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**FATORES DE RISCO PARA DISFUNÇÕES TEMPOROMANDIBULARES:
UMA REVISÃO SISTEMÁTICA DE ESCOPO**

Florianópolis
2020

Cecília Doebber Da Cas

**FATORES DE RISCO PARA DISFUNÇÕES TEMPOROMANDIBULARES:
UMA REVISÃO SISTEMÁTICA DE ESCOPO**

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Orientadora: Prof^a. Dr^a. Beatriz Dulcineia
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Cecília Doebber Da Cas

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O presente trabalho em nível de mestrado foi avaliado e aprovado por banca examinadora composta pelos seguintes membros.

Dra. Juliana Stuginski-Barbosa (Membro externo)

Dra. Giovana Fernandes (Membro externo)

Certificamos que esta é a **versão original e final** do trabalho de conclusão que foi julgado adequado para obtenção do título de mestre em Odontologia.

Coordenação do Programa de Pós-graduação

Prof^ª. Beatriz Dulcineia Mendes de Souza, Dr^a Orientadora

Florianópolis, 2020.

Este trabalho é dedicado à minha família e à equipe do CEMDOR.

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RESUMO

Objetivo: Analisar sistematicamente, por meio de uma revisão de escopo, a literatura disponível sobre os fatores de risco para disfunções temporomandibulares (DTM) e identificar as lacunas existentes sobre esse tema.

Métodos: A busca foi efetuada nas cinco principais bases de dados da área da saúde: PubMed, EMBASE, LILACS, Scopus e Web of Science, além da literatura cinzenta presente nas bases Google Scholar, Open Grey e ProQuest. Dois revisores analisaram cegamente os artigos encontrados considerando os critérios de elegibilidade pré-estabelecidos. Foram incluídos os estudos de coorte que analisaram os fatores de risco em populações com idade acima de 18 anos e que utilizaram como ferramenta diagnóstica para DTM o Research Diagnostic Criteria (RDC/TMD), Diagnostic Criteria (DC/TMD) ou as diretrizes da American Academy of Orofacial Pain (AAOP). Os estudos deveriam apresentar uma média de acompanhamento mínimo de um ano e os participantes não poderiam ter sofrido nenhum tipo de intervenção pelos pesquisadores. Não houve restrição quanto a data de publicação e foram incluídos estudos escritos apenas no alfabeto Latino-Romano.

Resultados: Dezenove estudos foram incluídos. Somente um estudo analisou a DTM com base nos critérios definidos pela AAOP e o restante utilizou o RDC/TMD. Onze estudos utilizaram a mesma amostra e somente 3 estudos dividiram o diagnóstico de DTM entre muscular e articular. Gênero feminino, idade média de 30 anos e raça afro-americana apresentaram risco maior quando comparadas com gênero masculino, idades mais novas e brancos, respectivamente. Sintomas somáticos de depressão e ansiedade, número de comorbidades, cefaleias, dores nas costas, Síndrome do Intestino Irritável, dores genitais, Apneia Obstrutiva do Sono, qualidade e distúrbios de sono, sintomas orofaciais não-específicos, dor em função ou palpação das estruturas do sistema estomatognático foram variáveis avaliadas por análises multivariadas e significativamente associada com DTM.

Conclusão: As variáveis significativas foram heterogêneas. No geral, gênero feminino e idade foram as características mais estudadas. Dores nas costas, trauma, cefaleias, variáveis relacionadas com sono, sintomas de depressão, presença de comorbidades, e sintomas faciais foram os grupos de mais significativamente relacionados com início de DTM. Entretanto, mais estudos de coorte utilizando análises multivariadas são necessárias para confirmar essas associações.

Palavras-Chaves: Doenças estomatognáticas. Doenças Musculoesqueléticas. Fator de risco. Dor facial.

ABSTRACT

Aim: The aims of this scoping review (ScR) were systematically evaluating the available evidence about risk factors involved to temporomandibular disorders (TMD) and identify the possible knowledge gaps present in the scientific literature concerning this topic.

Methods: The search was executed in five main databases for the topic, additionally to three databases of grey literature. Two reviewers assessed the studies blindly through a pre-determined eligibility criterion. Studies comprising the study topic in samples over 18 years old and using Research Diagnostic Criteria (RDC/TMD), Diagnostic Criteria (DC/TMD) or American Academy of Orofacial Pain (AAOP) to diagnoses TMD were included. No publishing data limits were applied, but only articles written in Latin Roman alphabet were accepted. In addition, a minimum average follow-up of one year were required and the participants must have not suffered any intervention by the researchers.

Results: Nineteen studies were included. Only one study assessed TMD by AAOP guidelines. Female gender demonstrated higher likelihood than males, as well as the age group around 30 years old and African race. Somatic symptoms, somatization, depression, anxiety, comorbidities, headache, back pain, irritable bowel syndrome, genital pain, obstructive sleep apnea, sleep quality, non-specific orofacial symptoms, jaw mobility pain and pain on palpation of stomatognathic structures were variables assessed by multivariate analyses and positively associated with TMD. Parafunctional habits and occlusal-related variables were also significantly related to TMD but were assessed by univariate analyzes.

