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Characteristics associated with high-impact pain in people with TMD: a cross-sectional study

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Abstract

High-impact (disabling) pain diminishes quality of life and increases health care costs. The purpose of this study was to identify variables that distinguish between high and low-impact pain among individuals with painful temporomandibular disorder (TMD). Community-dwelling adults (n=846) with chronic TMD completed standardized questionnaires assessing the following: 1) sociodemographic, 2) psychological distress, 3) clinical pain, and 4) experimental pain. We used high-impact pain, classified using the Graded Chronic Pain Scale, as the dependent variable in logistic regression modeling to evaluate contributions of variables from each domain. Cross-validated area under the ROC curve (AUC) quantified model discrimination. One third of participants had high-impact pain. Sociodemographic variables weakly discriminated between low and high-impact pain (AUC=0.61, 95% CI 0.57, 0.65) with the exception of race. An 18-variable model encompassing all four domains had good discrimination (AUC=0.79, 95% CI 0.75, 0.82), as did a simplified model (sociodemographic variables plus catastrophizing, jaw limitation, and number of painful body sites): AUC=0.79, 95% CI 0.76, 0.82). Duration of pain, gender, and experimental pain testing results were not associated. Characteristics that most effectively

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discriminated between people with low- and high-impact TMD pain included clinical pain features and ability to cope with pain.

Perspective: This article presents the results of a multivariable model designed to discriminate between people with high or low-impact pain in a community-based sample of people with chronic painful TMD. The findings emphasize the importance of catastrophizing, jaw limitation, and painful body sites associated with pain-related impact.

Keywords

Temporomandibular disorders; predictive value of tests; pain-related disability; AUC; quality of life

1 Introduction

1.1 TMD is a public health problem

Temporomandibular disorder (TMD) is characterized by pain in the jaw joint, face, and masticatory muscles that can become chronic. Although the hallmarks of TMD, as a regional pain disorder, are pain in the temporomandibular joints and masticatory muscles, people with TMD often experience pain in many other areas of the body[44].

Population-level prevalence of TMD range from approximately 5–10%, though case definitions vary among studies. Based on a single-item question, The National Health and Interview Survey (NHIS) estimated TMD-like pain at 6% in 1989[21] and 4.6% in data pooled from 2000–2005[35]. The prevalence of TMD combined with the paucity of effective treatments, and the likelihood of comorbid conditions such as headache and other idiopathic pain conditions, result in a significant individual and public health burden. For example, high-impact pain measured by Graded Chronic Pain Scale (GCPS) is predictive of healthcare spending. Specifically, among orofacial pain patients, movement from low to high GCPS status results in a $525 increase in healthcare costs over 6 months[6] (original reference reported 2012 £366 which we converted to 2012 US dollars using http://eppi.ioe.ac.uk/costconversion/).

1.2 High-impact pain

The National Pain Strategy identified as a target “Reducing the prevalence of high-impact chronic pain and its associated morbidity and disability”[18]. However, the extent of TMD-related disability is disputed. In a study of nursing students with signs or symptoms of TMD, 93.7% reported not having sought treatment, of whom nearly half (46%) reported that they were not bothered by the symptoms[38]. The authors inferred that the symptoms were not a problem for these individuals and concluded “most subjects with clinically detectable dysfunction are *functioning adequately* without significant symptoms” (p. 295) [emphasis added]. In one study of 399 TMD patients, only 49 (12%) met criteria for pain-related disability[20]. Reported prevalence of pain-related disability classified using the established taxonomy of Graded Chronic Pain Scale (GCPS) among people with TMD range from 2%[1] to 41%[4]. Using the same outcome assessment to obtain vastly different prevalences

warrants further investigation. In truth, the extent of the problem of high-impact pain among people with chronic TMD is unknown.

Research exploring pain-related disability among people with TMD has identified multiple potential characteristics associated with disability. Researchers have reported an association between pain-related disability, somatization and depression[25–27, 33, 51]. Catastrophizing has been associated with pain-related disability[41, 42]. Pain intensity and disability points have been associated with anxiety, somatization and depression[40]. Along with depression and somatization, duration of pain was linked to pain-related disability in Dutch, Italian, and Israeli samples[7]. Limitations of previous observational studies include potential selection bias from recruitment of participants from specialty pain clinics as some other factor may influence both treatment-seeking and pain-related disability. Many studies have reported a low number of people experiencing pain-related disability. Small sample size has prevented thorough examination of multiple factors in the respective population.

The purpose of this study was to identify variables that distinguish between high and low-impact pain.

2 Methods

2.1 Study overview

This cross-sectional study comprised 1088 people with chronic TMD recruited between May 2006 and October 2013 addresses characteristics associated with high-impact pain. The sample was nested in the parent study, the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA; Slade et al 2011[39]). The parent OPPERA study included a case-control study that compared chronic TMD cases with TMD-free controls. Human Research Ethics Committees at all study sites approved the study protocol. All participants signed an informed consent for study participation. Participants were compensated for their time.

2.2 Participants

Participants were individuals living near one of four study sites (University at Buffalo, NY, University of Florida Gainesville, FL, University of Maryland in Baltimore, MD, and University of North Carolina at Chapel Hill, NC) of the OPPERA study. We define the sample as “community-dwelling” because recruitment was conducted in the communities surrounding each study site utilizing radio advertisements, recruitment fliers, and local newspapers. Participants responded to advertisements seeking people with chronic jaw pain. Participants were aged 18–44 years and were required to be fluent in English. Exclusion criteria included recent facial surgery or facial injury, pregnancy, orthodontic procedures or positive report of any of ten major medical conditions. For more details about recruitment and sociodemographic composition of participants from each study site see Slade et al.[39].

Participants completed a telephone interview to assess eligibility prior to completing a battery of questionnaires about psychological distress and clinical pain, and a 3-hour clinic visit including clinical examination for verification of TMD status and experimental pain testing. Of the 1088 TMD cases recruited, 1042 had data for the outcome of interest and

hence were included in the current study (Figure 1). See supplemental material Figure A for a diagram of participants contacted, eligible and consented.

2.3 Procedures

Chronic TMD was defined as self-reported facial pain symptoms experienced for at least 6 months prior to enrollment and fulfillment of examination criteria described below. The 6-month threshold is consistent with the definition of chronic pain provided by the Institute of Medicine: “Chronic pain, by contrast, lasts more than several months variously defined as 3 to 6 months, but certainly longer than „normal healing‟‟”[17]. Potential participants had to report pain in the cheeks, jaw muscles, and/or jaw joints for at least 15 days in the prior month and at least 5 days per month for the previous 5 months. The Research Diagnostic Criteria for TMD (RDC/TMD) is a structured clinical examination conducted by a calibrated investigator who obtained measurements of jaw movement, records joint sounds, and palpates muscle and joint sites to determine the classification of painful TMD or normal[9]. Examination criteria to be classified as a TMD case required pain evoked by palpation in at least 3 masticatory muscle groups or pain in the temporomandibular joint. This examination was based on the established guidelines of the RDC/TMD[31].

