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Clinical Findings and Pain Symptoms as Potential Risk Factors for Chronic TMD: Descriptive Data and Empirically Identified Domains from the OPPERA Case-Control Study

Richard Ohrbach[*], **Roger B. Fillingim**[†], **Flora Mulkey**[‡], **Yoly Gonzalez**[*], **Sharon Gordon**[§], **Henry Gremillion**[¶], **Pei-Feng Lim**[‡], **Margarete Ribeiro-Dasilva**[#], **Joel D. Greenspan**[§], **Charles Knott**[‡], **William Maixner**[‡], and **Gary Slade**[‡]

[*]Department of Oral Diagnostic Sciences, University at Buffalo, State University of New York, Buffalo, New York [†]University of Florida, College of Dentistry, Gainesville, Florida, and North Florida/South Georgia Veterans Health System [‡]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina [§]Departments of Oral-Maxillofacial Surgery and Neural and Pain Sciences, and Brotman Facial Pain Center, University of Maryland Dental School, Baltimore, Maryland [¶]Louisiana State University Health Sciences Center School of Dentistry, New Orleans, Louisiana [#]Department of Community Dentistry and Behavioral Science, University of Florida, College of Dentistry, Gainesville, Florida [‡]Battelle Memorial Institute, Centers for Public Health Research and Evaluation, Columbus, Ohio

Abstract

Clinical characteristics might be associated with temporomandibular disorders (TMD) because they are antecedent risk factors that increase the likelihood of a healthy person developing the condition or because they represent signs or symptoms of either subclinical or overt TMD. In this baseline case-control study of the multisite Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) project, 1,633 controls and 185 cases with chronic, painful TMD completed questionnaires and received clinical examinations. Odds ratios measuring association between each clinical factor and TMD were computed, with adjustment for study-site as well as age, sex, and race/ethnicity. Compared to controls, TMD cases reported more trauma, greater parafunction, more headaches and other pain disorders, more functional limitation in using the jaw, more nonpain symptoms in the facial area, more temporomandibular joint noises and jaw locking, more neural or sensory medical conditions, and worse overall medical status. They also exhibited on examination reduced jaw mobility, more joint noises, and a greater number of painful masticatory, cervical, and body muscles upon palpation. The results indicated that TMD cases differ substantially from controls across almost all variables assessed. Future analyses of follow-up data will determine whether these clinical characteristics predict increased risk for developing first-onset pain-related TMD

Address reprint requests to Richard Ohrbach, DDS, PhD, Department of Oral Diagnostic Sciences University at Buffalo, Buffalo, NY 14214. ohrbach@buffalo.edu 1526-5900/$36.00.

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Supplementary Data
The supplementary data accompanying this article are available online at jpain.org and sciencedirect.com.

Perspective—Clinical findings from OPPERA's baseline case-control study indicate significant differences between chronic TMD cases and controls with respect to trauma history, parafunction, other pain disorders, health status, and clinical examination data. Future analyses will examine their contribution to TMD onset.

Keywords

TMD; chronic pain; trauma; parafunction; comorbid disorders; medical history; examination; pain

Temporomandibular disorders (TMD), a set of conditions affecting the masticatory muscles or joints and exhibiting pain as their primary characteristic, have historically been attributed to mechanisms related to dental or structural abnormalities, but with considerable controversy and little solid evidence.[12–14,34,89,90] Numerous psychological and behavioral factors are well-established influences upon a wide range of pain conditions including TMD pain.[20,22–27,42,66,83,91,100] Genetics and sensory processing also contribute to the etiology of TMD and other forms of chronic pain. [17–19,54,79] The abundance of data in support of psychological, genetic, and sensory processing factors within TMDs stands in sharp contrast to the far fewer reports of associations between TMD and factors which can be readily identified during clinical assessment, such as trauma, oral behaviors, and masticatory system status.

The scientific rationale for the project Orofacial Pain: Prosepctive Evaluation and Risk Assessment (OPPERA) is depicted in a heuristic model[53] in which clinical characteristics range from historical experiences (eg, trauma due to injury occurring before onset of TMD) to clinical manifestations that might represent signs or symptoms of subclinical TMD (eg, slightly limited jaw opening). Other relevant clinical characteristics form part of the case-classification for TMD (eg, orofacial pain during jaw movement) or represent consequences of experiencing the condition (eg, restriction in daily activities due to facial pain). However, for many other characteristics commonly assessed in clinical settings, it is far from clear whether they are an antecedent that increases the likelihood of developing the condition or are a consequence of the condition iteself. For example, parafunctional jaw behaviors are very likely both a cause and a consequence of TMD.[57]

In this paper, the term "risk factor" is used broadly to represent both etiologic events or experiences prior to onset of TMD as well as contributory events or experiences that occur in parallel with the onset of TMD or exacerbation of TMD symptoms. Despite the advances in the recognized factors of genetics, sensory processing, psychology, and behavior as contributing to TMD pain, no single risk factor for developing TMD has been identified as a necessary or sufficient cause. Hence, there is no causal smoking gun for TMD and, given the complexity of the conditions, it seems unlikely that one will emerge. Instead, multiple factors affect the masticatory system and pain perception, either as independent or interacting causal influences. This is consistent with virtually all major chronic diseases where the view of a multifactorial "web of causation" has long been used as a metaphor to describe the interplay of multiple risk factors on the occurrence of disease.[45]

Plausible risk factors for TMD which might be sufficient, either alone or more likely in combination, include: trauma, parafunction, other pain conditions or functional disorders, self-reported history of pain symptoms, pain reported in response to examination procedures, anthropometric variables, and health status. Many, if not most, of these proposed risk factors have been at least mentioned in the literature; but as of 1991, almost nothing was known about these factors in terms of their potential causal role for TMDs[89] and, to date, only modest progress has occurred.[80,87,98]

This paper reports findings from the OPPERA baseline case-control study, a component study examining chronic TMD within OPPERA. The aim of this paper was to characterize univariate differences in these clinical risk factors between people classified with chronic TMD arthralgia, myalgia, or both ("TMD cases") and people who had neither of those conditions ("controls") when examined. In order to accomplish this aim, a set of clinical assessment tools was applied to TMD cases and controls. The analyses presented here will serve as the foundation for future analysis of first-onset TMD that is being identified through longitudinal follow-up of the cohort of initially TMD-free controls.

Methods

Study Setting and Participants

As described elsewhere,[82] the OPPERA baseline case-control study used advertisements, emails, flyers, and word of mouth to recruit people who had chronic TMD ("cases") and people who did not ("controls"). For both groups, as described in the accompanying paper,[82] fewer than 10% reported hearing about OPPERA through research clinics; the majority heard either by word of mouth or from advertisements, flyers and emails. They were recruited between May 2006 and November 2008 from communities in and around academic health centers at 4 US study sites: Baltimore, MD; Buffalo, NY; Chapel Hill, NC; and Gainesville, FL. At each study site, the goal was to recruit 800 controls and variable numbers of cases based on local operational requirements, for a total of 3,200 controls and 200 cases. The actual number enrolled was 3,263 controls and 185 cases.

The classification of TMD was based on the Research Diagnostic Criteria for Temporomandibular Disorder.[21] In summary, cases met all 3 of the following criteria: during the telephone interview, 1) pain reported with sufficient frequency in the cheeks, jaw muscles, temples, or jaw joints during the preceding 6 months (at least 15 days in the preceding month and at least 5 days per month in each of the 5 months preceding that); during the examination, 2) pain reported in the examiner-defined orofacial region for at least 5 days out of the prior 30 days; and 3) pain reported in at least 3 masticatory muscles or at least 1 temporomandibular joint in response to palpation of the orofacial muscles or maneuver of the jaw. Examiners defined the orofacial region by touching the following anatomical areas bilaterally: temporalis, preauricular, masseter, posterior mandibular, and submandibular.

Chronic pain for the cases was defined as pain present for at least 6 months. We used a 6-month threshold as the time criterion to define chronic TMD, consistent with the 1994 IASP (page xi) recommended threshold for research in chronic pain, "pain which persists beyond the normal time of healing (Bonica, 1953) [which] may be less than one month, or more often, more than six months. With nonmalignant pain, three months is the most convenient point of division between acute and chronic pain, but for research purposes, six months will often be preferred."[62] In summary, case status was assigned on the basis of facial pain for at least the preceding 6 months including at least 5 days during the preceding month, and sufficient positive findings on examination.