Conclusion: The significant variables were greatly heterogeneous. In general, female gender and age were the characteristics most assessed. Back pain, trauma, headache, sleep-related variables, depression, comorbidities, somatization and facial symptoms were the most significantly related to TMD. However, more cohort studies including variables already appraised are necessary to confirm the results in other samples and fully understand the factors involved in TMD onset.

Keywords: Temporomandibular disorder. Risk factors. Systematic Review. Causality. Orofacial Pain.

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LISTA DE ABREVIATURAS E SIGLAS

AAOP – American Academy of Orofacial Pain
ATM – Articulação Temporomandibular
BS – Bruxismo do Sono
BV – Bruxismo em Vigília
DC/TMD – Diagnostic Criteria for TMD
DTM – Disfunção Temporomandibular
OPPERA – Orofacial Pain: Prospective Evaluation and Risk Assessment
RDC/TMD – Research Diagnostic Criteria for TMD

Do artigo em inglês:

AAOP – American Academy of Orofacial Pain
APS – Average Pain Sensitivity
BMI – Body Mass Index
BSI – Brief Symptom Inventory
CAD – Coronary artery Disease
CCI_R – Charlson Comorbidity Index Revised
CCI_A – Chronic Obstructive Artery
CHF – Congestive Heart Failure
CID-S – Composite International Diagnostic-Screener
CKD – Chronic Kidney Disease
COMT – Catecholamine-O-methyltransferase
CPQ-R – Comprehensive Pain and Symptom Questionnaire
CSPQ – Comprehensive Pain Symptom Questionnaire
CSQ-R – The Coping Strategies Questionnaire-Revised
DC/TMD – Diagnostic Criteria for TMD
EPQ-R – Eysenck Personality Questionnaire-Revised
GCPS – Grade Chronic Pain Scale
HPS – High Pain Sensitivity
HR – Hazard Ratio
HTN – Hypertension
IBS – Irritable Bowel Syndrome
ICDH – International Classification of Headaches Disorders
ICP – Intercuspal Position

IDR – Incidence Density Ratio
IHS – International Headache Society
IP – Insured Premium
JBI – Joanna Briggs Institute
JFLS – Jaw Functional Limitation Scale
LBP – Low Back Pain
LES – Life Experiences Surveys
LPS – Low Pain Sensitivity
LSL – Lifetime Stressor List
MV – Multivariate Analysis
NMD – Nonpsychotic Mental Disorders
NTD – New Taiwan dollars
OBC – Oral Behaviors Checklist
OPPERA – Orofacial Pain: Prospective Evaluation and Risk Assessment
OR – Odds Ratio
OSA – Obstructive Sleep Apnea
PCA – Principal Component Analysis
PCL-C - Checklist-Civilian Version
PCS – The Pain Catastrophizing Scale
PILL – Pennebaker Inventory of Limbic Languidness
POMS-bi – Profile of Mood States-Bi-Polar
PPT – Pressure Pain Threshold
PRISMA-ScR – Preferred Reporting Items for Systematic Review and Meta-Analyses
extension for Scoping Reviews
PSH – Pain Sensitivity Haplotypes
PSQI – Pittsburgh Sleep Quality Index
PSS – Perceived Stress Scale
PTSD – Post-Traumatic Stress Disorder
QHU – Quarterly Health Update
QST – Quantitative Sensory Test
RA – Rheumatoid Arthritis
RCP – Retruded Contact Position
RDC/TMD – Research Diagnostic Criteria for TMD
ref. – Reference

RR – Risk Ratio
SCLR-90 – Symptom Checklist 90-Revised
ScR – Scoping Review
SF12v2 – Short Form 12 Health Survey
SNP – Single Nucleotide polymorphisms
SQN-R – sleep Quality Numeric Rating Scale
SQR – Symptom Report Questionnaire
STAI – State-Trait Anxiety Inventory
TMD – Temporomandibular Disorder
TMJ – Temporomandibular Joint
TTH – Tension-type headache
TTH – Tensional-Type Headache
US – United States
USD – United State Dollars
UV – Univariate Analysis
WHO – World Health Organization
y.o – years old

LISTA DE SÍMBOLOS

% - Porcentagem

± - Mais ou menos

Do artigo em inglês:

% - Percentage

± - More or less than

≤ - Less than or equal to

°C - Degree in Celsius scale

> - Greater than

kg/m² - Weigh in kilos divided by the squared height in meters

mmHg - Millimetre of mercury

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1 INTRODUÇÃO

As disfunções temporomandibulares (DTM) são condições que envolvem os músculos da mastigação, a articulação temporomandibular (ATM) e estruturas anexas (LEEUEW e KLASSER, 2018). Estima-se que 10% da população mundial apresentem algum tipo de DTM (LERESCHE, 1997). As DTMs podem ser divididas em articulares, quando acometem a ATM, e musculares, quando a musculatura do sistema estomatognático é afetada. Os sinais e sintomas mais frequentes dessas disfunções compreendem dor nos músculos e/ou ATM, na palpação ou em função, ruídos articulares, assimetrias mandibulares e limitação de abertura (LEEUEW e KLASSER, 2018). Além disso, ela é considerada a causa mais comum de dor crônica na região orofacial (LIST e JENSEN, 2017) e influencia diretamente na qualidade de vida dos pacientes, aumentando a utilização dos serviços públicos de saúde e os custos relacionados ao atendimento (BITINIENE et al., 2018).