2.3.1. Outcome assessment: Disability—We measured pain impact using dichotomized scoring from the Graded Chronic Pain Scale (GCPS). The GCPS contains 7 items to assess pain intensity, interference in daily activities, and disability days (number of days with decreased or impaired functioning). These seven items were used to calculate five, hierarchical categories: grade 0 to grade IV[48]. Categories were subsequently dichotomized to denote low-impact (GCPS grades IIa-low or less) or high-impact (GCPS grades IIb-high or more) following the algorithm developed by Dworkin[8]. The GCPS has been used to evaluate pain-related disability in a number of research studies including studies of TMD[47, 50] and has been reported to be a reliable and valid instrument[48]. When the GCPS was published, the researchers used the term “pain-related disability” but recently the National Pain Strategy‟s Population Health Strategy for Pain report indicates that high-impact pain and pain-related disability refer to the same construct.

2.4 Explanatory variables

The multidimensionality of pain impact was assessed using variables from multiple domains. Sociodemographic data were collected upon entry (study site, age, self-reported sex and racial identity). Psychological distress variables measured positive and negative affect, catastrophizing, and somatic symptoms. Clinical pain features represent a mix of self-report measures related to jaw function such as jaw limitation and oral parafunction behaviors, and variables obtained during clinical examination. Experimental pain variables were collected during laboratory sensory testing. Although not previously explored in research addressing pain impact, experimental pain sensitivity has been linked to clinical pain expression[11]. Explanatory variables fit into four domains: sociodemographic, psychological distress, clinical pain, and experimental pain sensitivity. This categorization is consistent with domains of interest defined by OPPERA investigators[24].

2.4.1.1 Jaw mobility and painful body sites—

Examiners measured two aspects of jaw function that were not part of the RDC/TMD criteria for case classification: 1) maximum unassisted opening and 2) number of painful body sites. Instructions for the unassisted mouth opening measurement were “Open as wide as you can even if you feel pain or increase any pain you are feeling” and opening distance was measured in millimeters. To assess the number of painful body sites, pressure was applied to seven sites bilaterally including: the trapezius, supraspinatus, second rib, lateral epicondyle, medial gluteus, greater trochanter, and medial knee[31]. At each site, three pounds of pressure was applied. The respondent reported pain or no pain at each site for a sum score from 0–14.

2.4.1.2 Jaw limitation—

The Jaw Functional Limitation Scale (JFLS) is a self-administered 20-item instrument that measures limitations in three areas: chewing limitation, vertical jaw mobility or opening limitation, and limitation in verbal and emotional expression[32]. Participants were asked to rate their limitation in activities such as “chew tough bread” and “open wide enough to bite into a sandwich” using a 0 to 10 scale where 0 represented no limitation and 10 indicated severe limitation. The JFLS can also be used to calculate a combined global measure of jaw limitation. We used the global functional limitation measure as an overall summary of jaw limitation.

2.4.1.3 Oral Parafunction/Jaw overuse behaviors—

The Oral Behavior Checklist (OBC) is a 21-item instrument to assess the frequency of a variety of oral parafunctional behaviors such as grinding the teeth at night, chewing gum, and sustained talking[28]. The participants were asked to report how often they engage in these behaviors answering with ordinal responses from 0 to 4 indicating the frequency of the behavior. We used the summary score of all items.

2.4.1.4 Comorbid conditions—

Participants completed a questionnaire that asked about the presence or absence of 20 conditions: joint disease or arthritis, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, tendency to faint, ringing in ears, periodic heart racing or pounding, repeated trouble with neck, back, or spine, insomnia, depression, panic disorder, post-traumatic stress disorder, anxiety disorder, acid reflux, interstitial cystitis, prostatitis, multiple chemical sensitivity, dysmenorrhea, chronic pelvic pain, and sleep apnea. We used a sum score ranging from 0–20 corresponding to the number of conditions positively endorsed by participants.

2.4.1.5 Duration—

Participants reported the time (in years and months) since facial pain began. Duration was intended to measure the time since initial onset of the condition and not the time elapsed during the most current pain episode. A separate question was asked of participants to describe the pattern of duration of pain using the following categories: persistent, recurrent, or a single episode that had since ended.

2.5 Psychological Distress

2.5.1 Positive and Negative affect—

Participants completed the Profile of Mood States-Bipolar (POMS-Bi), a 72-item inventory used for assessing mood profiles. The scoring produces 6 dissimilar phases of mood that can be summed into two scores: overall

positive affect and overall negative affect[29]. These scores capture the multiple domains assessed with the POMS-Bi including feelings of confidence, confusion, hostility, anxiety, and depression. We hypothesized the negative summary score would encapsulate anxiety and depression that may be associated with high-impact pain.

2.5.2 Catastrophizing—Catastrophizing was classified according to the catastrophizing subscale of the Coping Strategies Questionnaire (CSQ-R). The CSQ-R is a revised version of the original CSQ[37] which consists of 27 items relating to how individuals cope with pain. Participants indicate the frequency with which they engage in specific coping activities when experiencing pain, using a 7-category numerical scale ranging from 0 (never do that) to 6 (always do that). The catastrophizing subscale is comprised of 6 questions indicating negative statements such as “I worry all the time about whether it will end”. This subscore addresses the concept of pain-related worry previously reported to be associated with high levels of pain-related disability[20].

2.5.3 Somatic symptoms—Participants completed the Symptoms Checklist 90-Revised (SCL-90R), a 90-item self-report inventory of symptoms the participant may have experienced. Participants were instructed to answer how much each problem distressed or bothered them during the past 7 days with the following ordinal scale: not at all, a little bit, moderately, quite a bit, or extremely. These items were scored 0 to 4 accordingly. The SCL-90R includes a somatization subscale that consists of questions about headaches, chest pain, lower back pain, nausea, sore muscles, faintness, trouble getting your breath, hot or cold spells, numbness, a lump in the throat, feeling weak in parts of the body and feeling heaviness in arms or legs[5].

2.6 Experimental pain

2.6.1.1 Thermal tolerance—A commercially available thermal stimulator (Medoc, Israel) was placed on the participant‟s arm, producing temperature increasing at a steady rate of 0.5ºC/second. Participants were asked to click a mouse button when they no longer wished to tolerate the pain from the heat and this temperature was recorded as the thermal tolerance. This procedure was repeated four times and the average was recorded as the participant‟s thermal tolerance.