Controls met all 6 of the following criteria: during the telephone interview, 1) pain reported infrequently in the cheeks, jaw muscles, temples or jaw joints (no orofacial pain in the preceding month and no more than 4 days per month in any of the 5 months preceding that); 2) no more than 4 headaches per month within the preceding 3 months; 3) having never been diagnosed with TMD; 4) no use of night guard occlusal splint; and during the examination, 5) pain reported in the examiner-defined orofacial region for no more than 4 days in the prior 30 days; and 6) classified as having neither myalgia nor arthralgia. However, controls could be positive or negative with respect to pain in response to palpation or jaw maneuver.

In summary, control status was assigned on the basis of infrequent report of facial pain during the preceding 6 months and infrequent headache during the preceding 3 months, no prior diagnosis of TMD or use of night guard, and no more than 4 days of facial pain in the preceding 1 month and thus not meeting 1 of the necessary criteria for either a myalgia or arthralgia diagnosis.

Additional studywide criteria required that all study participants were aged 18 to 44 years, fluent in English, not receiving orthodontic treatment, and not pregnant or nursing, and had negative responses to each of 10 questions regarding significant medical conditions and no history of facial injury or surgery.

This analysis uses data from all 185 recruited TMD cases and one-half of the 3,263 recruited controls (1,633 people). The controls for this analysis were selected at random so that data from people in the reserved sample could be used for validation studies that will be reported elsewhere. The accompanying paper[82] gives a more detailed account of study recruitment, case-classification methods, and inclusion and exclusion criteria.

Ethical Conduct of Research With Humans

The OPPERA study was reviewed and approved by institutional review boards at each of the 4 study sites and at the data-coordinating center (Battelle offices in NC). All study participants verbally agreed to a screening interview done by telephone and they provided informed, signed consent for all other study procedures.

Study Measures

Data about putative phenotypic risk factors were collected by self-administered psychological and clinical symptom questionnaires, physical examination, and quantitative sensory testing of responses to standardized noxious stimuli; these variables are described in more detail in other papers.[28,35,55] DNA extracted from blood samples collected at enrollment in order to provide information about putative genetic risk factors is described in greater detail elsewhere.[85] This paper focuses on questionnaire and examination data that quantify behaviors, symptoms, and signs of TMD that typically are considered in clinical settings when evaluating patients.

Measures collected in this study assessed trauma, parafunctional behaviors, other pain or functional disorders, diverse symptoms, clinical signs recorded during examination, anthropometric measures, and medical history. These data were collected using self-administered instruments, structured interview, and calibrated clinical examination procedures. The questionnaires and data collection forms developed for this study and reported in this paper are shown in Appendix A. The self-administered instruments consisted of: Comprehensive Pain and Symptom Questionnaire (CPSQ) which included the Graded Chronic Pain Scale (GCPS), Jaw Functional Limitation Scale (JFLS), Oral Behaviors Checklist (OBC), and medical history form. The Anthropomorphic Form (APM) was completed by study staff after measuring the participant. An examiner-completed form (OPPERA RDC Examination) contained the clinical examination data. An ongoing study is assessing the psychometric properties of the CPSQ and the results will be published separately. Most items from these instruments are reported in this paper; items deemed to be derivative or which represented a secondary level of detail are not reported here.

The CPSQ and OBC were completed by 1,626 controls and 185 cases. The JFLS was completed by 1,625 controls and 185 cases. The medical symptom checklist was completed by 1,633 controls and 185 cases. The APM instrument provided data for 1,627 controls and 185 cases; the form was missing for 6 controls. Examination data were recorded for all 1,633 controls and 185 cases.

Putative Etiologic Factors

Lifetime History of Regional Trauma—This was assessed using a checklist of potentially traumatic experiences, followed by a single question asking if any of those experiences had caused injury (see CPSQ Q33, Appendix A). For this paper, a binary, summary measure was computed to signify whether or not participants reported injury following 1 or more of 5 experiences: wisdom tooth extraction or other dental treatment; oral intubation; significant bump to the jaw; motor vehicle accident; or accident resulting in whiplash. Two other binary variables signified lifetime history of injury by yawning and by prolonged mouth opening (CPSQ Q34), and history of orthodontic procedures (CPSQ Q35).

Parafunctional Behaviors—The OBC[59,64] assesses the self-reported frequency over the preceding month of each of 21 activities involving the jaw such as clenching the teeth or bracing the jaw (5 ordinal response options, ranging from “none of the time,” coded 0, to “all of the time,” coded 4). Evaluations of this instrument suggest that it is valid, with terminology corresponding to the behaviors that are reliable and the recalled behaviors matching those measured using Ecological Momentary Assessment approaches.[59,64,69] An ordinal summary measure was computed based on adding the coded, ordinal responses to each of the 21 activities, and this was reduced to 4 categories using tertiles. More detailed data and alternate scoring will be available in a forthcoming manuscript.

Overlapping Conditions: Other Pain or Functional Disorders—Participants were asked about headaches in the prior year and number of headache types (CPSQ Q36, Q38) as a simple summary measure of headache severity for initial characterization. Participants were asked about presence of significant pains in the body other than the face (CPSQ Q42), current back pain (CPSQ Q51A), and number of back pain episodes in the past 12 months (CPSQ Q51C). An ordinal summary measure was computed based on a 20-item checklist of general symptoms such as joint disease, ringing in the ears, and acid reflux (CPSQ Q50). An ordinal summary measure was computed based on 4 abdominal pain questions adhering to the Rome III IBS criteria for irritable bowel syndrome (IBS; CPSQ Q52).[51] An ordinal summary measure was computed based on a 10-item checklist pertaining to bowel function (CPSQ Q53). A binary summary measure of genital symptoms was computed based on a presence of genital pain on contact (CPSQ Q57) but absence of genital itching (CPSQ Q54), consistent with self-reported criteria used in assessing vulvodynia.[5]

Clinical Status by Self-Report

Pain and Disability: Participants rated their facial pain and interference in functioning due to pain using the GCPS (CPSQ Q9-15, not 12A). The GCPS has been validated and exhibits good psychometric properties based on a large population survey and in large samples of primary care patients with pain.[94,95] More recently, the GCPS classification has demonstrated excellent reliability (Kappa = .87) and validity using TMD subjects.[70] The variables contribute to the chronic pain grade: 1) the characteristic pain intensity is the mean, multiplied by 10, of the 3 pain items (Q9-11);[24,94,95] 2) the pain-related activity interference score is the mean, multiplied by 10, of the 3 pain interference items (Q13-15);[94] and 3) participants reported the number of days of significant activity limitation due to pain in the past 6 months. Based on these 3 variables, individuals are classified into 6 chronic pain grades: 0 = no pain; I = low pain intensity and low pain-related disability; IIa = high pain intensity and low pain-related disability; IIb = high pain intensity and high activity interference; III = moderate pain-related disability; and IV = severe pain-related disability. “Disability” is a function of both high activity interference and high number of days of limited activity. Participants also reported the number of days that their efficiency had been reduced to less than 50% (CPSQ Q12A).

Modifying Factors: Factors that modify jaw pain (make it better or worse), for example, opening the jaw or yawning, were assessed with a 5-item checklist (CPSQ Q8), and an ordinal summary measure was computed for the number of activities modifying pain.

Limitations in Using the Jaw: Limitations were reported with the Jaw Functional Limitation Scale (JFLS), a 1-page, self-administered 20-item instrument that measures limitations across 3 domains: mastication, vertical jaw mobility, and verbal and emotional expression.[67,68] Reliability of the instrument is .87 (Cronbach's alpha) and .87 (temporal stability), while validity, as assessed via known groups comparison, is excellent. A response scale used 0 to 10 signifying degree of limitation (0 = "no limitation" and 10 = "severe limitation"); an option for "not applicable" is also available, and was scored as "missing." The subscales are computed as the mean response for all items in the subscale. Mastication is based on 6 items, vertical jaw mobility is based on 4 items, and verbal and emotional expression is based on 8 items; 2 items are not scored as part of these 3 subscales. A total score is also computed from the 3 subscales when all 3 component scores are available. The JFLS was designed based on item response theory, and consequently identical non-zero responses to all items within a subscale are highly improbable; non-zero responses that were the same within a subscale were regarded as invalid and recoded to "missing."