Buscando padronizar o diagnóstico e a classificação dessas disfunções, algumas ferramentas internacionais de diagnóstico foram criadas, como o Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (DWORKIN e LERESHE, 1992) que foi desenvolvido para padronizar as pesquisas envolvendo esse tópico. Uma versão atualizada, chamada Diagnostic Criteria (DC/TMD) foi lançada em 2014 (SCHIFFMAN et al., 2014) com o intuito de possibilitar seu uso tanto em pesquisas quanto no atendimento clínico de pacientes com DTM. Esses critérios diagnósticos são divididos em dois eixos: o eixo I corresponde aos aspectos físicos classificando as DTM em mialgia, mialgia local, dor miofascial, dor miofascial com referência ou espalhamento, artralgia, cefaleias atribuídas à DTM, deslocamento de disco com e sem redução, com travamento intermitente, limitação de abertura, doenças degenerativas da articulação e subluxação. Já o eixo II é relacionado com as questões psicossociais envolvidas com a DTM e pode ser avaliada através de questionários. Ainda, uma nova classificação internacional (International Classification of Orofacial Pain - ICOP) foi desenvolvida recentemente, com base nos critérios do DC/TMD, buscando facilitar a padronização dos termos utilizados em pesquisas e no âmbito clínico.

A Organização Mundial da Saúde (OMS, 2009) explica que um fator de risco para a saúde é aquele que aumenta a possibilidade de desenvolver determinada doença ou condição. As DTMs possuem uma etiologia multifatorial e a identificação de fatores de risco que podem contribuir ou aumentar as chances de desenvolvê-la é primordial para descobrir qual o papel dessas variáveis na etiologia dessas condições, visando a prevenção e a escolha da melhor forma de controle ou tratamento. Alguns fatores como gênero, hábitos parafuncionais, fatores

psicossociais, qualidade do sono e distúrbios relacionados, arranjos genéticos entre outros, são algumas variáveis prováveis que aumentam a incidência de DTM.

Para se indicar uma relação de causa-efeito, o padrão referência de desenho de estudo é o de coorte, que acompanha um paciente saudável por um período de tempo (SONG, CHUNG, 2010). Um dos maiores e mais conhecidos estudos de coorte na área é o Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) (SLADE et al., 2016) que analisou uma grande quantidade de variáveis potencialmente relacionadas com o desenvolvimento da DTM. Entretanto, a identificação de outros estudos de coorte possibilitam encontrar similaridades ou divergências em diferentes amostras populacionais (DIATCHENKO et al., 2005; KINDLER et al. 2012; LEE et al., 2020; LIM et al., 2010; MARKLUND, WÄNMAN, 2007; MARKLUND, WÄNMAN, 2008; MARKLUND, WIESINGER, WÄNMAN, 2010).

Algumas revisões sistemáticas (BAAD-HANSEN et al., 2019; DREWECK et al., 2020; FERREIRA et al., 2018; JIMENÉZ-SILVA et al., 2017; MANFREDINI, LOMBARDO, SICILIANI, 2017; REIS et al., 2019) contemplando alguns grupos de fatores de risco já foram publicadas, entretanto, nenhuma delas resumiu ou compreendeu todos os possíveis fatores envolvidos na DTM, além de incluírem desenhos de estudo diferente de coorte, influenciando na qualidade de evidência da relação de causa e efeito dos achados. Uma revisão sistemática que resume alguns fatores envolvidos para a dor musculoesquelética no geral foi encontrada (CLARK et al., 2017), entretanto, essa revisão adicionou somente dois artigos relacionados especificamente com DTM e apresentou informações limitadas sobre o tema proposto. Uma revisão de escopo sobre DTM foi encontrada (RINCHUSE E GREENE, 2018) entretanto, os achados foram baseados em resumos provenientes de revisões sistemáticas e apresentaram conclusões limitadas sobre a etiologia ou fatores envolvidos com DTM.

Por fim, devido a inexistência de uma revisão sistemática ou de escopo abrangendo os fatores de risco envolvidos no aparecimento das DTMs, essa revisão de escopo foi proposta. Os objetivos dessa revisão são mapear a literatura científica vigente para identificar os fatores já descritos e significativamente associados no aparecimento de DTM e encontrar lacunas ainda não explicadas ou compreendidas pelos estudos presentes, contribuindo para futuros estudos primários e revisões sistemáticas.

2 JUSTIFICATIVA

Apesar de haver algumas revisões sistemáticas já publicadas na literatura incluindo alguns aspectos potencialmente envolvidos na etiologia das DTM (BAAD-HANSEN et al., 2019; CLARK et al. 2017; DREWECK et al., 2020; FERREIRA et al., 2018; JIMENÉZ-SILVA et al., 2017; MANFREDINI, LOMBARDO, SICILIANI, 2017; REIS et al., 2019) a maioria deles incluíram desenhos de estudos que não são indicados como as melhores opções para investigar uma relação de causa e efeito, como os estudos de caso-controle, pesquisas laboratoriais, séries de casos e etc. Além disso, somente uma revisão resumiu os fatores envolvidos (CLARK et al. 2017) e os analisou de uma forma generalizada para disfunções musculoesqueléticas no geral, incluindo apenas dois artigos específicos para DTM.

