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Study Methods, Recruitment, Sociodemographic Findings, and Demographic Representativeness in the OPPERA Study

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Abstract: **This paper describes methods used in the project "Orofacial Pain Prospective Evaluation and Risk Assessment" (OPPERA) and evaluates sociodemographic characteristics associated with temporomandibular disorders (TMD) in the OPPERA case-control study. Representativeness was investigated by comparing sociodemographic profiles of OPPERA participants with population census profiles of counties near study sites and by comparing age and gender associations with TMD in OPPERA and the 2007 to 2009 US National Health Interview Survey. Volunteers aged 18 to 44 years were recruited at 4 US study sites: 3,263 people without TMD were enrolled into the prospective cohort study; 1,633 of them were selected as controls for the baseline case-control study. Cases were 185 volunteers with examiner-classified TMD. Distributions of some demographic characteristics among OPPERA participants differed from census profiles, although there was less difference in socioeconomic profiles. Odds of TMD was associated with greater age in this 18 to 44 year range; females had 3 times the odds of TMD as males; and relative to non-Hispanic-Whites, other racial groups had one-fifth the odds of TMD. Age and gender associations with chronic TMD were strikingly similar to associations observed in the US population. Assessments of representativeness in this demographically diverse group of community volunteers suggest that OPPERA case-control findings have good internal validity.**

Perspective: ***Demographic associations with TMD were consistent with population benchmarks and with other studies, suggesting broad applicability of these OPPERA findings. Greater occurrence of TMD in non-Hispanic-Whites than in other racial/ethnic groups and the lack of a socioeconomic gradient contradicts the disparities seen in many other health conditions.***

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The project "Orofacial Pain: Prospective Evaluation and Risk Assessment" (OPPERA) was designed to identify a broad range of genetic, physiologic, psychosocial, and clinical characteristics that influence development of painful temporomandibular disorders (TMD). Implicitly, putative risk factors should be understood within the context of sociodemographic factors associated with TMD. Hence, OPPERA's first specific aim was to determine whether sociodemographic characteristics generally considered predictive of TMD are associated with elevated risk of first-onset TMD and with increased odds of chronic TMD.

Because they are fundamentally related to causes of ill health, age, gender, race, and ethnicity feature prominently in the design and analysis of virtually all epidemiologic studies. Some studies limit the potential impact of demographic characteristics by restricting enrollment to 1 demographic subgroup or by matching when selecting cases and controls. Other studies apply statistical adjustments for demographic characteristics during data analysis. The scientific rationale stems from the fact that demographic characteristics determine exposure to a range of risk factors and protective health factors, and therefore might confound associations between those factors and the condition under study. Demographic characteristics also are at the core of public health policy. Age-related patterns of ill-health are critical when projecting health care needs in aging populations. The US Healthy People initiative lists reductions in racial and ethnic group health disparities as a primary objective for the nation.[25]

Socioeconomic status has a profound impact on many diseases and disorders, including an array of pain conditions such as musculoskeletal pain, sciatica, ulcer, and neuropathic pain.[18] Socioeconomic health inequalities have been characterized as "large, persistent, and even increasing" in developed countries.[22] An important finding is that socioeconomic inequalities are not confined to people who live in poverty.[17] Instead, they manifest as a gradient in disease risk that increases among progressively lower rungs of the socioeconomic ladder.

Given that demographic and socioeconomic influences on health are pervasive and the use of sociodemographic variables is orthodox, it is informative when exceptions to predominant trends are found or when there is uncertainty about the very nature of the association. Past studies of TMD provide examples of both. In the 2002 US National Health Interview Survey (NHIS), prevalence of TMD-like pain was greater in non-Hispanic-Whites than other racial-ethnic groups,[8] making it one of the few disorders that occurs less frequently in racial and ethnic minorities. In its request for applications that led to the OPPERA study, the National Institutes of Health stated: "The highest prevalence [of TMD] is observed in young adults (18–43 years)."[5] However, in one of the few examination surveys of a representative population sample, prevalence of TMD symptoms was greatest among 50- to 59-year-olds.[9]

The specific aims of this paper are to:

1. Describe the 4 study designs, methods of recruitment, data collection, and statistical analysis procedures used in the OPPERA baseline case-control study;
2. Describe outcomes from recruitment of participants in the baseline case-control study;
3. Evaluate representativeness of participants recruited into the OPPERA prospective cohort study using demographic benchmark data from the 2000 decennial census;
4. Describe distribution of symptoms and clinical signs of TMD among cases enrolled in the OPPERA baseline case-control study;
5. Evaluate associations between sociodemographic characteristics and chronic TMD using findings from the OPPERA baseline case-control study; and
6. Compare age- and gender-patterns of association with TMD in the OPPERA baseline case-control study with patterns of TMD-like symptoms reported in the US population.

Methods

The OPPERA project comprises: 1) a prospective cohort study of first-onset TMD; 2) a baseline case-control study of chronic TMD; 3) a matched case-control study of incident TMD; and 4) a prospective case-cohort study of the course of TMD (Fig 1). Collectively, these observational studies were designed to identify risk factors for onset and persistence of TMD. Methods for all 4 studies are described below, although results from OPPERA in this paper and others in this issue come solely from the OPPERA baseline case-control study mentioned above.

The OPPERA project was reviewed and approved by institutional review boards at each of4 study sites and at the data-coordinating center, Battelle Memorial Institute. All study participants verbally agreed to a screening interview by telephone and provided written consent for all other study procedures. The OPPERA study is being conducted under the auspices of a Certificate of Confidentiality (NIDCR-06-17) between the National Institutes of Health and Dr. William Maixner, Principal Investigator of OPPERA. The Certificate protects the privacy of research subjects.

Settings

Study participants were recruited from communities in and around 4US academic health centers: 1) The University of Maryland at Baltimore, MD, with a nearby population 651,154; 2) The University of Buffalo, NY, with a nearby population of 292,648; 3) The University of North Carolina at Chapel Hill, NC, with a nearby population 48,715; and 4) The University of Florida at Gainesville, FL, with a nearby population of 95,447. (All

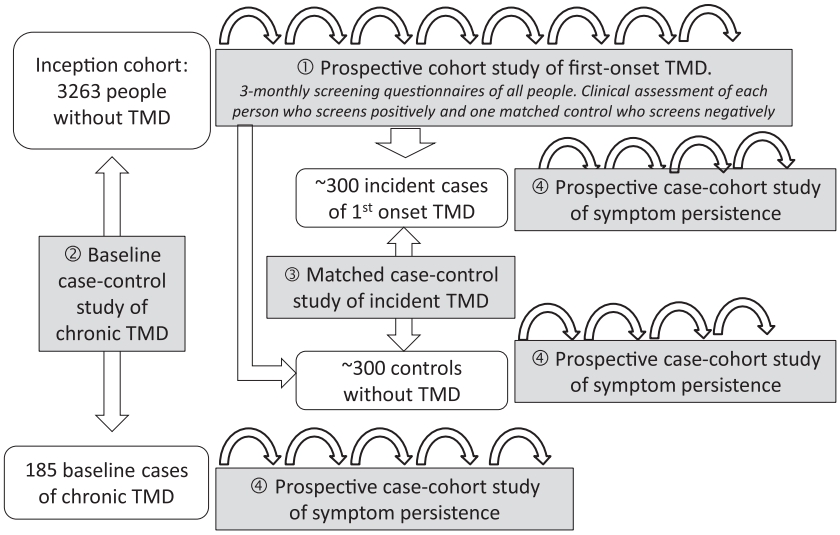

Figure 1. Components of the OPPERA Study.
Once every 3 months, a Quarterly Health Update (QHU) questionnaire is administered. It includes questions that screen for presence of temporomandibular disorder (TMD)-like symptoms.
① The prospective cohort study enrolled 3,263 people who had no history of TMD symptoms and who were found not to have TMD when examined clinically. During follow-up, those people who respond positively to QHU screening questions about TMD symptoms are invited to an OPPERA study site for clinical examination to determine TMD case-classification.
② For the baseline case-control study, 185 people with chronic TMD were enrolled as examiner-classified cases and their data were compared with baseline data from a randomly selected half of people in the prospective cohort study.
③ For each incident case in the inception cohort, 1 person who screens negatively for TMD symptoms is selected as a matched control and that person is also clinically examined. People classified without TMD are included in the matched case-control study of incident TMD.
④ Follow-up of first-onset cases of TMD and their matched controls is conducted through Quarterly Health Update questionnaires. Six months after case-classification, people with first-onset TMD are invited to an OPPERA study site for another clinical examination that classifies presence or absence of TMD.

population figures are from the 2000 US decennial census.) At baseline, all participants attended their local study sites for data collection by questionnaire, clinical examination, measurement of pain perception and autonomic function, and collection of a blood sample. Follow-up data collection will continue through 2012. All data and biological samples are managed by the study's data coordinating center, Battelle Memorial Institute, through its offices in Durham, NC.