2.6.1.2 Pressure pain threshold—Pressure pain thresholds (PPTs) were measured using a pressure algometer (Somedic, Sweden) placed on multiple body sites. The participants were given instructions to press a button when he/she first felt a sensation of pain from pressure. The rating is a single number, the average from two ratings on each side of the body reported in kilopascal units of pressure. For the analysis reported here, we used the pressure threshold measured on the trapezius. This site was selected to capture pain sensitivity outside the orofacial area. The trapezius site has been defined as a fibromyalgia tender point[49] and therefore may be a marker for widespread body pain. Interexaminer reliability of PPT was formally assessed and found to demonstrate a very good level of reliability across examiners and study sites (overall intraclass correlation coefficient=0.91) [16].

2.6.1.3 Mechanical pain rating and mechanical temporal summation—

Mechanical pain ratings and temporal summation of mechanical pain were assessed using a flat-tipped weighted pinprick stimuli applied to the skin. Participants were asked to rate the sensation from the weighted stimuli using the 0–100 pain intensity scale. Temporal summation of pricking pain was tested with the weighted mechanical probe applied in a series of ten applications over 10 seconds. Again, participants were asked to rate the pain intensity evoked by the series of stimuli using the 0–100 scale. Temporal summation was calculated as the difference between the rating of the series-of-10 stimuli and the rating of the single stimulus.

2.6.2 Data analysis—The outcome of interest was dichotomous pain-related disability score, classified using the GCPS. Student‟s t-tests were used to compare the mean values of continuous variables between low and high disability groups. Correlations between pairs of continuous variables were computed using Spearman‟s rank correlation coefficient to identify variables that should be excluded from analysis due to potential for multi-collinearity. There were no variables with correlation higher than 0.7 thus none were excluded. For descriptive purposes, tertiles of continuous variables were used to establish low, medium, and high-levels because category cut-points have not been previously defined. Categorical variable classification was used for frequency and stratified analysis by study site, sex, and race.

Binary logistic regression was used to evaluate associations between high-impact pain and the variables comprising sociodemographic, psychological distress, clinical pain, and experimental pain domains. Prevalence odds ratios from logistic regression were used to calculate area under the ROC curve (AUC) statistics in order to provide a simple numeric summary of a multivariable model‟s ability to discriminate between people with low- vs high-impact pain. To address the problem of overfitting when calculating AUC, we used a cross-validation method for estimating prediction error by creating divisions of the dataset for training and validation of the fitted model. The process involves simulation of model fitting without observations and then using that model-fit result to compute the result for the previously excluded observations[34]. Cross-validation is a more efficient substitute for the classic method of splitting a dataset and using one section to create the predictive model and then testing the model in the other section.

The model building strategy started with a model including only sociodemographic variables. Subsequent models explored the additional contributions of variables corresponding to the following domains: psychological distress (model 2), clinical pain (model 3), and experimental pain (model 4). Model 2 included model 1 variables plus psychological distress variables: positive and negative affect scores, somatization subscale, and catastrophizing subscale. Model 3 included all variables from previous models with the addition of clinical pain variables: JFLS global score, OBC summary score, maximum unassisted opening, number of painful body sites, duration of condition, and the number of comorbid pain conditions. Model 4 included all variables from previous models with the addition of experimental pain sensitivity testing results: thermal tolerance, pressure pain threshold of the trapezius, pain rating of mechanical stimulus, and mechanical stimuli windup.

Akaike Information Criterion (AIC) and Bayesian Information Criteria (BIC) were used to compare model fit. The AIC provides information about goodness of fit among these models. The BIC penalizes for more variables in the model and thereby complements the AIC by addressing the potential estimate inflation as the number of parameters increases. The model with the lowest BIC can be interpreted as the model with the maximum posterior probability[36]. The model with the highest cross-validated AUC represents the best model for discriminating between people with low- or high-impact pain. We considered an increase in AUC equal to or greater than 0.05 to indicate a substantial change. Deleting variables and assessing the AUC for change in estimate quantified the role of individual variable contribution to the model. This process resulted in the selected model (model 5). Statistical significance of the difference between two models was also measured to compare the models. Sensitivity and specificity were calculated for each model using predicted probabilities at the cut point of observed prevalence of high-impact pain.

To address potential sex differences indicated by previous research, the sample was stratified by sex and selected models were re-run in each population. Changes in the AUC between males and females would indicate a need to develop separate models based on sex.

We used SAS software Version 9.4 of the SAS System for Windows to perform all analyses. Copyright © 2012 SAS Institute, Cary, NC.

2.6.3 Missing data—Figure 1 shows the STROBE diagram of missing data from the sample of 1088 people, resulting in the final complete case sample restricted to 846 people. Participants with any missing data for the variables included in the modeling procedure were excluded from all analyses. Only 4% of the full sample exhibited missing data for the outcome of interest. Sample B shows restriction to the 99% of the sample that had complete data for addressing psychological distress variables (n=13). Sample C is restricted to 95% of Sample B when people with missing data about clinical pain features (n=52) were excluded. The final study sample was 87% of Sample C as the largest exclusion was due to missing experimental pain data (n=131). The percentage of participants with missing data were compared between low- and high-impact pain groups, according to variables used in the analyses. Chi-square tests were used to evaluate differences between groups. Individual items missing from questionnaires were imputed using the expectation-maximization (EM) algorithm in the datasets available for this analysis. OPPERA investigators describe the method in the following way: “In general, if a subject skipped at least 1 but less than half the items in a questionnaire, the missing items were imputed. If they failed to complete at least half of the items in the questionnaire, we treated their summary score as missing”[12].

3 Results

3.1 Descriptive data

One third of the study participants (33.5%) reported characteristics consistent with high-impact pain indicating interference with their day-to-day activities. The median age of participants was 28.0 years (SD 7.8). The ratio of female to male participants in both categories of disability was 3:1. Over 70% of the sample identified as white, while 14% of the sample identified as Black or African American.

Forty-one percent of the low-impact sample was in the 18–24 age range while 30% of the high-impact group was in this age category (Table 1), indicating older people were more likely to experience high-impact pain. There were race/ethnicity differences by impact with 76% of the low-impact group identifying as white while 62% of the high-impact group was white. Twenty-five percent of the high-impact group identified as Black or African American. Sex distribution by impact was very similar. There were more women than men in the sample of cases, with the 3:1 female to male ratio observed in both low and high-impact groups. People with low-impact pain scored higher on the POMS positive affect scale and lower on the negative affect scale. The low-impact group demonstrated lower scores in catastrophizing, somatic symptoms, jaw functional limitation, and oral parafunction behavior compared with the high-impact group. Other variables did not present with a monotonic relationship among the low, medium and high groups. The percentage of people with the lowest number of painful body sites among people with low impact was 35%, then 37% in the medium group and 28% for the highest group while the high impact group was distributed in the low, medium, and high categories at 32, 25, and 45% respectively.