As revisões de escopo são indicadas para analisar a literatura disponível sobre um determinado tópico, possibilitando uma análise geral sobre o tema. Além disso, através de um mapeamento das informações disponíveis, possibilita a identificação de possíveis lacunas ainda não preenchidas, podendo ser usadas como guia para futuros estudos primários e revisões sistemáticas (PETERS et al., 2015). Foi encontrada uma revisão de escopo envolvendo DTM como tópico principal, entretanto, as informações obtidas foram baseadas somente em resumos provenientes de revisões sistemáticas e as informações relacionadas com os fatores de risco envolvidos foram limitadas (RINCHUSE E GREENE, 2018). Em virtude dessas limitações na literatura científica atual, esse trabalho foi proposto.

3 OBJETIVOS

Objetivo geral

Analisar sistematicamente a literatura disponível acerca dos fatores de risco para as DTMs.

Objetivos específicos

- Identificar os fatores de risco mais estudados;
- Identificar e resumir as variáveis significativas;
- Identificar as lacunas existentes na literatura.

4 ARTIGO

Artigo formatado conforme as normas da revista *Journal of Oral Rehabilitation*

A scoping review of risk factors for temporomandibular disorders

Running title: Risk factors for temporomandibular disorder

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Conflict of interest

Authors have no conflicts of interest to declare.

Abstract

Aim: The aims of this scoping review (ScR) were systematically investigating the available data regarding the risk factors involved in onset of temporomandibular disorder (TMD), and finding the possible knowledge gaps in the scientific literature about the topic.

Methods: The search was executed in five primary electronic databases and in three grey literature databases. Two reviewers selected the studies blindly, based on a pre-determined eligibility criterion.

Results: Nineteen studies were included. Female gender demonstrated higher likelihood than males, as well as the age group around 30 years old and African race. Somatic symptoms, depression, anxiety, number of comorbidities, headache, back pain, irritable bowel syndrome, genital pain, obstructive sleep apnea, sleep quality, non-specific orofacial symptoms, jaw mobility pain and pain on palpation of stomatognathic structures were variables assessed by multivariate analyses and positively associated with TMD. Parafunctional habits and occlusal-related variables were also significantly related to TMD but were assessed by univariate analyzes.

Conclusions: The significant variables were greatly heterogeneous. In general, female gender and age were the characteristics most assessed. Back pain, trauma, headache, sleep-related variables, depression, number of comorbidities, somatization and facial symptoms were the most significantly related to TMD. However, more cohort studies comprising multivariate analysis are necessary to confirm it.

Keywords: Temporomandibular disorder. Risk factors. Systematic Review. Causality. Orofacial Pain. Musculoskeletal Diseases.

INTRODUCTION

Temporomandibular disorders (TMD) is an umbrella expression to comprise a group of condition that affect stomatognathic system such as masticatory muscles, temporomandibular joint (TMJ) and associated structures¹. The prevalence of this condition rounds 10% of general population². Moreover, according to American Academy of Orofacial Pain (AAOP), the most frequent signs and symptoms of TMD are pain on muscle and TMJ, on palpation or during function, joint sounds and asymmetric or restricted mandibular movements¹.

In order to standardize the diagnostic of TMD in researches, the Research Diagnostic Criteria (RDC/TMD)³ was proposed in 1992. Its updated version, the Diagnostic Criteria for TMD (DC/TMD)⁴ was created seeking out turn it enable to use in research and clinical assessment as well. The diagnostic of TMD based on these criteria is separated in two major axes: Axis I is related with physical assessments and Axis II is related with psychosocial appraisal throughout a series of validated questionnaires. According to World Health Organization (WHO), “health risk is defined as a factor that raises the probability of adverse health outcomes”⁶. TMD has a multifactorial and complex etiology. Some factors such as gender, parafunctional habits, psychosocial factors, sleep quality and disorders, genetic arrangements, emotional and physical trauma, among others, are examples of predictors related with increasing of risk of TMD onset. The identification of these risk factors and the understanding of how they are involved in the etiology of TMD may allow the prevention and effective management of this condition.

A well-known cohort study in this field, the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA)⁷ evaluated several variables related to TMD. However, other cohort studies^{8,9,10,11,12,13,14} indicated similarities and divergences on results. In addition, few systematic reviews regarding some risk factors involved in TMD were already published in the

literature^{15,16,17,18,19,20}. However, most of them included other study designs, different than cohort and they did not summarize and comprised all the potential risk factors, which could compromise the reliability of cause-effect evidences. Also, one²¹ systematic review about risk factors for general chronic musculoskeletal pain presented only limited information regarding TMD. Similarly, only one²² Scoping Review (ScR) about TMD was found, but it was based on abstracts from systematic reviews and also presented limited information about predictors of TMD.