Five cases and 42 controls had invalid responses (ie, blank, "not applicable," or invalid response patterns) for 10 or more JFLS items, and those people were excluded from further analysis of JFLS data. For the remaining 1,763 people, an unimputed summary score was computed when there were no missing items for that measure. For the 45 cases and 255 controls who had between 1 and 9 missing values from among the 19 JFLS items, missing values value were imputed from non-missing JFLS items as described below. The imputed data were added to the unimputed data for 135 cases and 1,331 controls who responded to all JFLS items, yielding an imputed dataset of 1,763 individuals.

Non-Pain Symptoms: Symptoms that may represent subthreshold pain experience or act as a substitute for pain were assessed over the past month with a 6-item checklist (CPSQ Q1); for this paper, an ordinal summary measure was computed regarding reports of stiffness, cramping, fatigue, pressure, soreness, and ache.

Temporomandibular Joint (TMJ) Clicking and Locking: The symptoms of temporomandibular joint noises, pain with those noises, and locking open or closed were assessed for the past month and for the period prior to the past month (CPSQ Q17-19, Q21, Q25, Q27, Q30).

Clinical Status by Examination—Examiners, trained according to RDC/TMD specifications,[21,75] collected clinical measures using physical assessments and structured interviews to determine whether jaw maneuvers produced pain and the anatomical location of the pain. The examination protocol was inclusive of the RDC/TMD protocol content but also included additional procedures. Their reliability in classifying TMD case status is summarized elsewhere.[82]

Jaw Mobility: Six jaw movements were assessed: pain-free opening; maximum unassisted opening; maximum assisted opening (when the examiner used moderate digital pressure to increase the degree of opening, if possible); left lateral excursion; right lateral excursion; and protrusion. When pain was reported during any of those movements (except for pain-free opening), examiners asked about its location and classified it into 1 or more of 10 muscle/joint groups, each assessed bilaterally: temporalis, masseter, lateral pterygoid area, posterior mandibular and submandibular area, and TMJ. The assignment of location was based on where the participant pointed; if inside the mouth at the superior lateral areas, the

location was “lateral pterygoid area;” if the location was overlying the TMJ and masseter area, the examiner used muscle contraction and joint movement to discriminate muscle versus joint versus both; and for all other areas, the assignment was based on the area pointed to.

Vertical range of motion, including vertical incisal overlap, was measured with a ruler according to instructions for maximum movement without pain (pain-free opening), maximum movement even if there was pain (maximum unassisted opening), and maximum movement as assisted by the examiner (maximum assisted opening). For the latter 2 measures, presence of pain was assessed as well as the location. As part of the maximum opening with assistance procedure, participants were instructed to indicate if they wanted the procedure to be terminated for any reason; the results were stratified according to whether the maximum opening procedure was terminated. The participant was instructed to move the jaw as much as possible, even if it was painful, to the left, right, and forward; each movement was measured with a ruler, and presence and location of pain was recorded.

TMJ Noises: Joint sounds from the TMJ were detected and recorded as follows. The examiner placed his or her fingers over the TMJ on the right side, and then on the left side, and felt for joint noises (click, crepitus) during opening and during closing.

Palpation Pain: The examiners calibrated their finger-tips with a hand algometer (Wagner Model FPK, 0–5 lb, Greenwich, CT) for each designated magnitude, in turn, as required during the exam. The calibrated finger was used to then apply pressure, over a 2-second period, at each location. The muscles of mastication and TMJ were palpated with finger pressure. Both the temporalis and masseter on each side were divided into 9 sections, and each section was palpated with a finger tip using the 2-lb (approximately 1 kg) magnitude. The temporalis was also examined intra-orally at the tendon using digital pressure at the 1-lb (approximately .5 kg) magnitude. To assess the masseter intra-orally, the examiner’s finger was placed between the buccal surfaces of the teeth and the cheek, and the participant was asked to clench firmly such that the masseter muscle pressed against the finger. The posterior mandibular and submandibular regions were palpated using the 1-lb magnitude. The lateral pterygoid muscle was palpated using the 1-lb magnitude. The TMJ was palpated at 3 locations: lateral pole, posterior attachment (via the external acoustic meatus), and dorsal aspect (with 25–30 mm of jaw opening); a magnitude of 1 lb was applied at each location. Any reports of pain in response to palpation was classified into the same 5 muscle/joint groups used to classify pain in response to jaw movement: temporalis, masseter, lateral pterygoid, submandibular, and TMJ.

The neck was examined on each of the right and left sides using 2 lbs of pressure for palpation at the following locations: upper, middle, and lower areas of the sternocleidomastoid muscle; upper, mid, and lower splenius capitus; and upper semispinalis capitus. The body was examined using 3 lbs of pressure for palpation at the following locations: middle part of upper belly of trapezius, supraspinatus, second rib, lateral epicondyle, medial gluteus, greater trochanter, and medial knee. This examination was intended to follow that used as part of the fibromyalgia examination.[99] Positive or negative pain responses were recorded.

Tooth Wear: Wear of the edges of the teeth, as generally found with bruxism, were assessed in 3 locations: incisors and the cuspids/bicuspids on each side. Wear at each of the 3 locations was recorded as positive if clear contact of at least 2 mm in length was evident between opposing tooth edges. The number of such areas (range: 0–3) was computed for this paper.

Anthropometric status—Weight (kg) and height (m) were measured using, respectively, a commercial scale and attached stadiometer (Seca 703; Seca North America East Medical Scales and Measuring Devices, Hanover, MD) and used to compute body mass index (BMI). Finger lengths of the index and ring fingers were measured to obtain an index of the ratio between the 2 fingers, as follows: the crease at the ventral base of each targeted finger was marked with a black pen, the ventral surface of each hand, in turn, was placed on the glass plate of an optical scanner. The scanned image was printed on paper, from which distances between the mark at the crease and the finger tip were measured with a digital caliper (Chicago Brand 6" Electronic Digital Caliper, .001" resolution; Chicago Brand Industrial, Inc, Fremont, CA). Later, a separate individual repeated the measurements using the same hardcopy in order to ensure reliable measurement. The ratios of the index finger (2D) to the ring finger (4D) from the 2 sets of measures were averaged to create 1, 2D:4D ratio measure for each hand.

Health Status—Health status was assessed with a checklist inquiring into past or current conditions (see Medical History Form, Appendix A). For this paper, a binary, summary measure was computed to signify whether or not participants reported 1 or more disorders among each of: 1) endocrine conditions (diabetes, hypothyroid disease, hyperthyroid disease); 2) cardiovascular conditions (mitral valve prolapse, high blood pressure, angina, heart attack, heart failure, pacemaker/defibrillator, stroke); 3) hematologic conditions (anemia, bleeding disorder, leukemia); 4) neural and sensory (earache or ringing in the ear, hearing loss, fainting or dizzy spells, epilepsy, seizures, or convulsions); and 5) respiratory conditions (sinus trouble, allergies or hives, asthma, tuberculosis, or breathing difficulties). A binary response was used for each of 4 single disorders of: 1) sleep apnea; 2) osteoarthritis; 3) rheumatoid arthritis; and 4) Sjogren's Syndrome. Tobacco use was computed from 4 questions: smoked 100 cigarettes in entire life, age of first tobacco use, current use, and age of first regular tobacco use. Participants were asked to describe overall health, and to report whether they had ever been hospitalized for any surgical operation or serious illness. An ordinal summary measure was computed based on reported prior use of 11 medications.

Statistical Methods—The primary analysis is the comparison of cases versus controls. As described in Results, a small number of the individuals who met our inclusion and exclusion criteria for recruitment into the study as controls reported low-level regional pain symptoms within the 6-month period prior to enrollment. For the case-control analysis, it is important to retain these individuals with subclinical conditions, because their exclusion produces estimates of association that are biased away from the null.[72]

Missing data were imputed using the expectation-maximization method in SAS procedure MI for summary scores derived from multiple-item scales such as the JFLS and as described elsewhere.[82] However, no imputation was done for individual items or from measures computed from small numbers of items (eg, characteristic pain intensity) because there were no clear grounds for selecting the additional variables that would be needed to impute such items.