Prospective Cohort Study of First-Onset TMD

Study Design

The prospective study of first-onset TMD recruited a cohort of adults aged 18 to 44 years who did not have TMD when examined at their baseline visit. Study participants continue to be followed to identify onset of TMD. Follow-up questionnaires, completed once every 3 months, identify people who develop significant symptoms suggestive of TMD, with examinations then performed to determine presence or absence of TMD in those reporting significant symptoms.

Participants

Recruitment took place between May 2006 and November 2008, when healthy volunteers were sought from communities in and around each study site. We sought to enroll individuals who varied in their risk of developing TMD and who covered the spectrum of major sociodemographic groups seen in counties near the study sites. However, there was no purposeful random sampling of residents in those counties.

The goal was to recruit 800 people without TMD from each study site. Volunteers were recruited using advertisements in local newspapers and radio stations, emails distributed through university networks, flyers posted in and around academic health centers, and word of mouth. Recruitment materials explained that healthy volunteers aged 18 to 44 years were needed for a study of muscle and jaw function. Respondents telephoned the local study site, at which point research personnel explained the study, administered a computer-assisted telephone interview to screen for study eligibility, and scheduled a clinic visit for people who met selection criteria.

Data Collection Procedures

Prior to their baseline clinic visit, potential enrollees completed 15 in-home questionnaires (Supplementary e-Table 1), either online or on paper forms that were mailed to them. The questionnaires asked about past experiences of potential risk factors and traitlike psychosocial characteristics thought to predict risk of TMD. Accompanying manuscripts describe specific details about the origins, reliability, and validity of these and other data collection procedures.

At the start of the 3-hour baseline clinic visit, study procedures were explained in detail and study participants signed the consent form approved by the study site's

IRB. They completed 7 more questionnaires evaluating statelike psychological characteristics and symptoms with timeframes anchored to the clinic visit (Supplementary e-Table 1).

A trained and calibrated examiner then assessed the head and neck to confirm absence of TMD and to measure clinical characteristics thought to predict risk of TMD. The examination protocol, which was based on the Research Diagnostic Criteria for TMD,[7] is described in detail in an accompanying paper [Ohrbach et al, in this volume]. To summarize, examiners first identified the relevant orofacial region by touching the following anatomical areas bilaterally: temporalis, preauricular, masseter, posterior mandibular, and submandibular areas. Examiners then asked a series of structured questions to evaluate symptoms regarding pain history, focusing on pain location, its history, and whether or not it was of orofacial origin. Signs of TMD were then assessed by determining responses to jaw movement and digital palpation of orofacial structures. The origin of any pain reported during those procedures was classified by the examiner into 1 or more of 10 anatomical locations, each considered bilaterally: temporalis, masseter, lateral pterygoid, submandibular, and temporomandibular joint (TMJ).

Quantitative sensory testing was performed after the examination to measure responses to standardized noxious stimuli delivered using pressure pain, mechanical cutaneous (pricking) pain, and heat pain. Full details of those measurements are provided in Greenspan et al [included in this volume]. Autonomic function was monitored at rest, during orthostatic challenge, and during the Stroop color-word test and pain-affect test. Full details of those measurements are provided in Maixner et al [Autonomic paper, in this volume.] Anthropometric measurements were recorded, and a 20-mL sample of peripheral blood was collected by venipuncture for subsequent DNA purification and genotyping.

At the end of the clinic visit, instructions were provided for a set of 28 daily pain diaries to be completed during the subsequent 4-week period. Study participants were told they would be contacted for quarterly health updates, described in more detail below. They received $100 payment for completing all baseline data collection procedures ($20 for preclinic questionnaires, $50 for physical assessments at the clinic, $20 for providing a blood sample, and $10 for the 4-week pain diary).

Examiner Training and Calibration

The clinical examiners from each study site were trained and calibrated together at University of Buffalo; calibration was made to a single expert dentist [YG] based at the Buffalo site who served as the reference examiner throughout the reported study period. Expert dentists from each site were calibrated according to the case classification decision rules. Three reliability studies were conducted in which examiners from each site conducted pairs of blinded, replicated examinations of non-OPPERA volunteers: 1 examination in each pair was conducted by the OPPERA examiner, and another by the reference examiner. The first reliability study regarding examiner performance was conducted at Chapel Hill; the study included 24 subjects (15 cases, 9 controls), and each of the clinical examiners and reference examiner independently performed the examination on each subject. At that study, the clinical examiners reviewed findings with their respective expert dentist, just as they would during actual study conduct, and both of them determined case classification. Over the next year, the examiner and expert dentist from each site, in turn, traveled to Buffalo in order for the expert dentists to be calibrated by the reference examiner. Immediately after calibration, the study site's pair of clinical examiner and expert dentist was evaluated for reliability, as judged against the reference examiner. At approximately 12- to 15-month intervals, repeat reliability studies were conducted in Buffalo. The overall Kappa reliability coefficients for the reliability in TMD case classification were: .87 (2006), 1.0 (2007), and .96 (2009).

Inclusion and Exclusion Criteria

Studywide inclusion and exclusion criteria were evaluated in the telephone interview (Supplementary e-Table 2). In summary, eligibility criteria 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 about significant medical conditions and no history of facial injury or surgery.

Criteria for Classification of TMD-Free Controls

To be eligible for the prospective cohort study, potential participants had to report absence of significant orofacial pain symptoms and they had to be free of TMD when examined (Supplementary e-Table 2). Symptoms were identified first in the telephone interview where all 4 of the following criteria had to be met: 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) never diagnosed with TMD; and 4) no use of night guard or occlusal splint.

The symptom criteria regarding orofacial pain were subsequently verified during structured questioning at the beginning of the clinical examination. After defining the relevant orofacial region by touch, examiners verified that participants had experienced pain of orofacial origin in the defined orofacial region for no more than 4 days in the prior 30 days. Furthermore, controls had to be classified by examiners as having neither myalgia nor arthralgia. Consistent with RDC criteria, signs of pain in response to jaw movement and digital palpation were not sufficient to classify TMD and, therefore, people who reported pain during examination procedures remained eligible for enrollment in the prospective cohort study.

The reference period of 30 days used in the examination was shorter than the 3-month reference period

of the telephone interview due to the increased complexity of defining the relevant anatomy and identifying the orofacial origin of pain in the examination inquiry. The intention was to restrict examinations to people whose initial telephone response signified a relatively long period with few or no symptoms. The clinic visit could then provide an opportunity for more in-depth probing of the most recent pain to permit valid reporting of potentially overlapping pain, such as headache.

Follow-Up of People Enrolled in the Prospective Cohort Study

Follow-up is continuing through mid-2012, with the expectation that approximately 300 people will be identified with first-onset TMD. Follow-up is by quarterly health update (QHU) questionnaires, administered once every 3 months, either online or on paper. Outside of that quarterly schedule, QHU questionnaires can also be administered to participants who contact their local study site describing symptoms. People who respond positively to QHU questions about TMD symptoms are asked to repeat most of the same questionnaires used at baseline and they are invited to the study site's clinic for clinical examination, quantitative sensory testing, measurement of autonomic function, and collection of a blood sample. A positive QHU response is based on criteria that are similar to the symptom questions used to recruit TMD cases for the case-control study (described below). To be classified as an incident case, these study participants must then be classified with TMD myalgia, arthralgia or both, using the same RDC-based examination criteria described below for TMD cases in the case-control study. Further details about identification of onset-cases will be reported in later papers that investigate incidence of TMD.

Baseline Case-Control Study

Study Design

The unmatched case-control study aimed to recruit 200 people with examiner-classified TMD myalgia, arthralgia or both ("TMD cases"). Controls were a 50% random sample of people without TMD who were enrolled in the prospective cohort study. The case-control study used data collected at baseline assessments for these TMD cases and controls.