Hence, the aims of this ScR were map the literature to identify the variables related with TMD and indicate the gaps concerning this field. The research question “Which are the risk factors involved in TMD disorders and the knowledge gaps regarding this topic?” was followed.

METHODS

This ScR was executed according to Joanna Briggs Institute (JBI) Reviewer’s Manual²³ and the Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)²⁴ was followed to this report.

Protocol and Registration

A protocol was performed following the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P)²⁵. The protocol was submitted to publication in the peer-reviewed JBI Database of Systematic Review and Implementation Reports.

Eligibility criteria

Participants

No restrictions about sex or ethnicity were applied, but only sample over 18 years old were included. Studies that investigated TMD outcome by a clinical examination based on RDC/TMD³, DC/TMD⁴ or following the guidelines of AAOP¹ were included. Additionally,

the participants must have not be diagnosed with TMD at baseline and must had been followed-up for an average time of at least one year. Also, the participants must had not undergone any type of interventions by the researchers along the study.

Concept

According to AAOP, TMD are a group of disorders involving the masticatory muscles, the TMJ and associated structures¹. The RDC/TMD³ and its updated version, the DC/TMD⁴, are international tools in order to standardized the assessment of TMD. These instruments splits TMD diagnostic in two major Axes: Axis I is associated to pain disability and Axis II is concerning psychosocial factors. The TMD diagnoses are classified as arthralgia, myalgia, local myalgia, myofascial pain, myofascial pain with referral, four types of disc displacement disorders, degenerative joint disease, subluxation, and headache related to TMD⁴. Risk factor are defined by WHO as any exposure or features that rises probability of developing a disorder or illness⁶.

Context

The context of this ScR were risk factors for TMD. No restriction about geographic location or health service level were applied.

Information sources and search strategy

This study included prospective and retrospective cohort studies, since it is the appropriate approach to analyze potential risk factors with significant evidence²⁶. Randomized controlled trial, case-control study, cross-sectional study, abstracts, reviews, case-reports and series, before-after, protocols, technique articles, guidelines, pilot studies, personal opinions, letters, posters, conference abstracts, and laboratory research (in vivo and in vitro studies) were excluded. In addition, only articles writing in Latin (Roman) alphabet were included and no limitations regarding time of publication was applied. If full text not available online, the

contact by e-mail with corresponding author or libraries was attempted two times, if not successful or corresponding e-mail not available, the study was excluded.

The search was performed on May 12, 2020 in five electronic databases more relevant to the topic: PubMed, EMBASE, Latin American and Caribbean Health Sciences (LILACS), Web of Science and SCOPUS. An additional search in grey literature was performed in Google Scholar, Open Grey and ProQuest Dissertations and Thesis (Supplementary Table S3). Also, a screening of reference lists from included articles were performed by two authors (C.D.C. and L.F.V.). All references were included in a Reference Management software (EndNote X8, Thomson Reuters) in order to exclude duplicated articles and organize references.

Study Selection

The study selection was performed in two phases. In phase one, after exclusion of duplicated articles, two authors (C.D.C. e L.F.V.) evaluated titles and abstracts, separately, using the online software Rayyan®²⁷ (Qatar Computing Research Institute, Doha, Qatar) and cross-checked the selection in a decision meeting. On the second phase, the potential eligible articles were appraised in full-text and blindly by the same authors, considering eligibility criteria and, if applicable, registering the reason for the elimination. A cross-checking meeting were performed and if any disagreement, a third author (L.P.N.) opinion was requested in order to obtain a final decision.

Data collection process and data items

One author (C.D.C.) gathered data from included studies using a standardized data sheet and, in order to warranty the integrity of contents, a crosschecking of the information was executed by another author (L.F.V.). Data collection included authors, year of publication, country, mean age of sample, sample size, time of follow-up, diagnostic criteria used for TMD diagnostic, risk factors assessed, and main results.

RESULTS

Study selection

The search resulted in 2,738 records after removing of duplicates and 183 were selected for the full-text analysis. After full-text assessment, 164 studies were excluded (Supplementary Table 2) and 19 were included (Figure 1) following the eligibility criteria. Main information data and significant variables presented by included studies were assessed in Table 1. A fulfilled data and results from each included study are presented in supplementary material (Supplementary Table S1).

Characteristics of sources of evidence

Eleven studies were from OPPERA cohort study^{28,29,30,31,32,33,34,35,36,37,38}. Only one⁹ used AAOP as guideline to identifies TMD, anyone used DC/TMD and three articles^{9,11,13} presented results for TMJ disorders and myofascial pain individually. The number of variables was countless and heterogenous.

Results of individual sources of evidence:

General Factors

“Female gender” was indicated as risk factor for TMD in six studies,^{11,13,14,29,31,37}, varying its ratio from 1.32 to 4.9 compared with male gender and demonstrated association in Univariate (UV)^{11,13,37} as well as in Multivariate (MV)^{14,29,31} analyses. “Age” was another variable widely studied, it was compared by groups in most of the studies and the middle age group around 30 years old (y.o) presented higher risk of TMD in both UV^{9,31,37} and MV^{29,30,37}, even though when weighed with psychological symptoms³³ or as continuous variable³¹. Also, “African American race” demonstrated a higher hazard of TMD in comparison with white people in UV^{28,31,37} and MV analyses^{36,37}. However, all values are referent to studies from OPPERA. Smoking history was indicated for two studies as a significant factor for TMD development, indicating that “Former and Current smoker” presented a two times greater risk

of TMD than people who never smoked, equally in UV and MV²⁹ and low ratings of ‘Satisfaction with material standards’ were a hazard for TMD, both in UV and MV³¹.