Descriptive statistics for each summary score were generated. Statistical significance of differences in mean scores was evaluated using the F-test derived from a least squares general linear model in which study site was a covariate. Study site was used as a covariate because operational requirements during recruitment created different proportions of cases among sites.

Summary scores were coded such that the reference category represented the healthiest state (eg., no pain, no joint locking, no medical conditions). The relationship between each

summary score and occurrence of TMD was expressed as the odds ratio, calculated from an unconditional, binary logistic regression model and the study site was a covariate. For continuous measures, the summary score was transformed to a unit-normal deviate. The transformation meant that odds ratios for continuous measures could be interpreted as the relative change in odds of TMD for each standard deviation of change in the summary score. For the majority of measures which are reported categorically, odds ratios represent conventional exposure odds ratios for case-control studies. A second logistic regression model generated a fully adjusted estimate of the relationship, using additional covariates of age (in years), gender, and race/ethnicity (dichotomized as white or non-white). For imputed measures from raw continuous data, a third logistic regression model using the imputed dataset calculated standardized odds ratios for each summary score among selected variables, as described above, with adjustment for study site, age, gender, and race/ ethnicity (as previously described).

All *P* values were computed without adjustment for multiple tests, and we therefore refrain from designating $P = .05$ as a threshold for statistical significance. In this paper's case-control analysis, 71 factors were investigated and therefore Bonferroni correction for the probability of type I error would yield a critical *P* value of .05/ 71 = .0007. Using the same rationale, rejection of the null hypothesis concerning odds ratios would occur only if the 99.93% confidence interval excluded the null value of 1. The smaller number of cases was the primary determinant of statistical power. As described in an accompanying paper,[82] there was sufficient power of 80% to detect ratios as small as 1.7 with exposure prevalence as low as 15%, and for continuous predictors, the minimum detectable standardized odds ratio was 1.25.

In general, though, drawing conclusions about statistical significance of associations is avoided, even with correction for multiple tests, because these papers report only univariate- or demographically-adjusted results. Furthermore, the Bonferroni adjustment is probably overly conservative in this setting, where several measures are moderately correlated. Instead, judgments about statistical significance will be reserved for subsequent papers that will use multivariable modeling to consider multiple characteristics simultaneously, as proposed in the OPPERA heuristic model. [53]

Results

Sociodemographic characteristics of this study sample are presented elsewhere in this compendium.[82] Only 10% of TMD cases had arthralgia alone and 5% had myalgia alone, while the remainder of the cases exhibited both myalgia and arthralgia; consequently, the case-control comparisons to follow are strongly influenced by the presence of both conditions within the cases. A study-site adjusted odds ratios (OR) was considered to be meaningful if it was less than .5 or greater than 2.0. In the text that follows, ORs are reported only if particular attention is warranted or if adjustment for sociodemographic characteristics produced substantial change in the fully adjusted OR or confidence interval (CI). Otherwise, the effect is considered stable and the ORs are available in the respective tables and not reproduced in the text.

Putative Etiologic Factors

TMD cases reported a greater occurrence of events causing injury to the jaw (Table 1), including jaw injury due to yawning or prolonged opening. History of orthodontic procedures was more common among TMD, with OR = 1.9, decreasing to 1.4 with adjustment. Parafunctional and overuse behaviors were more common among TMD cases primarily among the highest tertile.

Overlapping Conditions: Other Pain or Functional Disorders

TMD cases were more likely to report a headache (of any type) and more types of headache, compared to controls (Table 2). TMD cases reported more chronic pain elsewhere in the body, more current back pain, a greater number of back pain episodes in the past year, more functional disorder-related symptoms, and a greater number of Irritable Bowel Syndrome symptoms, and they met the Rome criteria for IBS more often, compared to controls. TMD cases were more likely to report genital symptoms than controls, although the adjusted effect was not significant.

Clinical Status by Self-Report

TMD cases registered higher characteristic pain intensity associated with the facial and jaw area, compared to the 247 controls who reported regional lifetime pain (Table 3); this result should be interpreted only as demonstrating that the cases reported regional pain as expected while the controls were, due to selection criteria, largely pain free. Even for those who reported pain, it was less than 5 days of pain in the past month (per stringent examination criteria) and clearly of a substantially lower intensity (mean 15.7 for those controls reporting pain versus mean 51.8 for cases). TMD cases also reported more interference from the pain in work, home, and recreation, compared to the controls who had pain, with SOR = 2.8. TMD cases registered a mean number of 20.1 days over the prior 6 months when their efficiency dropped below 50%, in contrast to the controls who registered a mean 3.2 days. Among TMD cases, 75% reported low-to-high pain with no interference and 25% reported problems in functioning, ranging from high interference to disability (Table 4); in contrast, only 7% of of the 160 controls reporting regional pain also reported any degree of interference or disability of the jaw. Among all controls, the number of individuals reporting interference or disability associated with any regional pain represented .7%.

TMD cases registered mean scores for limitation in mastication or opening of the jaw of approximately 2.0, contrasting with controls whose mean scores were less than .3 (Table 3). TMD cases also reported more limitation in verbal and emotional expression compared to controls, but the effect was smaller.

TMD cases reported more often than controls that their pain was modified by jaw function in the past month; only 22 of the cases reported 0 to 1 modifying activities and the remainder reported 2 to 5 modifying activities (Table 4). Only 54 controls responded to this question, compared to 247 controls reporting lifetime jaw-area pain and 160 controls reporting any pain in the prior 6 months. Among these 54 controls, half were in the reference category of 0 to 1 modifying activities.

TMD cases also reported nonpain symptoms such as stiffness or cramping at a much higher rate compared to controls, with 92.4% of cases reporting 3 or more such symptoms compared to only 4.8% of controls (Table 4). The computed OR = 294, with exceptionally wide CIs, is interesting and significant but obviously not a precise estimate.

Among TMD cases, 89% reported noises (click, crepitus) in either TMJ in the previous month, compared to only 19% of controls (Table 5). Pain associated with the TMJ noise was common among TMD cases (67%) and rare among controls (2%). The rates of reporting TMJ noise in the past month wereconsistent for the periodof time prior to the past month. In the past month, inability to open the mouth widely (on at least 1 occasion) was reported by 41% of TMD cases compared to only 2.2% of controls. In the past month, inability to close the jaw from a wide-open position (on at least 1 occasion) was reported by 25% of TMD cases compared to only 2.2% of controls.

Clinical Status by Examination

Across the measures of jaw opening, where a smaller value denotes greater problems, TMD cases exhibited significantly less mobility, on average, for each of the measures as compared to controls (Table 6). Mean pain-free opening was 12 mm less in TMD cases compared to controls, and for maximum unassisted opening the mean difference was 6 mm. Maximum assisted opening was stratified into those who did versus did not terminate the procedure. Among controls, the number of people who terminated the procedure was one-fourth the number who did not (347/1,260) whereas among TMD cases the ratio was one-half (62/121). Among people who did not terminate the procedure, the mean difference between TMD cases and controls was 4.5 mm, and the difference was very similar (4.1 mm) among people who did terminate the procedure. The SORs comparing maximum assisted opening for TMD versus controls were remarkably similar at .6.

TMD cases were far more likely to report pain with maximum unassisted opening (Table 7). TMD cases were even more likely to report pain with unterminated maximum assisted opening. Among the participants who terminated the maximum assisted opening procedure, 95% of cases and 76% of controls reported pain; note, however, that the CIs were quite wide for this variable.

Around 60% of TMD cases and 30% of controls reported noises in either TMJ.

Experience of pain during palpation of masticatory muscle was very similar for each of right and left side, within each case classification; for TMD cases, positive reports ranged from 57 to 97%, while for controls, positive reports ranged from 10 to 29% (Table 8).

TMD cases registered a mean of 6 neck muscle sites painful to palpation while controls registered a mean of 1.2 sites (Table 6). TMD cases also registered a mean of 7.4 body sites painful to palpation while controls registered a mean of 2.1 body sites.

Among TMD cases, 90% exhibited at least 2 bruxo-facets while 77% of controls exhibited at least 2 bruxo-facets (Table 7).

Anthropometric Status

TMD cases were slightly shorter in stature (mean difference of .03 m) with significant SOR = .7 that changed to a nonsignificant SOR = 1.1 after adjustment (Table 9). TMD cases also weighed slightly less (mean difference of 4.6 kg) with significant SOR = .8 that changed to a non-significant SOR = 1.0 after adjustment. The computed BMI did not differ between TMD cases and controls. The 2D:4D finger length ratios were significantly larger among TMD cases, compared to controls, with OR = 1.2 for each hand; after adjustment, these ORs decreased to 1.0 for each hand and were no longer significant.

