessment including a systematic review with network meta-analysis. J Oral Rehabil 2017;44:800–26.
73. Mujakperuo HR, Watson M, Morrison R, Macfarlane TV. Pharmacological interventions for pain in patients with temporomandibular disorders. Cochrane Database Syst Rev 2010; Cd004715. https://doi.org/10.1002/14651858.CD004715.pub2
74. Haviv Y, Rettman A, Aframian D, Sharav Y, Benoliel R. Myofascial pain: an open study on the pharmacotherapeutic response to stepped treatment with tricyclic antidepressants and gabapentin. J Oral Facial Pain Headache 2015;29:144–51.
75. Cairns BE. Pathophysiology of TMD pain–basic mechanisms and their implications for pharmacotherapy. J Oral Rehabil 2010;37:391–410.
76. Aggarwal VR, Fu Y, Main CJ, Wu J. The effectiveness of self-management interventions in adults with chronic orofacial pain: a systematic review, meta-analysis and meta-regression. Eur J Pain 2019;23:849–65.

77. Shimada A, Ishigaki S, Matsuka Y, Komiyama O, Torisu T, Oono Y *et al*. Effects of exercise therapy on painful temporomandibular disorders. J Oral Rehabil 2019;46:475–81.
78. Fernandes AC, Duarte Moura DM, Da Silva LGD, De Almeida EO, Barbosa GAS. Acupuncture in temporomandibular disorder myofascial pain treatment: a systematic review. J Oral Facial Pain Headache 2017;31:225–32.
79. Yuan Q-L, Wang Peng, Liu Liang, Sun Fu, Cai Yongsong, Wu W-T *et al*. Acupuncture for musculoskeletal pain: a meta-analysis and meta-regression of sham-controlled randomized clinical trials. Sci Rep 2016;6:30675.
80. Machado E, Machado P, Wandscher VF, Marchionatti AME, Zanatta FB, Kaizer OB. A systematic review of different substance injection and dry needling for treatment of temporomandibular myofascial pain. Int J Oral Maxillofac Surg 2018;47:1420–32.
81. Ceusters W, Nasri-Heir C, Alnaas D, Cairns BE, Michelotti A, Ohrbach R. Perspectives on next steps in classification of oro-facial pain - Part 3: biomarkers of chronic oro-facial pain – from research to clinic. J Oral Rehabil 2015;42:956–66.
82. Schiffman EL, Velly AM, Look JO, Hodges JS, Swift JQ, Decker KL *et al*. Effects of four treatment strategies for temporomandibular joint closed lock. Int J Oral Maxillofac Surg 2014;43:217–26.
83. Ferreira N, Masterson D, Lopes de Lima R, de Souza MB, Oliveira AT, da Silva K *et al*. Efficacy of viscosupplementation with hyaluronic acid in temporomandibular disorders: a systematic review. J Craniomaxillofac Surg 2018;46:1943–52.
84. Manfredini D. Occlusal equilibration for the management of temporomandibular disorders. Oral Maxillofac Surg Clin North Am 2018;30:257–64.
85. Manfredini D, Lombardo L, Siciliani G. Temporomandibular disorders and dental occlusion. A systematic review of association studies: end of an era? J. Oral Rehabil. 2017;44:908–23.
86. Porta M. A Dictionary of Epidemiology. New York, NY: Oxford University Press, 2014:p166.
87. Ulirsch JC, Weaver MA, Bortsov AV, Soward AC, Swor RA, Peak DA *et al*. No man is an island: living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision, and this effect is moderated by common genetic variation influencing HPA axis function. Pain 2014;155:2116–23.
88. Jordan KP, Thomas E, Peat G, Wilkie R, Croft P. Social risks for disabling pain in older people: a prospective study of individual and area characteristics. Pain 2008;137:652–61.
89. Santiago BM, Valença AMG, Vettore MV. Social capital and dental pain in Brazilian northeast: a multilevel cross-sectional study. BMC Oral Health 2013;13.
90. Aslund C, Starrin B, Nilsson KW. Social capital in relation to depression, musculoskeletal pain, and psychosomatic symptoms: a cross-sectional study of a large population-based cohort of Swedish adolescents. BMC Public Health 2010;10:715.
91. International Classification of Orofacial Pain, 1st edition (ICOP). *Cephalalgia* 2020;40:129–221. https://doi.org/10.1177/0333102419893823
92. Vardeh D, Mannion RJ, Woolf CJ. Toward a mechanism-based approach to pain diagnosis. J Pain 2016;17:T50–69.
93. Slade GD, Ohrbach R, Greenspan JD, Fillingim RB, Bair E, Sanders AE *et al*. Painful temporomandibular disorder: decade of discovery from OPPERA studies. J Dent Res 2016;95:1084–92.
94. Sharma S, Wactawski-Wende J, LaMonte MJ, Zhao J, Slade GD, Bair E *et al*. Incident injury is strongly associated with subsequent incident temporomandibular disorder: results from the OPPERA study. Pain 2019;160:1551–61.
95. Tchivileva IE, Ohrbach R, Fillingim RB, Greenspan JD, Maixner W, Slade GD. Temporal change in headache and its contribution to risk of developing first-onset TMD in the OPPERA study. Pain 2017;158:120.