General Health Factors

“Self-rating health status” indicates an 2.5 times greater risk to TMD when this rating is ‘poor or fair’, comparing to ‘excellent’, and it was significant even when the rating ‘good’ was chosen²⁹. Further, the usage of three or more medication indicates an increase around 40% for TMD onset, and history of neurosensory or respiratory conditions could be responsible of an increase of 50% of risk of TMD, considering UV results²⁹. “Mean arterial pressure” higher than 85mmHg³⁷ and “Heart rating”^{32,37} measured by beats per min were also significant, but only in UV analyses, as well as “Body Mass Index (BMI)” higher than 30, indicating obesity^{29,37}. Moreover, lower testosterone and higher estrogen exposure in uterus were significant predicting factors to TMD in UV and MV analyses, increasing around 15% the risk²⁹. “Osteoporosis” was presented by one study as also a significant predictor, corresponding to an increase of 80% in TMD development¹⁰.

Trauma

Trauma was demonstrated as a strong predictor for TMD. “Lifetime history of jaw injury due to prolonged opening” was significant in UV analysis³⁰. However, “First injury”, “Extrinsic injury”, “Intrinsic injury”, “Only one injury” or “Two or more injuries” were significant in MV and presented high values of hazard ratio³⁴.

Headaches

The presence of headaches was significantly associated with TMD by UV^{12,29} and MV analysis^{29,38}. In addition, frequency and severity of headaches events was also significant. Considering the types of headaches, “Tension-type (TTH)”²⁹, “Migraine”³⁸ and “Mixed headache”³⁸ demonstrated significant effect to TMD onset in UV and MV analyses.

Back pain

“Back pain” was significantly associated with TMD^{10,12,14,29}. In addition, one of the studies detected that even current low back at baseline has influence in UV and MV analyses and the number of episodes above 5, in one year, also predicts TMD in an UV analyses²⁹. Further, when spinal back pain was compared among gender, the female gender demonstrated a higher hazard of TMD in MV analyses¹⁴.

Other Pain Conditions

The “number of comorbidities” was a significant factor, also in UV^{28,29} and MV analyses²⁸. In the same way, presence of pains such as “Menstrual pain”, “Chest pain”, “Joint soreness or pain”, “Muscle soreness or pain”, “Abdominal pain” were described as significant, but only in UV analyses¹². Moreover, “Genital pain” presents a significant association in UV and MV, as well as “Positive diagnosed for Irritable Bowel Syndrome (IBS)”²⁹. Along with, “Three until five” or “more than six” IBS symptoms were positively associated with TMD in UV analysis²⁹.

Parafunctional Habits and Facial Symptoms

“Bruxism” in general demonstrated a significantly influence in both TMJ disorders¹¹ and myofascial pain¹³, as well as “Parafunctional habits” in general³⁰. Additionally, in UV analyses, “History or recent inability to open jaw widely”³¹ and “reported TMJ sounds”^{11,30} exhibited significant effect on TMD and, the last one, also specifically to TMJ disorders.

“Facial pain”³⁰ was also indicated to predispose TMD in UV analyses as well as “Pain sensitivity from mechanical and heat stimuli”³². In addition, a Grade Chronic Pain Scale (GCPS) score of 2-4 episodes increased in four times the chance of TMD³⁰. Moreover, “Pain from palpation” was significantly both in UV and MV analysis. An UV analysis demonstrated significance specifically to pain from palpation in “Temporalis”^{30,32}, “Masseter”^{30,32}, “Lateral pterygoid area” in all proposed adjustments, as well as “greater tenderpoints in neck and body”. Differently, pain from palpation in “TMJ” and “Posterior mandibular and submandibular area”

were no significant when imputed data was added³⁰. Further, “1-2 and 3 or more non-specific orofacial symptoms” were significant in UV^{28,30} and MV³⁰ as well as “Jaw mobility pain in opening: unassisted or assisted un-terminated”³⁰. Also, the “Quantity of days that efficiency dropped below 50%” was associated with TMD in UV analysis³⁰.

Occlusal Factors

“Crossbite”, “Unilateral Centric Relation”, “Any deviation of morphological occlusion” were positively associated with TMJ disorders in UV analyses¹¹. However, “Unilateral contact in the centric relation” and “Mandibular instability in intercuspal position” were significant for both, TMJ disorders¹¹ and Myofascial pain¹³.

Sleep Factors

Sleep quality was associated with TMD in UV^{29,30,36,37} and MV²⁹ analysis. In addition, “Time-varying covariate of sleep quality rating” were also significant in both analyses, even when perceived stress was added as mediator, sleep quality presented direct and indirect effect on TMD onset³⁶. Moreover, “High likelihood for Obstructive Sleep Apnea (OSA)” was a significant predictor for TMD in UV and MV analyses³⁷.