The mean history of orofacial pain was 7.0 years (SD 6.4). Among people with high-impact pain, the mean duration was 7.4 years while the low-impact group had a mean duration of 6.7 years with standard errors of 7.6 and 8.0 years respectively. Approximately 70% reported having ever seen a health care provider for facial pain. Among people with high compared to low-impact the frequency of reported treatment seeking was 76% and 67% respectively (not shown).

Among people with high-impact pain, the mean number of painful body sites was 7 while people with low-impact indicated a mean of 5 sites (rounded to the nearest whole number to represent pain sites). Table 2 shows people with low-impact pain reported one less painful condition from the 20 conditions compared to people with high-impact pain. Experimental pain testing results indicated people with low-impact pain had slightly higher thermal tolerance ($p=0.029$), higher pressure pain thresholds ($p=0.001$). The mechanical probe pain ratings were lower among the low-impact pain group ($p<0.001$), and the low-impact group demonstrated less mechanical temporal summation compared to the high-impact group ($p=0.001$).

3.2 Comparison of models

The initial multivariate model included sociodemographic variables: race, age, sex, and study site. These variables represent the minimum of controlling for study design and sociodemographic characteristics that may be associated with high-impact pain compared to models accounting for multidimensional aspects of high-impact pain. The area under the curve (AUC) of model 1 was 0.61 (Table 3), somewhat better than chance (0.50). Self-reported race was associated with parameter estimates of high-impact pain with individuals identifying as Black or African American more likely to experience high-impact pain compared to people who identified as white. People who identified as Asian, Hispanic, other or multiple racial or ethnic groups did not have elevated estimates of high-impact pain. There did not appear to be an effect of age or gender. Compared to the Chapel Hill study

site, people living in Gainesville had similar odds of high-impact pain while people living in either Buffalo or Baltimore had higher odds of high-impact pain.

Model 2 was comprised of 8 variables: 4 variables from model 1 plus 4 variables representing psychological distress: overall positive affect and negative affect scores from the POMS, the SCL-90R somatization subscale and CSQ-R Catastrophizing subscale score. While the POMS scores seemed to have no contribution to increasing the AUC, increased somatization and catastrophizing scores were associating with increased pain impact.

Model 3 included all variables from model 2 with the addition of 6 variables measuring clinical pain features including the combined global jaw functioning limitation score, oral behavior checklist, jaw opening, number of painful body sites, number of comorbid conditions, and duration of pain. Among the added variables, increases in jaw functional limitation and number of painful body sites were the only variables associated with an increase in impact. Model 4 is the full model, including all variables in model 3 plus the 4 experimental pain testing variables: thermal tolerance, pressure pain threshold, mechanical pain rating, and mechanical pain windup. Although temporal summation of mechanical pain and mechanical pain rating had different means between low versus high-impact groups in univariate analyses, the logistic regression model showed no increase in the AUC when experimental pain testing variables were added.

Based on the findings of the hierarchical model building process, we constructed a parsimonious selected model (model 5) designed to achieve the highest AUC with the lowest number of variables. This model included sociodemographic variables, catastrophizing, jaw limitation, and painful body sites. Though age and gender were not associated with impact, these variables were retained in the selected model because they have been identified as variables of interest in prior research. Also, though somatic symptoms were associated with high impact, removing this variable from the selected model did not cause a reduction in the AUC. Table 4 shows the results from all 5 models and Figure 2 shows all curves. There was overlap in the 95% confidence intervals for AUC from models 2, 3, 4, and the selected model. The chi-squared p-value comparing model 4 to the selected model and model 3 to the selected model were not statistically significant ($p=0.83$ and $p=0.64$ respectively).

Because models 3 (the model containing all sociodemographic, clinical pain and psychological distress variables) and 4 (the full model) were so similar in cross-validated AUC (Figure 2), we turned to model BIC and AIC to assess model fit. The AIC decreased from 1001 (model 2) to 872 with the addition of clinical variables (model 3). The smaller value, indicating better fit, did not fluctuate much with the addition of the experimental pain sensitivity variables (model 4) or the reduction in variables in the selected model (AIC= 871). The BIC decreased with the addition of mood variables (936), and again slightly with clinical variables (967), but increased with experimental pain variables indicating the penalty for additional variables that did not increase the model fit. The selected model had the lowest BIC (933).

Finally, when we ran models 4 and 5 stratified by sex, we found the AUC from model 5 was identical for both men (n=194) and women (n=652). When model 4 was performed with sex

stratification, the differences were in the third decimal place (women AUC=0.7717 and male AUC=0.7752).

3.3 Missing data results

Approximately 22% had incomplete data for one or more variables used in this analysis (supplementary material Table A). There was some variation in the percentage with incomplete data among racial groups, with African Americans having the most incomplete data. People in the oldest age group (35 and over) had the most incomplete data but there were no differences by sex. The Chapel Hill study site had the most incomplete data. The percentage of people with incomplete data increased as catastrophizing increased ($p=0.02$) and differed according to jaw function ($p<0.01$), although not in a monotonic manner. There was no statistically significant difference between missing and complete data by positive and negative affect scores, somatization score, oral behavior checklist sum score, maximum unassisted opening, reported duration of pain, pressure pain threshold, or mechanical pain testing.

Frequency of incomplete data varied according to the number of painful body sites and the number of comorbid painful conditions. There was less missing data in the highest thermal tolerance category. In summary, missing data was related to overall increased severity and symptoms, indicating that individuals with more comorbid pain conditions may have been less likely to complete all study components.

Because we performed complete case analysis, the sample was limited to n=846. As the selected model did not include experimental pain testing results which were the variables accounting for the most missing data, the model was repeated using the original sample with missing data only from the variables included in the model. This yielded a sample of n=1014 and an AUC of 0.79, 95% CI (0.76, 0.82) and BIC=1115. The results of multiple imputation for model 4 (the full model) was 0.80 (with individual imputations AUC ranging from 0.79 to 0.80), 95% CI (0.77, 0.83), SE=0.01. These results are nearly identical to results from the complete case analysis. We performed a sensitivity analysis using data from a more complete sample (Sample B in Figure 1). The results of the selected model in this larger population (n=1014) were the same AUC. We also performed multiple imputation and we found the AUC measure to be robust.

4 Discussion

4.1 Key Results

This is the first large study to identify variables that distinguish between high and low-impact pain among community-dwelling people with TMD. We found that catastrophizing, jaw functional limitation, and tenderness to body palpation were useful tools for discriminating between high- and low-impact pain. Specifically, people with TMD who reported greater pain catastrophizing, increased jaw limitation, and more painful body sites were more likely to experience high-impact pain than low-impact pain. Our selected model containing sociodemographic variables, catastrophizing, jaw limitation, and painful body sites performed as well as the full model with all 18 variables. The high-performing selected

model with 3 major contributors represents a simplified model of high-impact pain focused on 3 unique characteristics that can easily be evaluated in a clinical setting.