Participants

Recruitment of TMD cases reported in these papers occurred from May 2006 through November 2008. An additional round of recruitment began in April 2010, with the aim to enroll an additional 900 chronic cases of TMD for the purpose of a genome-wide association study. Enrollment will continue through July 2012, and data from those TMD cases will be reported in later papers. Recruitment of cases used the same procedures described above for the prospective cohort study. The goal was to enroll people representing the major sociodemographic groups found in counties nearby the study site. Specifically, enrollment of TMD cases was not limited to people who were seeking care for TMD.

Data Collection Procedures

Data collection procedures for TMD cases were identical to those described for the prospective cohort study.

Inclusion and Exclusion Criteria for Cases

To be enrolled as TMD-cases, volunteers had to meet the same studywide inclusion criteria used in the prospective cohort study (Supplementary e-Table 2). However, symptom and examination criteria differed with the aim of selecting people who had experienced facial pain symptoms for at least 6 months and who had examiner-confirmed classification of TMD myalgia, arthralgia, or both.

Criteria for Classification of TMD Cases

To conform with the symptom criteria, potential TMD cases first had to report pain with sufficient frequency in the telephone interview; that is, pain 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 [Supplementary e-Table 2]). The symptom criteria were then verified during a clinical examination, following the same protocol described for the prospective cohort study. For potential TMD cases, examiners confirmed that orofacial pain experienced during the preceding month was in the relevant orofacial area. If pain was described as headache located in the temporalis region, it was considered a sufficient symptom if it occurred in the relevant orofacial area during at least 5 days. However, pain in the orofacial area that was attributable to other causes, for example toothache, was not a sufficient symptom. The reference period of 30 days used in the examination was shorter than the 3-month reference period of the telephone interview for the same reasons described for selection of participants in the prospective cohort study.

In addition to symptoms of TMD, reports of pain in response to examination procedures were required to classify people as TMD cases. Specifically, TMD cases had to report pain in response to movement or palpation in at least 1 of the 2 TMJs or at least 3 of the 8 orofacial muscle groups (each assessed bilaterally): temporalis, masseter, lateral pterygoid, and submandibular.

Selection of Controls

A subset of people without TMD was selected from among all enrollees in the prospective cohort study using a stratified random sampling procedure. The rationale was to create a "reserve" sample of controls whose data could be combined with TMD cases who have been recruited since April 2009 for additional case-control analyses. Potentially, the reserve sample could also be used for validation of exploratory data analysis procedures conducted among the primary group of controls—for example, to validate findings from cluster analysis. Using the SAS SURVEYSELECT procedure, the cohort of 3,263

people who did not have TMD was stratified according to study site, and a simple random sample of 50% of enrollees was selected from within each site.

Statistical Power and Sample Size Justification

The number of people enrolled as controls was selected to meet statistical power requirements for the prospective cohort study. The baseline case-control study recruited 185 people with chronic TMD, comparing them with 1,633 controls drawn from the enrollees in the prospective cohort study. The smaller number of cases was the primary determinant of statistical power for hypotheses addressed in the case-control study. For binary predictor variables, odds ratios as small as 1.7 could be detected with 80% power, assuming type I error of $P = .05$, and exposure prevalence as low as 15%. For continuous predictor, the minimum detectable difference in standardized means between 185 cases and 1,633 controls was .22 standard deviations, corresponding to a minimum detectable standardized odds ratio of 1.25, again assuming type I error of $P = .05$ and power of 80%.

Data Management and Quality Assurance

A proprietary computerized tracking system was created by Battelle investigators using high-tiered programming languages (T-SQL, ASP, JAVASCRIPT, and VB.NET) to manage enrollment, capture data, and maintain records of consent. The tracking system also managed chain-of-custody of biologic samples from the time of their collection, storage at each study site, shipment for DNA purification and genotyping, and delivery of datasets to the data-coordinating center. The tracking system also initiated procedures for follow-up data collection from participants in the prospective studies, and it managed incoming data from questionnaires completed either online or on paper. The online versions used .pdf applications that managed input edits and enforced skip sequences. Paper forms were designed and scanned using Teleform® software that identified the same input edits and skip sequences used online so that errors could be corrected by research personnel at the time of scanning. Analytic datasets were created separately for each questionnaire or data form and exported in SAS format. They were stored securely on computer servers at the data coordinating center. Analysis of SAS datasets for this paper and others in this volume was performed at the UNC study site under the direction of the authors [GS, EB] with guidance from other OPPERA investigators.

OPPERA investigators convened 5 data-analysis working groups to develop data quality guidelines and to guide statistical analysis for 5 types of data: clinical assessments; psychological characteristics; quantitative sensory testing; autonomic function; and genetics. For continuous measures, quality assessment began with generation of box plots, separately for cases and controls, to identify potential outliers. Global editing rules were created to exclude values that were beyond the range of measurement or that were outside physiologic limits. Individual data forms with anomalous values were inspected visually to identify possible recording or scanning errors, and corrected when feasible. Accompanying papers describe specific quality control steps used for analysis of each set of putative risk factors.

In addition to examiner training and calibration procedures described above, 3 data quality assessment steps were used to assure quality of TMD case classification:

1. The paper forms used to record findings from the RDC/TMD clinical examination were reviewed at study sites by the OPPERA expert dentist at that site. Expert dentists, who had been through the same training procedures as OPPERA examiners, verified that signs and symptoms recorded on the examination were consistent with the classification criteria for presence or lack of TMD.
2. An expert pain panel was convened by 1 of the OPPERA principal investigators who is an expert in TMD case-classification [RO]. He and the expert dentists met by conference call to review online documents and resolve instances where the study site's expert dentist sought clarification of a case classification.
3. A software algorithm applied to the dataset of orofacial examination findings computed the case classification based on examiners records of symptoms and signs of TMD. The algorithm compared the computed classification with that provided by the examiner in order to identify any discrepancies.

Data Analysis and Statistical Methods for the Baseline Case-Control Study

For putative risk factors measured as continuous variables, summary measures were computed from responses to multiple items that formed subscales. Summary measures were calculated first for people with "complete data," meaning those for whom valid values were recorded for each item comprising a subscale or other summary measure. Typically, those measures yielded continuous scores that were analyzed to generate means, standard deviations, and quantiles describing their distribution.

Statistical Tests and Measures of Effect for Case-Control Comparisons

For putative risk factors measured as continuous variables, means were compared between TMD cases and controls and analysis of variance was used to test for statistical significance of the difference in means, adjusting for study site. Analysis of variance was used even for variables with markedly non-normal distributions because, in large samples, those least-squares methods are valid for any distribution.[15] Analysis of variance was used as well in instances where the variances of the 2 groups were unequal since the procedure is robust even when this assumption is violated. Exceptions were made when the precedent was to transform the variable to improve its interpretability; for example, some measures of heart rate variability were computed on the log scale.

For characteristics that were measured categorically, mutually exclusive groups were created and proportions were compared between cases and controls. This approach was used in addressing the fifth aim of this paper. In some instances, ordinal variables were managed in the same way, although some ordinal variables with many levels were treated as continuous variables (described above). The statistical significance of any differences in proportional distribution between cases and controls was evaluated by creating dummy variables for all but 1 reference category and evaluating the set of dummy variables using the likelihood ratio statistic from a binary logistic regression model, where the dependent variable was TMD case status. The model additionally adjusted for study site as a covariate. Parameter estimates and standard errors from the model were used to generate odds ratios and 95% CIs for the association between the characteristic and odds of TMD. As done for the continuous measures, a second logistic regression model generated odds ratios and 95% CIs that additionally adjusted for 3 demographic characteristics: age in years (modeled as a continuous variable), a single dummy variable for gender, and a single dummy variable signifying race/ethnicity as non-Hispanic-White or other.

All *P*-values were computed without adjustment for multiple tests, and $P = .05$ was therefore not nominated as a threshold for statistical significance. In this paper's case-control analyses, 11 sociodemographic characteristics were investigated so Bonferroni correction for the probability of type I error would yield a critical *P*-value of $.05 \div 11 = .004$. Using the same rationale, rejection of the null hypothesis concerning odds ratios would occur only if the 99.6% confidence interval excluded the null value of 1. In general, though, drawing conclusions about statistical significance of associations should be avoided, even with correction for multiple tests, because these papers report only univariate- or demographically-adjusted results. Instead, judgments about statistical significance will be made in subsequent papers using multivariable modeling to consider multiple characteristics simultaneously, as proposed in the OPPERA heuristic model (see Maixner et al, Overview paper, in this volume).