Health Status

TMD cases and controls did not differ in reporting 3 endocrine conditions, with rates of 2.2 and 3.1%, respectively (Table 10). TMD cases were more likely to report a history of cardiovascular or hematologic conditions, with rates of 8.2 and 14.2%, respectively, and with rates for controls of 4.7 and 7.7%, respectively; the ORs of approximately 2 decreased to no more than 1.5 after adjustment for demographic characteristics and were no longer significant. In contrast, approximately twice as many TMD cases versus controls reported at least 1 of 4 neural/sensory conditions or at least 1 among 5 respiratory conditions. In a pattern similar to that for the respiratory condition response rates, 6.3% of TMD cases compared to 2.4% of controls reported obstructive sleep apnea.

Approximately twice as many TMD cases versus controls reported prior history of smoking; in contrast, approximately equal number of TMD cases and controls reported current smoking (Table 11). TMD cases reported their general health as overall worse compared to controls among TMD cases, 50% reported hospitalization at sometime in their life for serious illness, compared to 37% of controls, with OR = 1.7 which decreased to a non-significant OR of 1.2 after adjustment. TMD cases reported more prior use of medications among the 11 types of medications assessed, with the increased utilization appearing at 2 medications (OR = 4.0) and at 3 or more medications (OR = 7.0); these ORs decreased after adjustment to 2.5 and 3.5, respectively.

Associations With Demographic Variables

Age, sex, and race variations among the variables are reported in Supplementary e-Tables 1–33. A majority of the comparisons were statistically significant, thereby supporting our use of fully adjusted models correcting for these variations. Further review of the demographic results is beyond the scope of the present paper.

Discussion

This exploration of clinical characteristics found that 59 of 71 assessed variables demonstrated a significant association with pain-related TMD. Some of these findings provide important confirmation and validation of previous studies, while others are presented for the first time (eg, selected health conditions and anthropometric findings). However, we believe this to be the first study to address all of these findings in 1 cohort. An important consideration when interpreting these findings is that TMD cases were volunteers recruited from communities in and around 4 US academic health centers. As reported in an accompanying paper,[82] clinical pain reports, symptom profiles, and history of treatment among TMD cases were consistent with TMD as it occurs in the community at large, rather than in treatment-seeking TMD cases. The accompanying paper also shows evidence that controls were selected from a similar community-based population of volunteers, and that the methods of selection produced good internal validity in estimates of associations.

All 3 forms of trauma were strongly associated with TMD. While the finding is consistent with previous studies, these case-control results do not resolve the controversy as to whether such trauma plays a direct causal role in TMD.[9,15,44] Equally strong was the association between TMD and yawning or prolonged opening, yet these everyday sources of plausible repeated strain have received no systematic research. Past orthodontic treatment was only weakly associated with TMD, a consistent finding with other studies showing that orthodontic treatment, considered alone, does not appear to either cause or improve TMD.[61,78,84]

Parafunctional activity such as teeth clenching has historically been considered a potential source of so-called microtrauma, but with limited evidence.[63,77] In this study, where parafunctional behaviors were assessed on a continuum using a comprehensive questionnaire, odds of TMD was elevated 17-fold among people in the upper tertile of the distribution relative to people in the lowest tertile, a strong relationship consistent with other findings.[11] Other studies that have reported weaker associations have asked only a few questions about parafunction.[33,92] Comprehensive item sets, such as the OBC used here, might be more valid because they have greater potential to elicit state-specific memory.[43] While findings from recent experimental and observational studies support a causal relationship between parafunction and pain,[11,31,32,41,56] parafunction may be both cause and consequence of the pain experienced in TMD, and the very magnitude of the odds ratio observed here suggests the presence of a bidirectional relationship, which casues doubt as to whether parafunction is a sufficient cause for TMD onset.[57]

Pain or other functional disorders were very strongly associated with TMD, most notably for headache. The OR of 10 for each additional type of headache represents a pragmatic though crude indicator of headache symptoms. While the ICHD-2 based headache symptoms will be further assessed in a future publication, we consider the present findings as an intriguing perspective regarding the underlying complexity of headache. Potential causal effects of headache on TMD should be interpreted cautiously; headache that co-occurs with TMD might represent the same disorder but called by another name, or it might be secondary.[6,88] Furthermore, enrollment criteria excluded controls, although not cases, who reported 5 or more headaches per month, thereby amplifying odds ratios. Our examination protocol sought to disentangle this possible confounding of headache with TMD, especially among the controls. Specifically, individuals who only had headache (less than 5 per month) but not jaw pain were accepted as "controls." Given that headache and TMD may coexist due to overlap in their classification, we refer to headache as an overlapping condition and will rely on future analysis of longitudinal data to examine causal direction.

Those caveats did not apply to back pain, abdominal pain and pelvic pain, each of which was moderately associated with TMD, as seen in other studies.[38,40,49,60,71,76] The strength of association with TMD was greater for sets of 2 or more of these "functional conditions" (OR = 6.7) than for individual functional conditions, suggesting that their co-occurrence has additive effects on the association with TMD and indicative perhaps of a shared set of pain regulatory pathways that have become dysregulated.[18]

Self-reported clinical status differed markedly between cases and controls. Consistent with clinical samples,[50] 1 in 4 TMD cases had facial pain-related disability, a proportion that was in stark contrast to controls (<1%). While some degree of facial pain, dysfunction and disability is an intrinsic consequence of TMD, the results are illuminating given that some of the facial pain symptoms are reported by at least some controls. Whether such symptoms are significant, however, might be usefully distinguished on the basis of impact to the individual; while the study's enrollment criteria permitted some history of TMD symptomatology among controls, people who reported having been diagnosed with TMD were excluded as controls.[82] Consequently, prior symptoms in controls, if present, would most likely qualify as subclinical in nature. In a related finding, the mean of 15 (0–100 scale) was not trivial amongst the 15% of the controls who responded to the 3 characteristic pain intensity questions based on the lifetime occurrence of regional but not diagnosed pain. A relevant methodological observation is that detailed questionnaires, such as the CPSQ, can elicit reports of symptoms even among people who, during an earlier telephone interview, reported no facial pain for the past 30 days. One explanation is that the questionnaire triggers state-specific memory.[37,43] Notably, only 53 individuals (3.2%) reported any regional pain in the past 30 days, and by examination criteria such pain occurred on fewer than 5 days.

Modifying factors that improve or worsen pain might also be intrinsic to musculoskeletal disorders. The large majority of TMD cases reported multiple modifying factors, suggesting that their presence may be important for disorder progression. In fact, rather than curtailing modifying behaviors, engaging in the behaviors might be a benefical part of TMD treatment.[30] Similarly, in the case of back pain, studies suggest that avoidance behaviors might contribute to progression of that condition.[46,81,93]

The expected finding that TMD cases had greater jaw functional limitation than controls is consistent with the disablement model.[65] While the mean levels of jaw functional limitation in OPPERA TMD cases was lower than a clinical sample,[68] mean levels in OPPERA controls were very low, yielding a strong association. It is worth noting that, among cases, limitation may also be part of avoidance behavior.[46]

TMJ noises were self-reported by nearly all TMD cases (89%) and only 19% of controls, consistent with the widely held view that such noises are an important part of TMD when combined with clinically significant pain and dysfunction. TMJ noises were identified during the examination in a majority of cases but also in 30% of controls. Given that 73% of OPPERA cases reported having consulted someone for their pain,[82] health-care services interaction could represent a possible source of reporting bias, resulting in elevated rate of self-reported noises by the cases relative to the noises detected by examination. Otherwise, individuals are often unaware of noises that clinicians readily detect,[86] perhaps accounting for the differential in self-report versus examiner detected among the controls. Other research indicates similar findings: 86% of cases self-reporting clicks,[96] 48% or 61% of cases with noises detected by examination,[73,96] and 37% of general dental practice patients (not screened for TMD) exhibiting TMJ noises during examination.[36] Collectively, these findings—self-report versus examination and cases versus controls—from 3 other studies are compatible with those found in this study, suggesting that bias due to participant recruitment methods or due to data collection methods is not a likely source of these statistics.