4.2 Interpretation

It is important to note that, even though we used a predictive modeling approach, the parameter estimates cannot be interpreted as causal as the data is cross-sectional and we have not controlled for confounding. The model building strategy was designed to assess the contribution of variables to the ability to discriminate between high- and low-impact pain, therefore the goal was the highest AUC achieved with the simplest model. Consistent with the TRIPOD statement[30], we have produced the first step in prediction by testing predictive performance in one data set. The large cross-sectional study provided an adequate number of chronic TMD cases in order to make multiple comparisons by identified variables of interest. The next step for understanding the etiology of pain impact requires a longitudinal setting that should be informed by the findings presented here.

Previous research implicated depression, pain duration, female gender, and somatization[26] as contributors to pain-related disability. We found no effect of gender or pain duration on pain impact. Restricting the sample by sex and running both the full and selected models further explored the effect of gender and found no differences. John[19] reported widespread body pain defined as self-reported pain in the head, back, stomach, or chest to be a risk factor for maintaining high GCPS scores and incidence of high GCPS at 1 to 2-year follow-up among women with TMD at baseline. After controlling for age, education, depression, and baseline GCPS, the authors found widespread pain was a risk factor for dysfunctional TMD (OR=1.9).

Our study supports the conclusion that widespread body pain is associated with higher GCPS scores, an effect we observed in both men and women. In a well-designed study with community and dental clinic recruitment, Velly and colleagues conducted an 18-month prospective study of TMD among 480 people with the aim of evaluating the effects of catastrophizing and depression on the progression of pain-related disability using the GCPS. They found disability score at follow-up was associated with baseline catastrophizing, depression, and widespread body pain at baseline[46]. No significant association was noted with sex or age, which is consistent with our findings. A small association was observed between widespread pain and disability. In contrast to our findings, the authors used the Beck Depression Inventory whereas we used the POMS-BI negative affect subscale. The use of different instruments may account the discrepancy between findings. Additionally, only 12% of the study population (n=70) at baseline and only 54 people met the high-GCPS criteria used for disability. This limited number of people with high-impact pain could have limited the statistical power needed to draw conclusions.

A 6-month study of 152 RDC verified TMD patients; Galli found that GCPS score at baseline was the only significant predictor of GCPS score at follow-up. Pain-related disability could be predicted at 3-month follow up by depression and anxiety scales, but this trend did not hold for 6-month follow-up[13].

We found Black or African American people were more likely to experience high-impact pain compared to other racial or ethnic categories including Asian, Hispanic, and Caucasian. Previous research has identified racial difference in clinical as well as experimental pain[10]. In univariate analyses, people who identified as Black or African American were older than participants from other racial groups and reported higher scores on catastrophizing and jaw limitation, but not more painful body sites. In a model of pain impact using race as the single predictor, people identifying as Black or African American had 3.5 times the odds of having high-impact pain compared to whites (AUC=0.34, 95% CI (2.4, 5.2)). Univariate findings suggest that African Americans in this sample were more likely to report features that we found associated with high-impact pain. However, the relatively small number of African Americans in the sample (n=120) is a limitation of this finding. Future research is needed to address race inequalities and pain impact to understand this relationship.

4.3 Limitations

The cross-sectional design, age range, potential for unmeasured variables, the difficulty assessing somatization, and missing data are limitations of this study. As discussed above, the cross-sectional design does not permit conclusions about whether or not high-impact pain is caused by functional limitation and catastrophizing or if the reverse could be true. The age range of 18–44 is a limitation because the sample over-represents younger people with TMD. The narrow age range of participants is not representative of the entire population living with chronic orofacial pain.

There is the possibility that unmeasured variables would have improved the performance of the predictive model. Potential unmeasured variables that may have contributed to a higher AUC in the model could include social support, socioeconomic status, sleep quality, medications, or factors as yet unknown.

Somatic symptoms were of interest because somatization has been associated with pain-related disability in previous research[3, 22], but the specific measurement of somatization in this study heavily influenced the decision to exclude it from the final model. A randomized controlled trial of 101 community-dwelling people with TMD assessed the effects of cognitive behavior therapy (CBT) at multiple time points after treatment and found somatization moderated the effect of treatment on pain-related interference[23]. That study used the same measure of somatization that we used: the SCL-90R. Our findings are consistent with previous research findings identifying an association with the SCL-90R somatization scale and high-impact pain, but the somatization scale was not included in the final model because the measure did not improve the AUC and other measures of somatization analyzed were not associated with high-impact pain (results not shown).

Missing data were an issue that required careful attention. Our examination of missingness was illuminating in two ways. We observed potential patterns in the data related to missingness and severity of the condition or symptoms. Based on sensitivity analysis and multiple imputation results, we conclude that the AUC is a robust measure that remained unchanged under different approaches to address missingness. If missing data was related to severity of pain or pain-impact, then it is difficult to conclude if we would expect bias towards or away from the null without knowing the reason for the missingness. For example,

if people with high-impact pain have more missing data for catastrophizing items and if they would have endorsed higher levels of catastrophizing, then we can conclude that missing data has resulted in a bias towards the null by tempering the association between pain impact and catastrophizing.

4.4 Generalizability

A major strength of this study is the community-dwelling sample. As opposed to a clinical sample recruited from tertiary pain clinics, participants in this study represent varying levels of treatment seeking and therefore, the results should be generalizable to the larger population of people with painful TMD. There is still potential for bias in this study. It is likely that residents dwelling around major academic centers can be different from residents dwelling randomly in the community. In addition, study participants in this article are responders to the advertisement, thus there can be selection bias involved. If people with high-impact TMD were more likely to respond to advertisements and participate in this study, then we may have overestimated the prevalence of high-impact TMD. If people with high-impact TMD did not participate in this study because the 3-hour appointment was too burdensome or for another reason, then we have not been able to assess those people. Approximately 70% of the sample reported having ever seen a healthcare provider for facial pain. The frequency of reported treatment seeking was 75.9% and 66.6% among people with high - and low-impact pain, respectively. This result points to the conclusion that almost a quarter of people meeting the criteria for high-impact pain reported never having seen a healthcare provider for treatment.

A second strength of our approach is the unique comprehensive assessment of study participants. In addition to self-reported questionnaire data, we were able to include examiner collected data and experimental pain sensitivity testing data. The diverse data collection allowed for a thorough assessment of multiple dimensions that could influence pain outcomes. Although experimental pain testing may have usefulness in clinical practice as demonstrated for identifying subgroups of patients[2] or predicting post-operative pain[15], our results support the conclusion that experimental pain testing has limited ability to differentiate high from low-impact TMD pain.