Population Benchmark Data for Demographic Comparisons

To address aim 3 of this paper, selected sociodemographic data items from the 2000 US decennial census were tabulated and the percentage distributions were compared with percentages and corresponding 95% confidence intervals among controls in the OPPERA baseline case-control study. The ratio of the OPPERA percentage relative to the Census percentage was used as an indicator of the degree to which people in the OPPERA prospective cohort study were representative of the major sociodemographic groups within the same age range in counties nearby each study site. Ratios of >1.5 and <.7 were used as thresholds to signify marked departure from representativeness. Relevant counties nearby recruitment sites are shown in Supplementary e-Fig 1. They were:

- NC: Chatham Co., Durham Co., Orange Co., Wake Co.
- NY: Erie Co.
- FL: Alachua Co.
- MD: Anne Arundel Co., Baltimore Co, Howard Co, Baltimore City.

County-specific data were selected from files downloaded from the US Census Bureau[23]:

- dc_dec_2000_sf1_u_data1.txt (race for categories of age and gender)
- dc_dec_2000_sf1_u_data2.txt (ethnicity for categories of age and gender)
- dc_dec_2000_sf4_u_data1.txt (marital status for categories of age and gender)
- dc_dec_2000_sf4_u_data2.txt (education and income for categories of age and gender).

For income, the census data were reported only for 2 relevant age groups (25–34 and 35–44 years), whereas other variables were reported for 3 relevant age groups (18–24, 25–34, and 35–44 years).

OPPERA data were from the 1,633 study participants in the prospective cohort study selected at random for the baseline case-control study. They reported relevant sociodemographic characteristics in the telephone interview and the self-completed demographic questionnaire. People with invalid or missing responses to OPPERA questions were omitted from analysis for that item. Within each study site, percentage distributions were tabulated permitting comparison between census benchmarks and participants in the OPPERA prospective cohort.

Prevalence of TMD-Like Symptoms Reported in the US Population

To address the sixth aim of this paper, the age and gender patterns of association with TMD in the OPPERA baseline case-control study were compared to age- and gender-related patterns of association with self-reported TMD-like symptoms in the US population. US population estimates were generated using data from the 2007–2009 NHIS, a nationally representative cross-sectional survey that interviews, annually, a sample of the civilian, noninstitutionalized US population. Datasets for each of the 3 years were downloaded from the Centers for Disease Control and Prevention.[24] This analysis was limited to people aged 18 years or more. Cases of TMD-like symptoms were defined as individuals who answered "Yes" to the following question: "During the past 3 months, did you have facial ache or pain in the jaw muscles or the joint in front of the ear"? The 69 individuals who responded "don't know" or who did not answer the question were excluded from the analysis, resulting in a sample size of 72,836 people. Age was defined as a categorical variable with 7 levels: 18 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, and 75+. The prevalence of TMD-like symptoms, cross-classified by age group and gender, was computed using sampling weights that were part of NHIS's complex multistage survey design. Standard errors were estimated using the Taylor-series approximation method.[14] Since 3 years

of NHIS data were pooled, weights from the pooled data were divided by 3 to avoid overestimation. All calculations were performed using the SAS SURVEYFREQ procedure.

Results

Recruitment of Study Participants (Aim 2)

Telephone interviews were conducted with 5,781 people who expressed interest in the project identifying 4,057 who were eligible for the prospective cohort study. Of those, 3,350 (83%) attended the clinical assessment (Supplementary e-Table 3). All but 87 were confirmed as eligible during the clinical assessments, yielding 3,263 people without TMD who were enrolled into the prospective cohort study. Random sampling selected 1,633 of those people whose baseline data were used for the baseline case-control study. The telephone interview identified an additional 280 people who were putative cases of TMD, of whom 202 (72%) attended the clinical assessment. Examiners confirmed TMD in 185 of them, and they constituted the sample of TMD cases enrolled into the baseline case-control study.

For both cases and controls, word of mouth was the most commonly reported way in which enrollees heard about the OPPERA study, followed by email, posted flyers, and advertisements (Table 1). Only 7% of TMD cases and 9% of controls said that they had been referred from a research clinic.

The number of enrolled TMD cases varied more than 2-fold among study sites, while there was less site variation, in relative terms, in enrollment of controls (Table 2). Baltimore enrolled more people aged 35 to 44 years than either of the other 2 age groups, whereas 35 to 44-year-olds represented the smallest age group at the other sites. Baltimore had nearly equal numbers of males and females, while females were a clear majority at each of the other 3 study sites. Baltimore had the largest number of Black/African American study participants, Gainesville had the largest number of Hispanics, and Buffalo had the largest number of people in other racial/ethnic groups, many of them Asian.

Demographic characteristics are cross-classified in Supplementary e-Table 4 to provide additional details about study participants at each study site.

Table 1. How Study Participants Learned about the OPPERA Study

Percent Who Heard By*	TMD Cases (n = 185)	Controls (n = 1633)
Word of mouth	50	42
Email	17	24
Posted flyers	17	14
Newspaper advertisement	14	18
Referred from research clinic	7	9
Other	1	0

*Percentages sum to more than 100 because more than 1 source of information could be reported.

Comparison of Sociodemographic Characteristics of TMD-Free Controls and Population Benchmarks (Aim 3)

At the Baltimore study site, age distributions were generally similar for controls in the baseline case-control study and people living in nearby counties (Table 3). In contrast, at the other study sites, OPPERA participants had a younger age distribution than people living in nearby counties. Percentages of males and females did not differ markedly between OPPERA study sites and the nearby counties. In Baltimore, there was a markedly higher proportion of Blacks/African Americans in OPPERA than in nearby counties (percentage ratio = 2.4)—a discrepancy that was not observed at other study sites. Hispanics of both genders were overrepresented at the Florida site, and male Hispanics were overrepresented at Buffalo. For most of the OPPERA percentage estimates, 95% confidence intervals were approximately $\pm$5%, which did not markedly alter these interpretations regarding representativeness.

At all study sites, OPPERA participants were more likely to have never married than people living in nearby counties. At most study sites, OPPERA participants were more likely than residents of nearby counties to have educational qualifications beyond high school, although at Baltimore, the OPPERA sample was fairly representative with respect to educational attainment. In Baltimore and Buffalo, OPPERA participants had a lower income distribution than households in nearby counties. At other study sites, there were generally small differences in most categories of income, although all 3 sites were overrepresented with people in the highest income category.

Distribution of Symptoms and Clinical Signs of TMD Among Cases (Aim 4)

Among people classified with TMD in the baseline case-control study, more than 90% reported facial pain that began at least 1 year before enrollment into the study, with the majority reporting a history of at least 3 years (Table 4). Pain was experienced in recurrent bouts by most. Nearly three-quarters of TMD cases reported episodes of pain that lasted for at least 15 days in the preceding month, and approximately one-half had individual episodes that usually lasted at least 1 day. Most had seen a health care provider for their pain at some time, although only about one-third had done so within the preceding 6 months.

Using the Characteristic Pain Intensity scale from the Graded Chronic Pain Scale, cases registered a mean pain intensity of moderate (51/100) as integrated over the present and prior 6 months (Table 5). Cases also registered mean levels of approximately 2/10 with respect to interference in each of daily activities, social activities, and work activities due to facial pain. The mean number of days cases were prevented from attending to their usual activities was 11, though the distribution was skewed, with the maximum reported value at the scale maximum of 180. Cases registered mean pain intensity of approximately 7 and unpleasantness of nearly 8 using

Table 2. Number of Participants in the OPPERA Baseline Case-Control Study Classified According to Sociodemographic Characteristics

		Study Site				TMD Case Classification	
	All OPPERA	Baltimore, MD	Buffalo, NY	Chapel Hill, NC	Gainesville, FL	Cases	Controls
All people	1,818	430	422	463	503		
TMD cases	185	46	23	56	60	185	
Noncases of TMD	1,633	384	399	407	443		1,633
Age (years)							
18–24	910	90	220	240	360	72	838
25–34	511	127	120	161	103	60	451
35–44	397	213	82	62	40	53	344
Gender							
Female	1,080	227	246	313	294	155	925
Male	738	203	176	150	209	30	708
Race-ethnicity							
White-NH	984	101	249	307	327	145	839
Black/African-American	533	291	86	102	54	25	508
Hispanic	108	8	18	16	66	8	100
Other/not stated	193	30	69	38	56	7	186
Detailed race and ethnicity							
White							
Non-Hispanic	947	96	248	294	#	138	809
Hispanic	16	1	—	9	6	4	12
Black/African American							
Non-Hispanic	525	287	86	101	#	25	500
Hispanic	4	1	—	—	3	—	4
Asian							
Non-Hispanic	162	18	60	33	#	6	156
Hispanic	2	—	—	—	2	—	2
Native Hawaiian or other Pacific Islander							
Non-Hispanic	4	2	—	1	1	—	4
American Indian or Alaskan Native							
Non-Hispanic	6	3	1	1	1	—	6
Multiple races							
Non-Hispanic	27	7	1	5	#	3	24
Hispanic	106	8	18	16	#	8	98
Not stated	19	7	8	3	1	1	18

the Gracely scale for pain intensity and unpleasantness. Responses on both scales were skewed toward the maximum score of 20.