Psychosocial Factors

“Depression” was significant related to TMD in UV^{33,39} and MV^{9,39} analyses. In addition, it was also significant, specifically to ‘joint pain’ or ‘joint pain or discomfort’ group and ‘muscle pain or discomfort’, however, for ‘muscle pain’ group it was not significantly in all adjustments⁹. “Depression” presented significance even when adjusted for Catecholamine-O-methyltransferase (COMT)³⁹, demonstrating an independent effect on TMD onset.

“Anxiety” was also described as a predictor for TMD in UV³³, comprising ‘State anxiety’ as well as ‘Strait anxiety’. In MV analyses, it was significant to ‘joint pain or discomfort’, ‘muscle pain’ or ‘muscle pain or discomfort’, however for ‘joint pain’ group the significance was not met in all adjustments⁹.

Higher levels of “Somatic symptoms”^{28,33} was significant in UV and MV analyses, as well as “Perceived stress”^{33,36,39}. Higher scores in “POMS confident-unsure” unsure was also significant in UV³⁹ analyses and “Somatization”, “Obsessive-compulsive” behavior, “Interpersonal sensitivity”, “Hostility”, “Phobia”, “Paranoid”, “Psychotic”, “Post traumatic events”, “Personality (through EPQ-R Neuroticism)”, “Impact of negative events” and “Negative affect (through POMS-bi)” were related to TMD onset in only UV analyses, as well as “Helplessness” and “Passive coping”, however these ones only when imputed data was added³³. In MV analyses, high loadings from “Global psychological” (SCL-90-R scales, the PILL, and the LSL/PCL-C PTSD symptom scale) were a strong predictor together with its associations with “Age” and “Lifetime residency”. Conversely, “Stress and Negative Affectivity” (loadings from State and Trait Anxiety, Perceived Stress, POMS Negative Affect, and EPQ-R Neuroticism; negative loadings for POMS Positive Affect and EPQ-R Extraversion) was significant only when “Global psychological symptoms” were low and in not all proposed adjustments³³.

Genetic Factors

COMT haplotype demonstrated an effect in TMD onset in two studies^{8,39}. No specific Single Nucleotide polymorphisms (SNP) were significantly associated directly to TMD onset; however, some genes present indirectly effect because they have influence on pain phenotypes. As an example, SCN1A and ACE2 were associated with non-painful orofacial symptoms; a SNP of PTGS1 gene was associated with psychosocial factors; a SNP from APP gene was associated with stress and negative affectivity; and MPDZ gene was associated with QST phenotype (heat pain temporal summation)³⁵.

Data synthesis:

The variables presented by the studies were greatly heterogeneous. In general, ‘Female gender’ and ‘Age’ were the characteristics most assessed. ‘Back pain’, ‘Trauma’ and

‘Headaches’ were significantly related to TMD in all studies that contemplated these variables. In addition, ‘Parafunctional Habits’ and ‘Facial symptoms’ were both cited and indicated risk for TMD by 4 studies. Further, ‘Depression’ was assessed by 4 articles and 3 of them encountered positive association with TMD, similarly with ‘Perceived Stress’, cited by 4 and significantly in 3 studies, and ‘Anxiety’, cited by 3 articles and indicated as significant in 2. ‘Sleep-related’ factors were present in 4 studies and all of them established association with TMD, nonetheless OSA was assessed by 2 articles and only 1 found significance. The most assessed significant variables are presented in Table 2. All assessed variables and respective results by each article are shown in Supplementary Table 1.

DISCUSSION

The present ScR explored the existing evidence concerning the risk factors related with TMD. Following that it presents a multifactorial etiology, the detection of possible variables that have influence on TMD outcome is fundamental to help the clinician in TMD prevention, effective management of this condition or in order to promote more specific public health strategies. In addition, the other aim of this ScR is mapping the scientific literature regarding these issues, exposing the existing gaps and allowing focused upcoming studies.

In order to enhance the reliability in assess the potential risk factors involved in TMD, cohort studies were chosen since this study design consistently detect the hazard for a specific condition or disease²⁶. However, this type of study, where patients are observed during a period of time, is expensive and involves a temporal framework, depending of the patient’s availability and willingness, being more susceptible to withdrawals²⁶. As a result, in this study it was not possible found a large variety of studies that comprised both the cohort design and TMD outcome. Since eleven included studies were from the OPPERA study^{28,29,30,31,32,33,34,35,36,37,38}, a same sample was used for different analyses and the numbers of variables were greatly heterogeneous. In addition, the included studies, even those not from

OPPERA, comprised different variables and most of them did not distinguish the TMD diagnosis into at least muscle or articular disorder, interfering on information summarizing. Moreover, most of them used only the RDC/TMD³ criteria. It can be explained due to the DC/TMD⁴ had been translated in some languages recently and a minimal of one year of follow-up were an eligibility criterion for this study.