4.5 Conclusion

The Federal Strategy for Pain report says: “*High-impact chronic pain* is associated with substantial restriction of participation in work, social, and self-care activities for six months or more”[45]. The report recommends an assessment of high-impact pain based on the response to 3 questions about how often people experience interference due to pain in “usual work, regular social and recreational activities, and taking care of myself” with the answers never, rarely, sometimes, usually or always. Based on this scale, high-impact chronic pain is defined as at least one of the 3 items rated “usually” or “always”. The difference in this proposed method and the GCPS used in our research is the GCPS asks participants to rate extent, rather than frequency, of interference on the 0 to 10 scale and the GCPS classification is also based on pain intensity and work days missed.

Managing high-impact pain is imperative for clinicians treating chronic TMD. Information about characteristics associated with high-impact pain therefore is valuable clinically for targeting and modification to improve patient outcomes. Several research studies have produced evidence that CBT and biofeedback training may reduce pain impact[8, 14, 43]. Patients who received combined CBT and biofeedback training experienced greater change in pain-related disability measured with the GCPS compared to the control group[14]. When "usual treatment" (described as typically physiotherapy, patient education, medications, and occlusal appliance therapy) was compared with usual treatment plus a 6-session cognitive behavioral intervention, researchers found pain-related interference was reduced among those receiving CBT but the benefit was temporary[8]. In a sample of 115 TMD patients, researchers reported pain-related beliefs mediated CBT effects on disability at one-year follow-up[43].

The current study demonstrated an association between catastrophizing, jaw functional limitation, and painful body sites with high-impact pain while gender, duration of condition, and experimental pain sensitivity were not associated with high-impact pain. We found one third of people with chronic TMD experienced high-impact pain and that catastrophizing, jaw limitation, and painful body sites were associated with high-impact pain while pain duration, gender, and experimental pain sensitivity were not. This finding is consistent with the hypothesis that pain impact is a complex construct associated with clinical pain features as well as ability to cope with pain. Assessing catastrophizing and jaw functional limitation requires two brief questionnaires while assessing painful body sites can be performed with a brief physical exam. Understanding and improved targeting of catastrophizing, jaw limitation, and body pain for therapeutic intervention is important to reduce the impact of pain among people with chronic TMD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AIC	Akaike information criterion
BIC	Bayesian information criterion
AUC	Area under the curve
CBT	Cognitive behavior therapy
CI	Confidence interval
CSQ	Coping Strategies Questionnaire

GCPS	Graded Chronic Pain Scale
JFLS	Jaw Functional Limitation Scale
OBC	Oral Behavior Checklist
POMS	Profile of Mood States-Bipolar
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorder
ROC	Receiver operating characteristic
SCL_90	Symptom Checklist 90r
SD	Standard deviation
SE	Standard error
TMD	Temporomandibular Disorder

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Highlights:

1. One third of people with temporomandibular disorder (TMD) had high-impact pain
2. High-impact pain was distinguished by catastrophizing and clinical features of TMD
3. Pain sensitivity and duration of TMD did not distinguish high vs. low impact pain