Associations Between Sociodemographic Characteristics and Chronic TMD (Aim 5)

Distributions of all 3 demographic characteristics differed markedly between TMD cases and controls (Table 6). Odds of TMD increased across successively older age groups, and females had more than 3 times the odds of TMD as males. Relative to non-Hispanic-Whites, other racial groups had lower odds of TMD, with fully adjusted odds ratios ranging from .2 (for Black/African American and for other groups) to .4 (for Hispanics). Because of the overall similarity of odds ratios for specific minority groups, their data were pooled, yielding a fully adjusted odds ratio of .2 (95% CI = .2, .3) for the combined group of non-Whites. Odds ratios for individual demographic characteristics tended to be consistent, whether or not they were adjusted for other demographic characteristics.

While country of birth was not associated significantly with occurrence of TMD, people whose first language was not English had half the odds of TMD relative to people whose first language was English (Table 7). However, the latter effect ceased to be statistically significant after adjustment for age, gender, and race. Higher educational attainment was associated with greater odds of TMD, and although odds ratios were attenuated after adjustment for demographic characteristic, there remained an approximate 2-fold increase in odds associated with any level of education beyond high school (Table 7). In contrast, there was a conspicuous lack of association between TMD and income, satisfaction with socioeconomic position, and health insurance coverage.

Demographic Variation in Prevalence of TMD-Like Symptoms in the US Population and in OPPERA (Aim 6)

Population estimates from the NHIS for females revealed an inverted-U relationship between age and prevalence of TMD-like symptoms (Fig 2A). Prevalence reached 7.1% among women age 35–44 years whereas it was 5.1% in

Table 3. Race, Ethnicity, Income and Educational Attainment: US Census 2000* and Controls in the OPPERA Baseline Case-Control Study

	Baltimore, MD			Buffalo, NY			Chapel Hill, NC			Gainesville, FL		
	Census	OPPERA	Ratio‡	Census	OPPERA	Ratio	Census	OPPERA	Ratio	Census	OPPERA	Ratio
Age group (% of people)												
18–24 years	20.2	21.4 (17.3, 25.5)	1.1	21.5	52.8 (47.9, 57.6)	2.5	21.6	53.3 (48.5, 58.2)	2.5	41.6	74.2 (70.1, 78.3)	1.8
25–29 years	16.7	18.8 (14.8, 22.7)	1.1	15.8	17.3 (13.5, 21.0)	1.1	19.8	23.3 (19.2, 27.5)	1.2	17.3	12.4 (9.4, 15.5)	.7
30–34 years	19.2	10.9 (7.8, 14.1)	.6	18.6	11.5 (8.4, 14.6)	.6	19.5	11.1 (8.0, 14.1)	.6	13.1	6.1 (3.9, 8.3)	.5
35–39 years	22.0	17.4 (13.6, 21.2)	.8	21.3	7.5 (4.9, 10.1)	.4	20.4	6.4 (4.0, 8.8)	.3	13.5	3.4 (1.7, 5.1)	.3
40–44 years	22.0	31.5 (26.9, 36.2)	1.4	22.9	11.0 (7.9, 14.1)	.5	18.8	5.9 (3.6, 8.2)	.3	14.5	3.8 (2.1, 5.6)	.3
Gender (% of people)												
Male	47.5	51.3 (46.3, 56.3)	1.1	48.5	43.8 (38.9, 48.6)	.9	49.9	34.9 (30.3, 39.5)	.7	49.2	43.9 (39.3, 48.5)	.9
Female	52.5	48.7 (43.7, 53.7)	.9	51.6	56.3 (51.4, 61.1)	1.1	50.1	65.1 (60.5, 69.7)	1.3	50.8	56.1 (51.5, 60.7)	1.1
Race/ethnicity†												
% white: males	62.5	81.5 (76.1, 87.0)	1.3	81.3	41.5 (34.1, 48.9)	.5	67.3	28.2 (20.8, 35.6)	.4	75.2	59.1 (52.1, 66.0)	.8
% White: females	59.5	20.0 (14.2, 25.8)	.3	79.7	57.1 (50.7, 63.6)	.7	66.4	56.8 (50.8, 62.8)	.9	73.1	62.1 (56.1, 68.1)	.8
% Black: males	30.7	72.8 (66.6, 79.1)	2.4	12.8	15.8 (10.3, 21.3)	1.2	20.7	14.8 (8.9, 20.6)	.7	15.2	9.8 (5.6, 14.1)	.6
% Black: females	34.1	68.6 (62.0, 75.3)	2.0	14.7	25.9 (20.2, 31.6)	1.8	24.9	30.3 (24.8, 35.9)	1.2	17.8	12.1 (8.0, 16.2)	.7
% Hispanic: males	3.1	2.6 (.3, 4.8)	.8	3.9	6.9 (3.1, 10.7)	1.8	10.7	5.0 (1.4, 8.6)	.5	7.5	14.4 (9.5, 19.4)	1.9
% Hispanic: females	2.4	2.2 (.1, 4.2)	.9	3.7	2.2 (.3, 4.2)	.6	5.6	5.7 (2.9, 8.5)	1.0	7.3	16.1 (11.5, 20.7)	2.2
	Baltimore, MD			Buffalo, NY			Chapel Hill, NC			Gainesville, FL		
	Census	OPPERA	Ratio‡	Census	OPPERA	Ratio	Census	OPPERA	Ratio	Census	OPPERA	Ratio
Age group (% of people)												
% Never married: males	49.2	63.2 (56.3, 70.0)	1.3	49.0	72.5 (65.8, 79.2)	1.5	46.9	74.6 (67.5, 81.8)	1.6	68.2	83.4 (78.2, 88.7)	1.2
% Never married: females	43.1	71.2 (64.6, 77.7)	1.7	39.9	72.5 (66.5, 78.4)	1.8	42.2	70.2 (64.7, 75.7)	1.7	62.1	79.8 (74.8, 84.8)	1.3
Educational attainment: males												
High school or less	44.3	53.0 (45.8, 60.2)	1.2	41.7	13.3 (8.2, 18.4)	.3	32.7	4.2 (.9, 7.5)	.1	25.9	3.6 (1.0, 6.2)	.1
Post high school or some college	28.8	28.6 (22.1, 35.2)	1.0	34.7	41.0 (33.7, 48.4)	1.2	29.4	44.4 (36.2, 52.5)	1.5	46.4	57.7 (50.8, 64.7)	1.2
College graduate	17.7	13.0 (8.1, 17.8)	.7	16.5	27.2 (20.5, 33.8)	1.7	25.8	38.0 (30.0, 46.0)	1.5	16.9	25.3 (19.1, 31.4)	1.5
Post graduate level	9.3	5.4 (2.1, 8.7)	.6	7.2	18.5 (12.7, 24.3)	2.6	12.1	13.4 (7.8, 19.0)	1.1	10.9	13.4 (8.6, 18.2)	1.2
Educational attainment: females												
High school or less	37.4	42.3 (35.1, 49.5)	1.1	33.8	21.2 (15.8, 26.6)	.6	25.0	5.7 (2.9, 8.4)	.2	21.8	5.2 (2.5, 8.0)	.2
Post high school or some college	32.9	28.6 (22.0, 35.1)	.9	40.3	37.8 (31.5, 44.2)	.9	33.8	43.8 (37.8, 49.8)	1.3	50.0	49.2 (43.0, 55.4)	1.0
College graduate	20.2	17.6 (12.0, 23.1)	.9	17.8	26.6 (20.8, 32.4)	1.5	29.8	25.3 (20.0, 30.5)	.8	18.7	28.6 (23.0, 34.3)	1.5
Post graduate level	9.5	11.5 (6.9, 16.2)	1.2	8.1	14.4 (9.8, 19.0)	1.8	11.4	25.3 (20.0, 30.5)	2.2	9.5	16.9 (12.3, 21.6)	1.8
Annual household income: M + F												
<$20,000	13.8	33.5 (27.6, 39.3)	2.4	20.2	27.8 (22.6, 33.0)	1.4	11.6	10.9 (7.6, 14.2)	.9	26.1	14.9 (11.2, 18.6)	.6
$20,000–$39,999	22.8	29.9 (24.2, 35.6)	1.3	25.6	21.5 (16.8, 26.3)	.8	23.6	26.5 (21.8, 31.2)	1.1	30.6	15.5 (11.7, 19.3)	.5
$40,000–$59,999	21.4	17.5 (12.8, 22.2)	.8	23.2	17.0 (12.7, 21.4)	.7	21.5	17.6 (13.6, 21.7)	.8	20.5	13.2 (9.7, 16.8)	.6
$60,000–$99,999	27.2	14.3 (10.0, 18.7)	.5	23.0	20.1 (15.5, 24.8)	.9	27.1	23.8 (19.3, 28.4)	.9	16.0	24.8 (20.3, 29.3)	1.5
$100,000–$149,999	9.9	2.4 (.5, 4.3)	.2	5.9	8.3 (5.1, 11.5)	1.4	11.2	12.4 (8.9, 15.9)	1.1	4.9	14.1 (10.5, 17.7)	2.9
$150,000 or more	4.9	2.4 (.5, 4.3)	.5	2.2	5.2 (2.6, 7.8)	2.3	5.0	8.8 (5.8, 11.8)	1.8	1.9	17.5 (13.5, 21.4)	9.2