Similarly, reported locking was also significantly more common among TMD cases than controls. When TMJ noises and locking are prominent features in the clinical history, it is common for substantial muscular dysfunction and pain to also be present, an explanation that is also consistent with high levels of parafunction observed in TMD cases.[11] Moreover, longitudinal studies show that clicking and locking often resolve over time with minimal intervention.[16] Multivariate and longitudinal analyses will be needed to understand the significance of joint noises and locking in OPPERA's cases and controls.

Differences in clinical status by examination between cases and controls were also in part a consequence of case-classification, yielding expected differences in all clinical parameters. One notable finding concerns the 17% of controls (n = 262) who reported pain after terminating the assisted mouth-opening procedure, contrasting with the 11% of TMD cases (n = 20) who did not terminate the procedure and furthermore said it was not painful. The former may be a group at high risk for first-onset TMD, while the latter group may represent individuals coping well with TMD.

The number of neck and body sites that were painful to palpation was conspicuously greater in TMD cases than controls. This is the somatic equivalent of case-control differences in self-reported pain disorder symptoms and supports growing evidence for the overlap among pain disorders.[1–4,7,8,74,97] Meanwhile, positive clinical findings occurred at a substantial rate among the controls (Tables 6–8). Whether it represents variation of a normal phenotype, as traditionally viewed, or a marker for elevated risk of TMD onset remains to be discovered in our prospective cohort study.

There are reasonable grounds to compare anthropometric measures between cases and controls. The condition might limit mastication, thereby affecting diet and weight. Another proxy, given the greater prevalence of TMD in women, is gonadal hormones in TMD.[47,48] Multiple lines of evidence suggest this sexually dimorphic index reflects prenatal exposure to estrogens versus androgens, such that lower 2D:4D ratios reflect higher androgen exposure, while lower ratios indicate greater prenatal estrogen[52,58] and may thereby account for greater occurrence of TMD in women than men. However, none of the anthropometric measures in OPPERA were associated with TMD after adjusting for demographic variables.

Health status revealed generally poorer health in TMD cases than controls, consistent with other studies.[10,39] Relative to controls, TMD cases reported more neural/ sensory conditions, respiratory conditions, and medication usage, and they were more likely to rate their health

as fair or poor. Of note, these associations were not confounded by demographic characteristics.

Several potential limitations of the present study warrant highlighting. One limitation is that many self-reported clinical measures were assessed using single-item questions. Although widely used in clinical practice and ubiquitous in medical research, such measures rarely have supporting evidence of reliability or validity. Multiple items are almost always needed for assessing latent variables (such as complex mood states), whereas single items are often considered sufficient for assessing straight-forward concepts, such as “do you have pain?” For some conditions, such as obstructive sleep apnea, validated multi-item instruments are available, although it was not feasible to add them to the already large number of questions asked in OPPERA. For other areas, such as perception of TMJ clicking, the face validity and presumably content validity of the single item are strong, and, assuming clear operationalization, at issue is the items’ reliability which is directly testable. Two of the self-report instruments, the CPSQ and the medical history, ask multiple questions about health status using single-item measures, although we are only now in the process of evaluating their reliability.

Another caveat is that the case-control study design does not allow us to establish whether the characteristic developed before or after onset of TMD, thereby hindering conclusions about possible causal effects. A third limitation is that the analyses consider each measure independently of other clinical measures. Odds ratios likely will be attenuated when multiple clinical variables, and other characteristics assessed in OPPERA,[28,35,55] are considered simultaneously using a multivariate approach.

In conclusion, TMD cases and controls differed on most (59 of 71) of the measures from among this broad array of self-reported and clinical characteristics. Most of the findings confirmed results from other studies. Many odds ratios exceeded 5, signifying very strong associations, and most remained stable after adjustment for demographic characteristics. For several sets of clinical characteristics, we believe marked associations with TMD occurred because they are implicitly part of the condition. Yet many of those same characteristics were found in at least some controls. Consequently, we do not regard large ORs as prima facie evidence of causality; instead, we regard larger ORs as suggestive of more complex patterns of interaction, perhaps iterative over time, between pain, the person, and the variable. The importance of these findings lies in the comprehensiveness of the collected data and their relevance for the clinical domain which primarily serve as a reference against which to compare findings reported in the other papers in this series. Because this study is of moderate power, limited by selection of only 185 cases, observed findings should also be considered as a base for developing additional hypotheses. A future goal of the OPPERA prospective cohort study is to determine whether those characteristics represent early signs of TMD, useful markers signifying elevated risk of first-onset TMD, or variation in normal phenotypes.[29]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Putative Etiologic Factors Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
Lifetime Hx of external injury to jaw	Yes	126	8.2	46	30.5	<.0001	4.5	3.0, 6.7	4.2	2.8, 6.5
	No [ref]*	1,408	91.8	105	69.5					
Jaw injury due to yawning	Yes	44	2.7	30	16.2	<.0001	7.0	4.2, 11.6	7.3	4.2, 12.7
	No [ref]	1,579	97.3	155	83.8					
Jaw injury due to prolonged opening	Yes	36	2.2	26	14.1	<.0001	7.2	4.2, 12.4	8.3	4.5, 15.2
	No [ref]	1,587	97.8	159	85.9					
Ever had orthodontic procedures	Yes	694	42.9	110	59.8	<.0001	1.9	1.4, 2.7	1.4	1.0, 2.0
	No [ref]	925	57.1	74	40.2					
Oral behaviors-checklist: sum score	25–62	458	29.4	147	83.1	<.0001	19.2	10.0, 36.9	16.8	8.6, 32.9
	17–24	514	33.0	20	11.3		2.3	1.1, 4.9	1.8	.8, 3.9
	0–16 [ref]	585	37.6	10	5.6					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§Odds ratio.

¶95% confidence interval for OR.

Table 2

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Overlapping Conditions Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
Any headaches in last year	Yes	1,178	72.6	179	96.8	<.0001	11.6	5.1, 26.4	8.8	3.8, 20.1
	No [ref] *	444	27.4	6	3.2					
No. of different type of headache in last year	4	151	9.4	51	27.9	<.0001	24.7	10.4, 58.8	16.2	6.7, 39.2
	3	147	9.1	42	23.0		21.7	9.0,52.2	15.0	6.1, 36.6
	2	392	24.3	57	31.1		10.6	4.5,25.0	7.8	3.3, 18.6
	1	476	29.6	27	14.8		4.3	1.7,10.5	3.9	1.6,9.7
	0 [ref]	444	27.6	6	3.3					
Chronic pain other than face	Yes	201	12.6	87	47.3	<.0001	6.8	4.8,9.4	5.1	3.6,7.3
	No [ref]	1,333	87.4	97	52.7					
Current low back pain	Yes	204	12.6	53	29.0	<.0001	3.0	2.1,4.3	2.9	2.0, 4.3
	No [ref]	1,415	87.4	130	71.0					
Episodes of low back pain in last year	11 or more	147	9.1	47	25.5	<.0001	6.5	4.1,10.2	5.2	3.2,8.4
	5–10	167	10.4	50	27.2		6.0	3.9, 9.4	4.8	3.0,7.6
	2–4	325	20.1	34	18.5		2.0	1.3, 3.2	1.7	1.1,2.8
	1	136	8.4	10	5.4		1.4	.7, 2.9	1.2	0.6,2.4
	0 [ref]	838	52.0	43	23.4					
Count of 10 IBS symptoms	6 or more	107	6.6	28	15.2	<.0001	3.5	2.2,5.7	3.8	2.2,6.3
	3–5	263	16.7	50	27.2		2.4	1.6,3.5	2.6	1.7,3.9
	1–2	328	20.3	31	16.8		1.2	.8,1.9	1.3	.8,2.0
	0 [ref]	909	56.4	75	40.8					
ROME IBS classification	Yes	43	2.7	16	8.7	<.0001	3.6	2.0,6.6	2.7	1.4,5.1
	No [ref]	1,558	97.3	168	91.3					
Genital symptoms	Yes	48	3.0	11	6.4	.0219	2.4	1.2,4.7	1.4	.7,3.0
	No [ref]	1,528	97.0	162	93.6					
Count of 20 comorbidities	2 or more	245	15.2	92	50.5	<.0001	8.5	5.8,12.4	6.6	4.4,9.8
	1	298	18.5	37	20.3		2.4	1.6,3.8	2.1	1.3,3.3
	0 [ref]	1,065	66.2	53	29.1					

[*] Reference group used to calculate odds ratios.