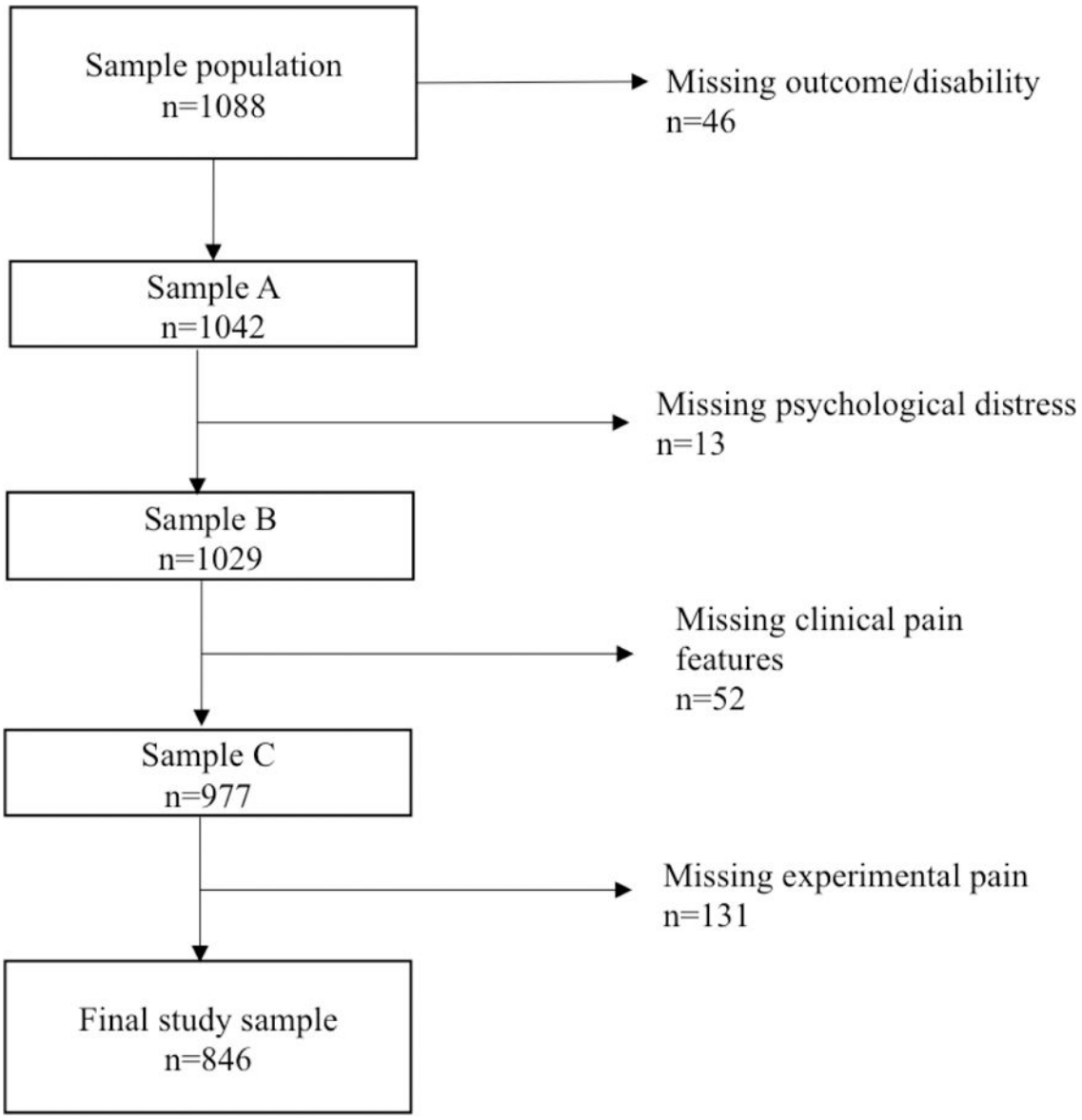

Figure 1.
Diagram showing exclusion of missing data by domain

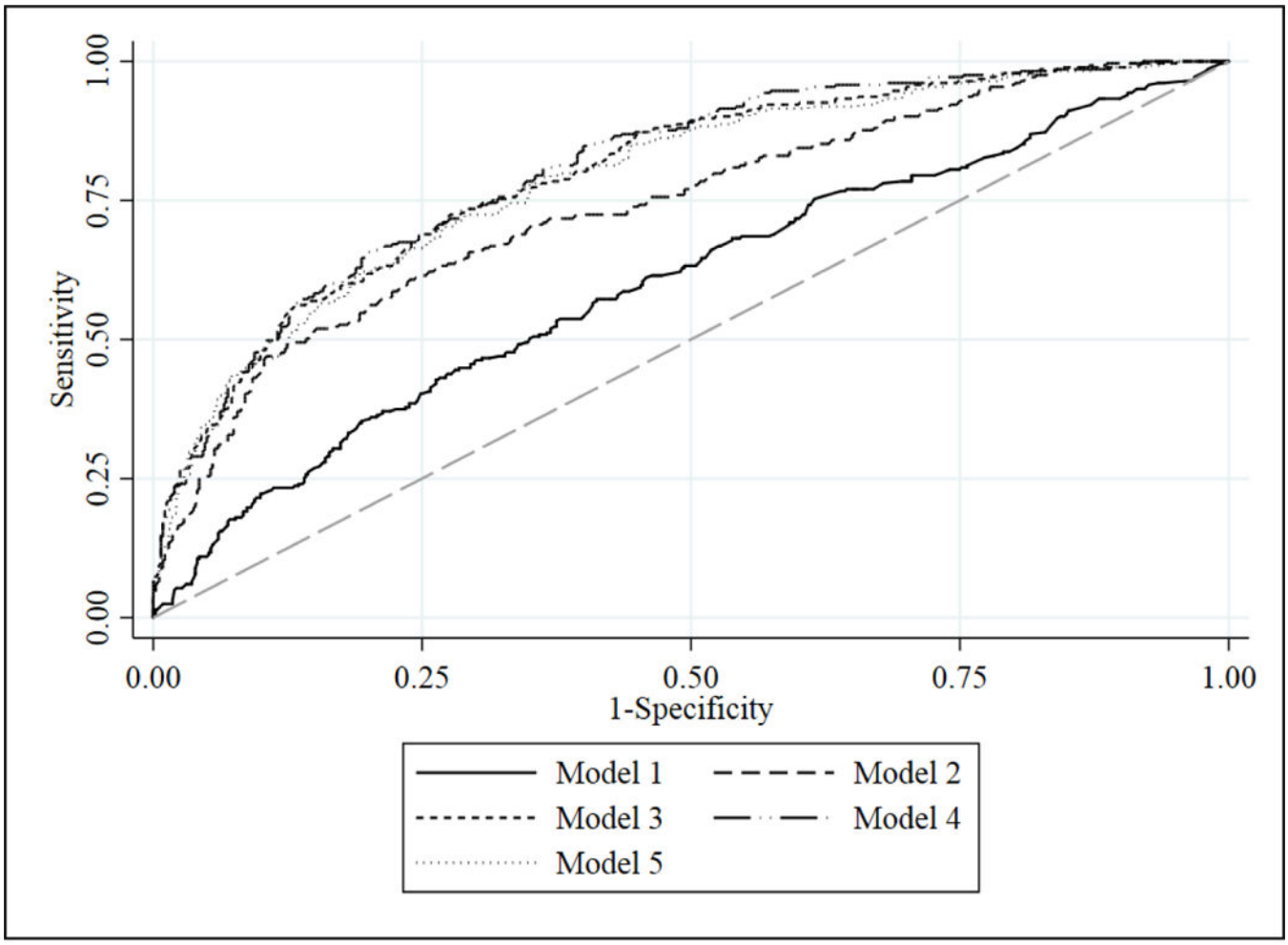

Figure 2.

The cross-validated AUCROC comparing the selected model to models with demographic variables and patient characteristics. The full model is shown as the first model, represented by a solid line. Model 1 includes race, gender, age, and study site. Model 2 includes demographics plus mood variables. Model 3 includes demographics plus mood and clinical variables. The selected model includes race, age, gender, study site, catastrophizing, JFLS score, and number of painful body sites.

Table 1.

Demographic and clinical characteristics of the sample of people with chronic TMD. Pain-related disability classification: high-impact is GCPS II-high, III, IV (n=283) and low-impact is GCPS I and II-low (n=563).

		Low-Impact Pain (n=563)		High-Impact Pain (n=283)	
	Total	**N**	**%**	**N**	**%**
Race/Ethnicity					
White	604	429	76.2	175	61.8
Black/African American	120	49	8.7	71	25.1
Asian	38	29	5.2	9	3.2
Hispanic	56	38	6.8	18	6.4
Other	28	18	3.2	10	3.5
Age (years)					
18–24	314	229	40.7	85	30
25–34	305	205	36.4	100	35.3
35–44	227	129	22.9	98	34.6
Sex					
Male	194	126	22.4	68	24
Female	652	437	77.6	215	76
Study site					
UNC	239	177	31.4	62	21.9
UB	201	122	21.7	79	27.9
UF	237	173	30.7	64	22.6
UMD	169	91	16.2	78	27.6

Abbreviations: UNC= University of North Carolina at Chapel Hill; UB=University of Buffalo, NY; UFL=University of Florida at Gainesville; UMD=University of Maryland at Baltimore

Table 2.

Continuous variables in the sample of people with chronic TMD by pain impact classification. Low-impact is GCPS I and II-low and high-impact is GCPS II-high, III, and IV.