*For all characteristics other than income, census data are from people aged 18 to 44 years living in counties nearby OPPERA study sites. Census data for income are for 25 to 44 year olds; the same age range was used for OPPERA income data. Numbers in parentheses are 95% confidence intervals for percentage estimates at OPPERA sites.

†Percentages of racial/ethnic groups within gender do not sum to 100% because other racial/ethnic categories are not reported here.

‡Ratio of percentage at OPPERA site relative to percentage in Census.

women aged 18–24 years and 3.5% in women aged 75 years or more. Prevalence in men was about half that of women in the corresponding age group. The age-gradient among men followed a weak inverse relationship, although age variation in men was less apparent than in women.

Very similar patterns of age- and gender-related variation were observed when the proportion of TMD cases was plotted for the OPPERA baseline case-control study (Fig 2B), albeit within the truncated age distribution of OPPERA study participants. Specifically, among females, the proportion of cases increased in successively older age groups, while among males, there was little age variation. As observed with the NHIS data, the gender difference in proportion of TMD cases was greatest among OPPERA participants aged 35 to 44 years, and was much smaller among 18- to 24-year-olds.

Table 4. History of Facial Pain among 185 Temporomandibular Disorder (TMD) Cases

	*n**	%
Time since facial pain began		
<1 yr	17	9.2
1 to <3 yrs	36	19.5
3 to <10 yrs	75	40.5
≥10 yrs	57	30.8
Temporal pattern of facial pain		
Persistent	53	29.0
Recurrent bouts	129	70.5
One time	1	.6
Number of days with facial pain during last month		
<15 days	46	46.0
15 days to persistent	138	184.0
Duration of each episode of facial pain during last month		
Less than a day	85	46.7
More than a day but does stop	51	28.0
Continuous pain	46	25.3
Ever seen a health care provider for facial pain		
Yes	133	72.7
No	50	27.3
Most recent visit to health care provider for facial pain		
Within 1 to 6 months	46	38.3
More than 6 months ago	74	61.7

*Numbers do not necessarily add to 185 people due to missing or "don't know" responses.

Discussion

This paper addresses OPPERA's first scientific aim regarding sociodemographic associations with chronic TMD, and it provides information to gauge representativeness of the study groups. Representativeness is important for 2 reasons. First, case-control studies should select controls who represent the same population from which cases arise[20] (p 116). This is 1 critical requirement for internal validity of associations estimated in case-control studies. Case-control studies are internally valid when "comparison groups are selected and compared in such a manner that the observed differences between them may, apart from sampling error, be attributed only to the hypothesized effect under investigation,"[13] (p 184) while sampling error is "that part of the total estimation error of a parameter caused by the random nature of the sample"[13] (p 163). For example, when cases are recruited from clinics, it is essential that controls be selected in such a way that if the controls developed the condition, their potential to be detected as cases at those clinics would be similar to that of cases. The OPPERA project sought volunteer participants from communities in and around academic health centers. Fewer than 10% of cases reported hearing about OPPERA through research clinics; the majority of cases heard either by word of mouth or from advertisements, flyers, and emails. This result, coupled with findings regarding clinical pain reports, symptom profiles, and history of treatment among TMD cases, is consistent with TMD as it occurs in the community at large, rather than in treatment-seeking TMD cases. Likewise, controls reported hearing about OPPERA primarily by word of mouth or from advertisements, flyers, and emails. Age and gender associations with TMD observed in the OPPERA baseline case-control study were very similar to the associations observed in the US population, suggesting that the methods used to select cases and controls did not seriously distort estimates of demographic associations with chronic TMD. Taken together, these suggest that both cases and controls were selected from a community-based population of volunteers, and that the methods of selection produced good internal validity.

Representativeness of the OPPERA controls is of additional importance to gauge generalizability of findings that will emerge from the prospective cohort. Generalizability, also termed external validity, occurs when unbiased inferences regarding a target population can be inferred from associations observed among participants in a specific study[13] (p 185). A target population is a larger group of people than those studied, and usually refers to people living in similar places (eg, an entire county, state or nation) and at similar times as the study sample. In OPPERA, controls were a nonprobability sample of

Table 5. Quantitative Measures of Symptom Experiences among 185 Cases With Temporomandibular Disorder (TMD)

						Percentiles					
Measure	Units and Potential Range	N	Mean	Sd	Min	5th	25th	50th	75th	95th	Max
Intensity* of current facial pain at clinic visit	0–20 scale	182	7.8	4.8	0	0	5	8	11	16	20
Unpleasantness* of current facial pain at clinic visit	0–20 scale	184	7.2	4.3	0	0	5	7	9	16	20
Rating of current facial pain preclinic visit	0–10 scale	185	3.2	2.4	0	0	1	3	5	7	10
Rating of average facial pain in last 6 months	0–10 scale	185	5.1	2.2	1	2	4	5	7	10	10
Rating of worst facial pain in last 6 months	0–10 scale	185	7.2	2	1	4	6	7	8	10	10
Characteristic pain intensity†	0–10 scale	185	51.8	19.2	10	23	37	50	67	83	97
Interference in daily activities due to facial pain	0–10 scale	185	2.2	2.3	0	0	0	2	4	7	10
Interference in social activities due to facial pain	0–10 scale	184	1.8	2.5	0	0	0	1	3	7	10
Interference in work due to facial pain	0–100 scale	185	2.0	2.6	0	0	0	1	3	8	10
Number of days kept from usual activities because of facial pain	0–180 days	182	10.7	29.9	0	0	0	0	6	48	180

*The Gracely scales use the verbal descriptor of "mild" for pain intensity of 7 and "unpleasant" for pain unpleasantness of 8.
†Characteristic pain intensity is the mean of current, average and worst ratings, rescaled as a 0 to 100 measure.