[†] *P* value is from binary logistic regression model evaluating overall association between putative risk factor and case-status.

[‡] Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

[§] Odds ratio.

[¶] 95% confidence interval for OR.

Table 3

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Self-Reported Pain and Functional Limitation of the Jaw Measured as Continuous Variables

									Unimputed Effect Estimates†				Imputed Effect Estimates†		
		Controls			TMD Cases				Site-Adjusted Effect‡		Fully-Adjusted Effect‡		Fully-Adjusted Effect‡		
Putative Risk Factor	Units and Potential Range	N	Mean	SE	N	Mean	SE	P Value*	SOR§	95% CI¶	SOR	95% CI¶	N	SOR	95% CI
Facial characteristic pain intensity#	0–100	247	15.71	1.11	185	51.84	1.41	<.0001	13.9	8.7,22.3	16.9	9.9,29.0			
Facial pain interferenc#	0–100	246	5.01	.84	184	19.71	1.69	<.0001	2.8	2.1,3.8	2.9	2.2, 4.0			
No. days when efficiency dropped below 50%#	0–180 days	232	3.19	1.19	181	20.24	3.08	<.0001	2.8	1.7,4.5	2.6	1.6,4.1			
JFLS: chewing limitation	0–10	1,402	.28	.02	162	2.22	.13	<.0001	3.2	2.7, 3.8	3.3	2.8,3.9	1,763	3.0	2.6,3.5
JFLS: opening limitation	0–10	1,541	.18	.02	162	2.22	.13	<.0001	3.4	2.9,4.0	3.3	2.8,3.9	1,763	3.0	2.6,3.5
JFLS: verbal & emotional expression limitation	0–10	1,510	.14	.02	156	.72	.10	<.0001	1.5	1.3, 1.6	1.6	1.4,1.8	1,763	1.6	1.4,1.8
JFLS: combined global measure	0–10	1,331	.16	.02	135	1.74	.11	<.0001	3.7	3.1,4.5	3.7	3.0,4.5	1,763	2.9	2.5,3.4

*P values are from analysis variance model comparing mean values of putative risk factor between cases and controls, with adjustment for study site.

†Unimputed effect estimates are for complete case analysis using numbers of subjects in columns headed N under case classifications. Imputed effect estimates are for the full sample where missing data have been estimated.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor as the main explanatory variable and study site as covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender and race/ethnicity.

§SOR is standardized odds ratio from a logistic regression model evaluating the linear effect of the risk factor that was standardized by z-score transformation.

¶95% confidence interval for SOR.

#The CPI assesses pain in the past 6 months, and the data reported encompass all who have ever had pain in the masticatory system; of these, N = 80 reported no pain in the past 6 months.

Table 4

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Self-Reported Pain-Related Disability, Factors That Modify Pain, and Nonpain Characteristics Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
Facial graded chronic pain status#	IIb–IV	11	6.9	46	25.4	<.0001	9.5	4.4, 20.4	10.3	4.6, 23.4
	IIa	3	1.9	44	24.3		29.9	8.8, 102	27.3	7.9, 94.5
	I [ref] *	146	91.3	91	50.3					
Number of activities that modified facial pain last month≠	4–5	7	13.0	83	46.9	<.0001	12.1	4.6, 32.0	11.4	4.1, 31.3
	2–3	21	38.9	72	40.7		3.1	1.4, 6.7	3.1	1.3, 7.1
	0–1 [ref]	26	48.1	22	12.4					
Number of face/jaw symptoms	3 or more	78	4.8	171	92.4	<.0001	294	158, 548	248	131, 468
	0–2 [ref]	1,546	95.2	14	7.6					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§Odds ratio.

¶95% confidence interval for OR.

#Applicable only for those individuals reporting jaw-area pain of GCPS grade of 1 or more, which requires reporting pain over the prior 6 months. Compare this to footnote 7, Table 3.

≠Applicable only for those individuals reporting jaw-area pain during the prior month.

Table 5

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Self-Reported Jaw Clicking and Jaw Locking, Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect[3]		Fully-Adjusted Effect[‡]	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value[†]**	**OR[§]**	**95% CI[¶]**	**OR**	**95% CI**
TMJ noises in last month	1 or more	297	18.5	165	89.2	<.0001	37.1	22.8, 60.3	30.2	18.4, 49.5
	0 [ref][*]	1,305	81.5	20	10.8					
Pain with TMJ noises in last month	Yes	24	1.5	123	67.2	<.0001	148	86.8, 253	132	74.9, 234
	no [ref]	1,570	98.5	60	32.8					
TMJ noises before last month	1 or more	338	21.0	162	90.0	<.0001	34.8	21.0, 57.8	27.2	16.2, 45.6
	0 [ref]	1,271	79.0	18	10.0					
In last month, could not open mouth wide	Yes	35	2.2	75	40.8	<.0001	31.2	19.8, 49.0	30.5	18.6, 50.1
	No [ref]	1,581	97.8	109	59.2					
Prior to 1 month ago, could not open mouth wide	Yes	109	6.8	94	50.8	<.0001	14.1	10.0, 20.1	11.1	7.7, 16.1
	No [ref]	1,497	93.2	91	49.2					
In the last month, could not close jaw from wide-open position	Yes	35	2.2	46	25.3	<.0001	15.2	9.4, 24.5	12.5	7.4, 20.9
	No [ref]	1,569	97.8	136	74.7					
Prior to 1 month ago, could not close jaw from wide-open position	Yes	74	4.6	65	35.3	<.0001	11.2	7.6, 16.5	8.5	5.6, 12.9
	No [ref]	1,535	95.4	119	64.7					

Abbreviation: TMJ, temporomandibular joint.

[*] Reference group used to calculate odds ratios.

[†] *P* value is from binary logistic regression model evaluating overall association between putative risk factor and case-status.

[‡] Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender and race/ethnicity.

[§] Odds ratio.

[¶] 95% confidence interval for OR.

Table 6

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Jaw Mobility and Body Palpation Scores Measured as Continuous Variables

		Controls			TMD Cases				Site-Adjusted Effect†		Fully-Adjusted Effect†	
Putative Risk Factor	**Units and Potential Range**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**P Value***	**SOR‡**	**95% CI§**	**SOR**	**95% CI**
Pain-free jaw opening	mm	1,617	47.78	.19	184	35.11	.83	<.0001	.2	.2, .3	.3	.2, .3
Maximum unassisted jaw opening	mm	1,617	53.31	.18	184	47.43	.65	<.0001	.4	.4, .5	.5	.4, .6
Maximum assisted jaw opening (unterminated)	mm	1,260	55.93	.20	121	52.40	.74	<.0001	.6	.5, .8	.8	.7, 1.0
Maximum assisted jaw opening (terminated)	mm	347	56.05	.41	62	51.84	1.21	.0002	.6	.4, .8	.7	.5, .9
Number of neck sites tender to palpation	0–14	1,633	1.18	.06	185	5.99	.32	<.0001	3.6	3.1, 4.2	3.5	3.0, 4.1
Number of body sites tender to palpation	0–14	1,633	2.13	.07	185	7.43	.29	<.0001	4.3	3.6, 5.1	4.1	3.4, 4.9

*P values are from analysis variance model comparing mean values of putative risk factor between cases and controls, with adjustment for study site.

†Site-adjusted effects were computed in logistic regression models where the putative risk factor as the main explanatory variable and study site as covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

‡SOR is standardized odds ratio from a logistic regression model evaluating the linear effect of the risk factor that was standardized by z-score transformation.

§95% confidence interval for SOR.