	Total		Low-impact pain		High-impact pain		Comparison
	Mean	SD	Mean	SD	Mean	SD	P-value†
Age (years)	29.0	7.8	28.2	7.6	30.5	8.0	<0.001
POMS: Overall positive affect*	80.7	16.2	82.0	15.8	78.0	16.7	0.008
POMS: Overall negative affect*	58.2	18.8	56.0	17.5	62.6	20.4	<0.001
Catastrophizing*	0.7	0.6	0.6	0.5	1.0	0.7	<0.001
Somatization*	1.4	1.2	1.1	1.1	2.0	1.3	<0.001
JFLS global measure*	2.0	1.5	1.6	1.3	2.9	1.7	<0.001
OBC total score*	32.8	11.0	31.9	10.2	34.7	12.2	0.001
Maximum unassisted opening (mm)	46.9	8.9	47.3	8.4	46.2	9.8	0.085
Number of painful body palpation sites	5.8	4.0	5.4	3.6	6.6	4.5	<0.001
Number of pain comorbid conditions	2.6	2.6	2.2	2.1	3.6	3.0	<0.001
Duration of pain (years)	6.9	6.4	6.7	6.2	7.4	6.7	0.155
Thermal tolerance (^{o}Celsius)*	45.6	2.4	45.7	2.3	45.3	2.5	0.029
Pressure pain threshold: trapezius (kPa)*	278.8	125.0	288.5	127.9	259.5	116.7	0.001
Mechanical probe pain rating*	11.8	14.8	10.3	11.9	15.0	19.0	<0.001
Mechanical Temporal summation*	13.4	14.5	12.1	13.0	15.8	16.8	0.001

Abbreviations: POMS, Profile of Mood States: Bi-polar Form; JFLS, Jaw Functional Limitation Scale; OBC, Oral Behaviors Checklist

*Variable includes imputation of up to 50% missing items

†P-value from t-test comparing low- and high-impact pain groups

Table 3.

Results of binary logistic regression models predicting presence of high-impact pain

	Demographic only	Model 1 + psychological distress	Model 2 + clinical pain features	Model 3 + experimental pain sensitivity	Selected model
Number of subjects	846	846	846	846	846
AUC	0.65	0.76	0.81	0.82	0.8
AUC cross validated	0.61	0.74	0.79	0.79	0.79
95% CI	0.57, 0.65	0.70, 0.77	0.75, 0.82	0.75, 0.82	0.76, 0.82
SE	0.02	0.02	0.02	0.02	0.02
Model BIC	1088.36	935.53	967.32	985.68	932.53
Model AIC	1040.95	1001.9	872.51	871.9	870.9
Race (ref= white)					
Asian	0.92 (0.40, 1.94)	0.86 (0.34, 1.96)	0.99 (0.38, 2.36)	0.86 (0.32, 2.08)	1.00 (0.38, 2.34)
Black	2.83 (1.83, 4.39)	2.64 (1.64, 4.28)	2.74 (1.63, 4.63)	2.39 (1.40, 4.10)	2.72 (1.64, 4.54)
Hispanic	1.24 (0.67, 2.22)	1.19 (0.61, 2.25)	1.24 (0.63, 2.39)	1.09 (0.54, 2.11)	1.22 (0.62, 2.34)
Other	1.38 (0.59, 3.03)	1.32 (0.55, 3.03)	1.36 (0.52, 3.32)	1.23 (0.47, 3.09)	1.39 (0.54, 3.41)
Age	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)	1.02 (1.00, 1.05)	1.03 (1.00, 1.06)	1.02 (1.00, 1.05)
Sex (ref=male)					
Female	1.07 (0.75, 1.54)	1.07 (0.72, 1.60)	0.92 (0.59, 1.45)	0.90 (0.57, 1.45)	0.84 (0.55, 1.30)
Study site (ref=UNC)					
UB	1.68 (1.12, 2.55)	1.29 (0.82, 2.04)	1.35 (0.83, 2.19)	1.48 (0.91, 2.41)	1.35 (0.84, 2.18)
UF	1.06 (0.69, 1.61)	1.04 (0.66, 1.63)	1.18 (0.74, 1.90)	1.14 (0.69, 1.88)	1.16 (0.73, 1.86)
UMD	1.70 (1.09, 2.67)	1.49 (0.92, 2.43)	1.72 (1.00, 2.95)	1.74 (1.00, 3.03)	1.70 (1.00, 2.91)
POMS: Overall Positive Affect *		1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	
POMS: Overall Negative Affect *		1.00 (0.99, 1.01)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)	
Somatization *		2.04 (1.47, 2.84)	1.54 (1.04, 2.30)	1.52 (1.02, 2.26)	
Catastrophizing *		1.59 (1.37, 1.84)	1.45 (1.24, 1.70)	1.46 (1.24, 1.71)	1.46 (1.25, 1.70)
JFLS Global Measure *			1.63 (1.44, 1.86)	1.63 (1.44, 1.87)	1.59 (1.41, 1.79)
OBC total score *			0.99 (0.98, 1.01)	0.99 (0.98, 1.01)	
Maximum unassisted opening			1.01 (0.99, 1.04)	1.01 (0.99, 1.04)	
Number of painful body sites			1.08 (1.03, 1.13)	1.07 (1.01, 1.13)	1.08 (1.03, 1.13)
Number of comorbid conditions			1.03 (0.95, 1.13)	1.02 (0.94, 1.12)	
Duration of pain (years)			1.00 (0.97, 1.03)	1.00 (0.97, 1.03)	
Thermal tolerance (oCelsius)				0.99 (0.92, 1.08)	
Pressure pain threshold *				1.00 (1.00, 1.00)	

	Demographic only	Model 1 + psychological distress	Model 2 + clinical pain features	Model 3 + experimental pain sensitivity	Selected model
Mechanical probe pain rating *				1.01 (0.99, 1.02)	
Mechanical temporal summation *				1.02 (1.00, 1.03)	

Abbreviations: AUC, Area under the curve; CI, confidence interval; BIC, Bayesian information criteria; AIC, Akaike information criteria; UNC, University of North Carolina at Chapel Hill; UB, University of Buffalo, NY; UF, University of Florida at Gainesville; UMD, University of Maryland at Baltimore, POMS, Profile of Mood States: Bi-polar Form; JFLS, Jaw Functional Limitation Scale; OBC, Oral Behaviors Checklist; kPA, kilopascals

*Variable includes imputation of up to 50% missing items

Table 4.

Comparison of models

ROC Model	AUC	SE	Sensitivity	Specificity	LCL	UCL	BIC
Model 1 (4 variables)	0.612	0.02	48.4%	67.1%	0.57	0.65	1088.36
Model 2 (8 variables)	0.736	0.02	62.2%	72.8%	0.70	0.77	953.53
Model 3 (14 variables)	0.785	0.02	67.1%	75.3%	0.75	0.82	967.32
Model 4 (18 variables)	0.786	0.02	67.1%	75.1%	0.75	0.82	985.68
Selected model (7 variables)	0.787	0.02	67.1%	75.5%	0.76	0.82	932.53

Model 1 includes race, age, gender, and study site. Model 2 includes model 1 variables and mood variables. Model 3 includes model 2 variables and clinical jaw features. Model 4 includes model 3 variables and experimental pain testing. Selected model includes model 1 and JFLS, catastrophizing, and number of painful body sites. Sensitivity and specificity were calculated using the cutpoint of predicted probability that coreesponded with the observed prevalence of high-impact pain