Table 6. Associations Between Demographic Characteristics and Temporomandibular Disorder (TMD) in the OPPERA Baseline Case-Control Study

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect	
Demographic Characteristic	Category*	N	Column %	N	Column %	P Value†	OR§	95% CI¶	OR	95% CI
Age (years)	35–44	344	21.1	53	28.6	.0044	2.2	1.4, 3.3	2.3	1.5, 3.6
	25–34	451	27.6	60	32.4		1.7	1.2, 2.5	1.8	1.2, 2.6
	18–24 [ref]	838	51.3	72	38.9					
Gender	Female	925	56.6	155	83.8	<.0001	4.0	2.7, 6.0	4	2.6, 6.0
	Male [ref]	708	43.4	30	16.2					
Race-ethnicity	Other/not stated	186	11.4	7	3.8	<.0001	.2	.1, .5	.2	.1, .5
	Hispanic	100	6.1	8	4.3		.4	.2, .9	.4	.2, 1.0
	Black/African American	508	31.1	25	13.5		.2	.1, .3	.2	.1, .3
	White non-Hispanic [ref]	839	51.4	145	78.4					
Race-ethnicity	Other/not stated	794	48.6	40	21.6	<.0001	.2	.2, .4	.2	.1, .3
	White non-Hispanic [ref]	839	51.4	145	78.4					
Born in USA	No	251	15.7	25	13.5	.4426	.8	.5, 1.3	1.4	.8, 2.2
	Yes [ref]	1,351	84.3	160	86.5					

*Reference group used to calculate odds ratios.
†*P* value is from Chi-square test evaluating overall association between demographic characteristic and case-status.
‡Site-adjusted effects were computed in logistic regression models where the demographic characteristic was the main explanatory variable and study site was the sole covariate. Fully-adjusted effects were computed in logistic regression models that further adjusted for age, gender, and race/ethnicity.
§Odds ratio.
¶95% confidence interval for odds ratio.

volunteers, rather than people who agreed to participate after being selected at random from a sampling frame. Statistical sampling theory dictates that measures of association and other statistics computed from nonprobability samples cannot be construed as population estimates[1] (page 116). Even when random samples are selected, nonparticipation and loss-to-follow-up is inevitable, and it is important to evaluate representativeness of the study participants. A common technique is to compare characteristics of study participants with

Table 7. Associations Between Socioeconomic Characteristics and Temporomandibular Disorder (TMD) in the OPPERA Baseline Case-Control Study

		Controls		TMD Cases			Site-Adjusted Effect‡		Fully-Adjusted Effect	
Socioeconomic Characteristic	Category*	N	Column %	N	Column %	P Value†	OR§	95% CI¶	OR	95% CI
First language spoken	Other than English	220	13.6	13	7.0	.0119	.5	.3, .8	.8	.5, 1.6
	English [ref]	1,402	86.4	172	93.0					
Marital status	Never married	1,184	73.5	107	58.5	<.0001	.5	.4, .7	.7	.5, 1.1
	Other [ref]	427	26.5	76	41.5					
Highest level of schooling	Post graduate	249	15.5	42	23.0	.0005	3.7	1.9, 7.1	2.0	1.0, 4.0
	College	403	25.0	57	31.1		3.1	1.6, 5.8	2.2	1.2, 4.3
	Post HS/some college	673	41.8	69	37.7		2.2	1.2, 4.0	2.0	1.1, 3.9
	High school or less [ref]	286	17.8	15	8.2					
Family annual household income	$80,000 or more	365	29.6	47	30.9	.7322	1.1	.6, 1.8	.9	.5, 1.6
	$40,000–$79,999	333	27.0	46	30.3		1.2	.7, 2.0	.9	.5, 1.5
	$20,000–$39,999	282	22.9	31	20.4		1.0	.6, 1.7	.8	.5, 1.4
	$0–$19,999 [ref]	254	20.6	28	18.4					
Satisfaction with financial situation	10–7	469	29.1	59	32.1	.6424	1.2	.8, 1.7	1.0	.7, 1.5
	4–6	619	38.4	70	38.0		1.1	.7, 1.6	.9	.6, 1.4
	0–3 [ref]	526	32.6	55	29.9					
Satisfaction with material standards in life	9–10	378	23.6	42	22.8	.4234	1.1	.7, 1.7	.8	.5, 1.3
	6–8	744	46.4	94	51.1		1.3	.9, 1.8	1.0	.7, 1.5
	0–5 [ref]	483	30.1	48	26.1					
Covered by health insurance	No	305	19.3	29	16.5	.3686	.8	.5, 1.2	1.1	.7, 1.8
	Yes [ref]	1,277	80.7	147	83.5					

*Reference group used to calculate odds ratios.
†*P* value is from Chi-square test evaluating overall association between demographic characteristic and case-status.
‡Site-adjusted effects were computed in logistic regression models where the demographic characteristic was the main explanatory variable and study site was the sole covariate. Fully-adjusted effects were computed in logistic regression models that further adjusted for age, gender, and race/ethnicity.
§Odds ratio.
¶95% confidence interval for odds ratio.

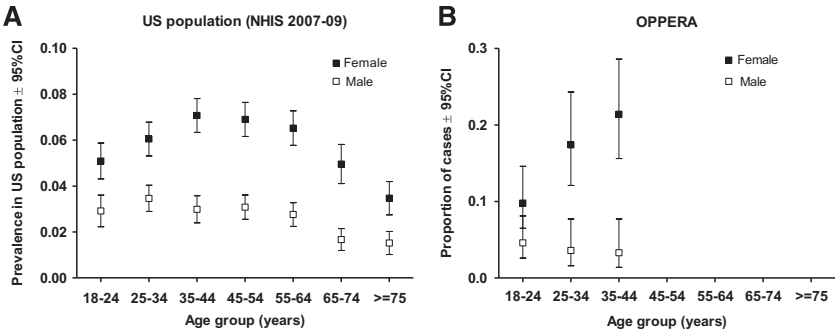

Figure 2. Temporomandibular disorder (TMD) prevalence in the US population and proportion of cases in the OPPERA Baseline Case Control Study.
A: Prevalence of self-reported TMD-like pain in the US population from the 2007 to 2009 National Health Interview Survey (NHIS; n = 72,836 people). Cases were people who responded positively to the interview question: "During the past 3 months have you had facial ache or pain in the jaw muscles or the joint in front of the ear"?
B: Site-adjusted proportion of cases in the OPPERA case-control study (n = 185 TMD cases and 1,633 controls). Proportions are predicted probabilities computed from a logistic regression model with predictor-variables age-group, gender, and age-group by gender interaction. Because the number of cases was determined by study design, the proportions are not estimates of population prevalence. However, the demographic patterns of variation in proportions seen in the OPPERA case-control study is comparable to demographic patterns of variation in prevalence within the US population.

population benchmarks. Despite not having used probability sampling methods, we also investigated representatives by comparing sociodemographic characteristics of OPPERA controls with Census 2000 data. Not surprisingly, there was evidence of nonrepresentativeness, most notably for age distribution, marital status, and educational attainment. Furthermore, the degree of nonrepresentativeness varied among study sites. In the case-control study, different numbers of cases were enrolled at each site for operational reasons. We therefore adjusted for study site and demographic characteristics to produce internally valid estimates of association in the case-control study. However, it is important to note that those statistical adjustments do not guarantee external validity.

Generalizability is not essential when investigating putative risk factors in epidemiological studies. Even in studies that lack generalizability, a characteristic found to be a risk factor provides "proof of principle" that the characteristic can influence health. Furthermore, if a study enrolls sufficient numbers of people in major demographic groups, the "proof of principle" potentially can be evaluated separately in those groups. Indeed, it is unusual for prospective cohort studies to use probability sampling methods, and doing so might even threaten internal validity, for example, by making it more difficult to obtain uniformly accurate measurement among all study participants[20] (p 146).

Demographic diversity was an explicit recruitment goal for OPPERA, in part because the project was funded by a request for applications that required inclusion of "subjects from both genders, all racial and ethnic groups (and subgroups)."[5] When the study was designed, relatively little was known about age-related and racial/ethnic variations in rates of examiner-determined TMD for US community-based samples drawn from nonclinical settings. For that reason, it was important that an unmatched case-control study design be used, and that cases and controls reflected demographic variation in the United States. Hence, the OPPERA sites were selected because they included large metropolitan areas and smaller rural communities.

Another goal of recruitment for the prospective cohort study was to select people who reported no history of TMD but who varied in characteristics that likely were associated with risk of developing the condition. Specifically, it was important not to exclude "sub-clinical" individuals who had some (but not sufficient) signs and symptoms of TMD. We therefore permitted enrollment of people who reported infrequent pain in the orofacial area (ie, less than 5 days per month) or who reported some headaches (fewer than 5 episodes in the past month), provided they were not found to have TMD when examined. People were not enrolled in the prospective cohort study if they reported 5 or more headache episodes per month because that number of temple region headaches potentially could be regarded as a variant of TMD.[3] A variety of other overlapping pain conditions was permitted without qualification.