Table 7

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Pain With Opening, Temporomandibular Joint (TMJ) Sounds, And Bruxofacets Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
Pain on unassisted opening	1 or more	552	34.7	154	86.0	<.0001	11.7	7.5, 18.2	12.9	8.2, 20.5
	0 [ref]*	1,037	65.3	25	14.0					
Pain on assisted opening (unterminated)	1 or more	389	31.4	98	83.1	<.0001	11.3	6.8, 18.6	11.9	7.1, 20.0
	0 [ref]	849	68.6	20	16.9					
Pain on assisted opening (terminated)	1 or more	262	76.4	58	95.1	.0009	6.6	2.0, 22.6	6.9	2.0, 24.0
	0 [ref]	81	23.6	3	4.9					
TMJ palpation sounds: right	1 or more	488	30.2	110	59.5	<.0001	3.4	2.4, 4.6	3.0	2.1, 4.2
	0 [ref]	1,129	69.8	75	40.5					
TMJ palpation sounds: left	1 or more	525	32.5	109	58.9	<.0001	3.2	2.3, 4.4	2.6	1.9, 3.7
	0 [ref]	1,092	67.5	76	41.1					
Number of locations with bruxofacets	2–3	1,233	76.6	164	90.1	<.0001	2.3	1.3, 3.9	2.1	1.2, 3.7
	0–1 [ref]	377	23.4	18	9.9					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§Odds ratio.

¶95% confidence interval for OR.

Table 8

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Clinical Palpation Characteristics of Masticatory Muscles Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
RIGHT SIDE										
Temporalis	1 or more	412	25.2	166	89.7	<.0001	45.8	27.1, 77.4	39.2	23.0, 66.8
	0 [ref]*	1,221	74.8	19	10.3					
Masseter	1 or more	474	29.0	180	97.3	<.0001	135	54.6, 334	121	48.5, 301
	0 [ref]	1,159	71.0	5	2.7					
Posterior mandibular and submandibular	1 or more	236	14.5	114	61.6	<.0001	25.2	16.8, 37.8	22.5	14.6, 34.8
	0 [ref]	1,397	85.5	71	38.4					
Lateral pterygoid area	1 or more	303	18.6	119	65.0	<.0001	11.0	7.8, 15.6	13.3	9.0, 19.5
	0 [ref]	1,329	81.4	64	35.0					
Temporomandibular joint	1 or more	170	10.4	130	70.3	<.0001	32.4	21.3, 49.3	30.3	19.5, 47.0
	0 [ref]	1,463	89.6	55	29.7					
LEFT SIDE										
Temporalis	1 or more	347	21.2	156	84.3	<.0001	34.7	22.0, 54.8	31.2	19.6, 49.9
	0 [ref]	1,286	78.8	29	15.7					
Masseter	1 or more	417	25.5	169	91.4	<.0001	48.5	27.9, 84.1	42.8	24.4, 75.0
	0 [ref]	1,216	74.5	16	8.6					
Posterior mandibular and submandibular	1 or more	222	13.6	105	56.8	<.0001	19.9	13.4, 29.4	19.7	12.8, 30.3
	0 [ref]	1,411	86.4	80	43.2					
Lateral pterygoid area	1 or more	299	18.3	106	57.9	<.0001	7.8	5.5, 10.9	8.7	6.1, 12.6
	0 [ref]	1,332	81.7	77	42.1					
Temporomandibular joint	1 or more	194	11.9	131	70.8	<.0001	28.7	19.0, 43.6	26.0	16.9, 40.2
	0 [ref]	1,439	88.1	54	29.2					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

[§] Odds ratio.

[¶] 95% confidence interval for OR.

Table 9

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Clinical Anthropometric Variables

		Controls			TMD Cases				Unimputed Effect Estimates†			
									Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Units and Potential Range**	**N**	**Mean**	**SE**	**N**	**Mean**	**SE**	**P Value***	**SOR§**	**95% CI¶**	**SOR§**	**95% CI¶**
Height	m	1,622	1.70	.00	185	1.67	.01	.0002	.7	.6, .9	1.1	.9, 1.3
Weight	kg	1,614	76.77	.52	185	73.12	1.33	.0277	.83	.7, 1.0	1.0	.8, 1.2
Body mass index	kg/m_2	1,609	26.45	.16	185	26.09	.46	.5922	1.0	.8, 1.1	1.0	.8, 1.2
Left hand finger length ratio (Index:Ring)	mm	1,621	96.32	.09	185	97.00	.26	.0167	1.2	1.0, 1.4	1.0	.9, 1.2
Right hand finger length (Index Ring)	mm	1,621	96.03	.09	185	96.71	.24	.0054	1.2	1.1, 1.4	1.0	.9, 1.2

*P values are from analysis variance model comparing mean values of putative risk factor between cases and controls, with adjustment for study site.

†Unimputed effect estimates are for complete case analysis using numbers of subjects in columns headed N.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor as the main explanatory variable and study site as covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§SOR is standardized odds ratio from a logistic regression model evaluating the linear effect of the risk factor that was standardized by z-score transformation.

¶95% confidence interval for SOR.

Table 10

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Medical Conditions Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
History of 3 endocrine conditions#	1 or more	50	3.1	4	2.2	.4974	.7	.3, 2.0	.5	.2, 1.4
	0 [ref]*	1,578	96.9	180	97.8					
History of 7 cardiovascular conditions#	1 or more	76	4.7	15	8.2	.0418	1.9	1.0, 3.3	1.5	.8, 2.8
	0 [ref]	1,545	95.3	169	91.8					
History of 3 hematologic conditions#	1 or more	126	7.7	26	14.2	.0028	1.9	1.2, 3.0	1.3	.8, 2.0
	0 [ref]	1,500	92.3	157	85.8					
History of 4 neural/sensory conditions#	1 or more	374	23.0	106	57.9	<.0001	4.7	3.4, 6.4	3.7	2.6, 5.2
	0 [ref]	1,254	77.0	77	42.1					
History of 5 respiratory conditions#	1 or more	626	38.5	122	66.7	<.0001	3.1	2.3, 4.3	2.5	1.7, 3.4
	0 [ref]	1,000	61.5	61	33.3					
History of obstructive sleep apnea	Yes	37	2.4	11	6.3	.0026	3.2	1.6, 6.4	3.1	1.4, 6.7
	No [ref]	1,530	97.6	164	93.7					
History of osteoarthritis≠	Yes	11	.7	5	2.7					
	No [ref]	1,616	99.3	179	97.3					
History of rheumatoid arthritis≠	Yes	7	.4	3	1.6					
	No [ref]	1,620	99.6	181	98.4					
History of Sjogrens syndrome≠	Yes	1	.1	1	.5					
	No [ref]	1,627	99.9	182	99.5					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§Odds ratio.

¶95% confidence interval for OR.

[#] See Methods for the particular conditions included in this category.

[≠] *P* value and ORs not computed due to cells having expected frequencies of <5.

Table 11

Variation Between Temporomandibular Disorder (TMD) Cases and Controls in Health Status Variables Measured Categorically

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect‡	
Putative Risk Factor	**Category**	**N**	**Column %**	**N**	**Column %**	**P Value†**	**OR§**	**95% CI¶**	**OR**	**95% CI**
Smoking history: current, former or never	Current	294	18.4	25	13.7	.0003	.8	.5, 1.4	.8	.5, 1.4
	Former	125	7.8	30	16.4		2.3	1.5, 3.6	1.7	1.0, 2.8
	Never [ref] *	1,175	73.7	128	69.9					
Self rated general health	Fair/poor	77	4.7	13	7.1	.0001	3.0	1.5, 5.8	3.5	1.7, 7.4
	Good	850	52.4	121	66.1		2.2	1.5, 3.1	2.2	1.5, 3.2
	Excellent [ref]	696	42.9	49	26.8					
Ever hospitalized for surgery/ serious illness	Yes	598	36.9	92	49.7	.0006	1.7	1.2, 2.3	1.2	.9, 1.7
	No [ref]	1,023	63.1	93	50.3					
Past use of 11 medications	3 or more	239	14.7	60	32.6	<.0001	7.0	3.7, 13.2	3.4	1.8, 6.7
	2	542	33.4	77	41.8		4.0	2.2, 7.4	2.4	1.3, 4.6
	1	473	29.1	34	18.5		2.1	1.1, 4.0	1.8	.9, 3.5
	0 [ref]	370	22.8	13	7.1					

*Reference group used to calculate odds ratios.

†*P* value is from binary logistic regression model evaluating overall association between putative risk factor and case status.

‡Site-adjusted effects were computed in logistic regression models where the putative risk factor is the main explanatory variable and study site is the covariate. Fully-adjusted effects were computed in logistic regression models that additionally include covariates of age group, gender, and race/ethnicity.

§Odds ratio.

¶95% confidence interval for OR.