People with these sub-clinical and overlapping conditions were not excluded from the prospective cohort study for 2 reasons: 1) the aims of the prospective cohort study might be compromised by enrolling a highly pain-resistant group which may have a very low incidence rate of first-onset TMD—the endpoint for the main scientific goals of OPPERA; and 2) sub-clinical and overlapping conditions are highly prevalent in the US population, which may have limited OPPERA's generalizability by excluding people with those conditions. Likewise, for the case-control analysis, it is important to retain people with sub-clinical conditions, because their exclusion produces estimates of association that are biased away from the null.[19]

The OPPERA baseline case-control findings confirmed that TMD occurs more frequently in females than in males.[6,16] Although there is less published evidence about racial and ethnic group variation in TMD, these OPPERA findings are consistent with results from the NHIS showing that non-Hispanic whites have higher prevalence of TMD-like pain than racial and ethnic minorities in the US.[8] Our own analysis of NHIS data

revealed patterns of age- and gender-specific prevalence in the US population that were strikingly similar to patterns observed in the observed proportion of cases among the 18 to 44 year-olds in OPPERA. Together with results from an examination survey of women in New York,[9] these findings demonstrate a positive association between age and occurrence of TMD among women within the 18 to 44 year age range. The findings clarify ambiguity in the literature regarding the association between age and TMD in early- and mid-adulthood. For example, a systematic review noted that most cross-sectional studies of TMD prevalence found "a negative linear relationship between prevalence and age,"[16] a premise echoed by the National Institutes of Health in its request for applications[5] that led to the OPPERA study.

Because of its rigorous sampling design and its large sample size, the NHIS represents the gold standard for prevalence of self-reported health conditions in the United States. Prevalence of TMD-like symptoms in the NHIS was based on a single-item question that is similar to the question used in other national interview surveys.[11] In the study of women in New York City,[9] a comparable single-item screening question yielded prevalence (10.1%) that was very similar to prevalence of examiner-determined TMD (10.5%). This was despite the fact that the screening question had low sensitivity (42.7%), a limitation that was balanced by excellent specificity (94.7%). If the NHIS screening question for TMD had similar validity, the NHIS prevalence figures represent only slight underestimates of the true population prevalence. Taken together, the age- and gender-related associations with TMD in the OPPERA case-control study suggest that OPPERA should have broad applicability for the populations at these 4 US study sites.

Past studies provide inconsistent evidence regarding the relationship between socioeconomic status and TMD.[16] A questionnaire-based survey of 50- and 60-year-olds in Sweden reported significantly greater odds of orofacial pain for people in blue-collar occupations than in white-collar occupations, although there was no significant association with education.[10] In the United Kingdom, self-reported prevalence of orofacial pain was elevated 1.5-fold for people living in areas of the country that were the most socioeconomically deprived relative to people living in affluent areas.[2] In that study, orofacial pain included reported pain in the jaw joints and other parts of the face, pain during jaw function, tenderness of facial muscles, and other forms of oral pain such as burning and shooting pain. These case-control findings from OPPERA showed a general lack of association between examiner-classified TMD and indicators such as income and health insurance, and only a modest increase in odds of TMD associated with greater educational attainment. Satisfaction with financial and material circumstanace reflect financial strain[12] which is 1 aspect of subjective social status, a construct found to be informative in social epidemiologic studies of health inequalities.[21] Despite the fairly consistent null associations with chronic TMD observed using a number of socioeconomic indicators, the relationship warrants more detailed investigation. For example, these analyses adjust only for demographic characteristics, yet other risk factor for TMD might have confounded socioeconomic associations towards the null. Also, results from the prospective cohort study should provide additional insight into effects of socioeconomic status on risk of developing TMD.

Nonetheless, the very absence of a marked inverse social gradient in TMD makes it 1 of the few health conditions to defy that trend. In contrast, reviews of other pain conditions report a consistent, inverse gradient of reducing prevalence in higher socioeconomic groups.[18] In the case of widespread bodily pain, a large, population-based prospective cohort study was able to attribute the inverse gradient to an array of psychological characteristics: psychological distress, anxiety, depression, illness behavior, somatic symptoms, sleep problems, and threatening life events.[4]

In summary, these finding from the OPPERA baseline case-control study revealed an array of demographic associations: TMD was more likely in older than in younger age groups, in females than in males, and in non-Hispanic-Whites than in other racial/ethnic groups. This latter result, and the general absence of a socioeconomic gradient in TMD, are counter to the patterns of health disparities seen in many other diseases and disorders.

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Supplementary Data

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

References

1. Aday LA: Designing and conducting health surveys: A comprehensive guide, 2nd ed. San Francisco, CA, Jossey-Bass Publishers, 1996

2. Aggarwal VR, Macfarlane TV, Macfarlane GJ: Why is pain more common amongst people living in areas of low Socio-economic status? A population-based cross-sectional study. Br Dent J 194:383-387, 2003

3. Ballegaard V, Thede-Schmidt-Hansen P, Svensson P, Jensen R: Are headache and temporomandibular disorders related? A blinded study. Cephalalgia 28:832-841, 2008

4. Davies KA, Silman AJ, Macfarlane GJ, Nicholl BI, Dickens C, Morriss R, Ray D, McBeth J: The association

between neighbourhood Socioeconomic status and the onset of chronic widespread pain: Results from the EPIFUND study. Eur J Pain 13:635-640, 2009

5. Department of Health and Human Services (DHHS): Prospective studies on craniofacial pain and dysfunction. RFA Number: RFA-DE-05-007. http://grants.nih.gov/grants/guide/rfa-files/RFA-DE-05-007.html Cited: February 9, 2011

6. Drangsholt ML, L.: Temporomandibular disorder pain, in Epidemiology of Pain, (Crombie IK, Croft PR, Linton SJ, LeResche LVK, M., Eds.) Seattle, WA, IASP Press, 1999. pp. 43-52

7. Dworkin SF, LeResche L: Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. J Craniomandib Disord 6: 301-355, 1992

8. Isong U, Gansky S, Plesh O: Temporomandibular joint and muscle disorder-type pain in U.S. adults: The National Health Interview Survey. J Orofac Pain 22: 317-322, 2008

9. Janal M, Raphael K, Nayak S, Klausner J: Prevalence of myofascial temporomandibular disorder in US community women. J Oral Rehabil 35:801-809, 2008

10. Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A: Risk factors associated with symptoms of temporomandibular disorders in a population of 50- and 60-year-old subjects. J Oral Rehabil 33:473-481, 2006

11. John MT, Hirsch C, Drangsholt MT, Mancl LA, Setz JM: Overbite and overjet are not related to self-report of temporomandibular disorder symptoms. J Dent Res 81:164-169, 2002

12. Krause N, Baker E: Financial strain, economic values, and somatic symptoms in later life. Psychol Aging 7:4-14, 1992

13. Last JM, Spasoff RA, Harris SS, Thuriaux MC: International Epidemiological Association: A Dictionary of Epidemiology. New York, NY, Oxford University Press, 2001

14. Lohr SL: Sampling: Design and Analysis. Pacific Grove, CA, Duxbury Press, 1999

15. Lumley T, Diehr P, Emerson S, Chen L: The importance of the normality assumption in large public health data sets. Annu Rev Public Health 23:151-169, 2002

16. Macfarlane TV, Glenny AM, Worthington HV: Systematic review of population-based epidemiological studies of orofacial pain. J Dent 29:451-467, 2001

17. Marmot MG, Wilkinson RG: Social Determinants of Health. New York, NY, Oxford University Press, 1999

18. Poleshuck EL, Green CR: Socioeconomic disadvantage and pain. Pain 136:235-238, 2008

19. Poole C: Controls who experienced hypothetical causal intermediates should not be excluded from case-control studies. Am J Epidemiol 150:547-551, 1999

20. Rothman KJ, Greenland S, Lash TL: Modern epidemiology. Philadelphia, PA, Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008

21. Singh-Manoux A, Adler NE, Marmot MG: Subjective social status: Its determinants and its association with measures of ill-health in the Whitehall II study. Soc Sci Med 56: 1321-1333, 2003

22. Smedley BD, Syme SL: Promoting health: Intervention strategies from social and behavioral research. Washington, DC, National Academy Press, 2000

23. U.S. Census Bureau: American Fact Finder. http://factfinder.census.gov/home/saff/main.html?_lang=en Cited: February 9, 2011

24. U.S. Centers for Disease Control and Prevention: National Health Interview Survey. Questionnaires, Datasets, and Related Documentation 1997 to the Present. http://www.cdc.gov/nchs/nhis/quest_data_related_1997_forward.htm Cited: February 9, 2011

25. U.S. Department of Health and Human Services. The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020: Phase I report: Recommendations for the framework and format of Healthy People 2020. Section IV. Advisory Committee findings and recommendations. http://www.healthypeople.gov/hp2020/advisory/Phasel/sec4.htm#_Toc211942917 Cited: February 9, 2011