Due to the multifactorial nature of TMD, multivariate (MV) analyses are important to comprise some important confounders that may impact on the results. Some interesting variables were assessed only by univariate (UV) analysis and these results must be interpreted with caution, because it can super estimate or underestimate the effect⁴⁰. Thus, in this ScR, the number of studies and the type of analysis performed by them were considered.

First of all, female gender is considered a relevant risk factor by several studies^{11,13,14,29,31,37}. It confirms that women have greater risk to develop TMD and supports the higher prevalence of TMD in women, as previously demonstrated in systematic reviews^{41,42,43}. Regarding the age, the group most affected by TMD were around 30y.o. Although it is known that age peaks can variate depending of specific diagnoses, in general TMD, this age-peak were also already comprised by the scientific literature^{44,45,46} and systematic review⁴³.

The role of occlusal factors in TMD is controversial. In this ScR some occlusal problems such as crossbite, deviation of morphological occlusion, unilateral centric relation in centric relation position and mandibular instability were significant to TMD by included studies^{11,13}. However, more recent studies did not found an evident association of occlusal factors as predictor for TMD^{18,41}, as well as problems linked with centric-relation intercuspal position¹⁷ and chewing dysfunctions¹⁹. A 20-years follow-up study indicated that no single occlusal factor is responsible to cause TMD, nevertheless, a lateral forced bite between retruded contact position and intercuspal position and unilateral crossbite could be considered as risk factors⁴⁷. Also, some occlusal interferences associated with higher levels of

parafunctional habits may lead to TMD, because this type of patients present higher perceptions of pain⁴⁸. In addition, some researchers believe that the occlusal factors no significance is due the lack of longitudinal controlled studies⁴⁹ and others implies that these interferences could be a result of TMD and depends of patient's ability to overcome this discrepancy⁴¹. Conversely with occlusal factors, physical trauma^{30,34} presented a strong correlation with TMD onset in both types of analysis and it is also confirmed by systematic reviews^{50,51}.

Similarly, bruxism^{11,13} was also a significant factors for TMD outcome. This significance is confirmed, for children, by a systematic review¹⁶. To adults, a systematic review established a relationship, but reinforce the necessity of higher-quality and cohort studies in order to precisely affirm it⁵². An umbrella review contemplating TMD and bruxism suggested a plausible evidence between bruxism and signs and symptoms of TMD⁵³. Further, a systematic review also pointed out the conflicting evidence available, but suggested a relation in some extent and indicated that this association can also be mediated by other risk factors, such as age, the method of investigation and the period when the event occurs, awake or sleep bruxism¹⁵. Following, the included studies in this ScR did not differentiate awake bruxism and sleep bruxism. This distinction is essential for a reliable evaluation, since they have different mechanisms involved⁵⁴. As an example, although the evaluation of awake bruxism by studies are relatively recent, some of them indicates that sustained clenching (more common in awake bruxism) is more involved to articular disorders than gridding (more common in sleep bruxism)⁵⁵. Also, due to the increased muscle activity, the bruxism and other parafunctional habits, also significant to TMD in UV analysis³⁰, may play a role in temporary facial pain and other non-specific symptoms¹⁵, also being significantly related with TMD in included studies^{28,30} by UV and MV analysis.

In addition, the detection of bruxism in the included studies were analyzed only through self-related episodes, thus, only possible bruxism diagnostic can be draw. It may influenced in

the analysis, once the bruxism can be active or inactive and some episodes could not be detectable by the patient, mainly during sleepiness^{56,57}. Also, according to International Consensus of Bruxism, the bruxism could be considered a risk factor, a protective factor or nor a protective or risk factor⁵⁴, being considered a behavior. It implicates that the bruxism occurrence could be a protective factor in response of some parallel disorder, such as OSA⁵⁴, which was also a significant risk factor of TMD onset³⁷.

Likewise, sleep-related factors were also related with TMD among all four studies that comprised these variables. Most of the results were from PSQI and SQN-R questionnaires, both validated and adequate methods to investigate the sleep quality of patients^{58,59}. The sleep quality is indicated as an important regulator of our physiologic and psychological system^{60,61} and although the complexity of this connection, the increased likelihood of TMD could be explained due to the fact that sleep deprivation could influence in pain sensitivity threshold because it alters the function of key endogenous pain modulatory pathways⁶². In addition, the association of sleep quality with TMD was already demonstrated in a recently systematic review²⁰ and it presents a bidirectional relationship with TMD⁶⁰.

Additionally, primary headaches such as tensional-type headache and migraine were also associated with TMD outcome^{12,29,38}. It is confirmed by the scientific literature available^{63,64,65} and it presents a bidirectional relationship with TMD because both conditions are related with central sensitization and impairment of the descending pain inhibitory system⁶⁵. Moreover, migraine was demonstrated as a risk factor for TMD and, although TMD is not considered a risk factor for primary headaches, it plays a role in their chronification³⁸. Similarly, back pain was also related with TMD^{10,12,14,29} as well as presence of other painful comorbidities^{12,29}, that also shares similar pain pathways⁶⁵.

Furthermore, all of aforementioned variables can be mediated by psychosocial aspects. Symptoms of depression^{9,33,39} and anxiety^{9,33}, perceived stress^{33,36,39} and somatization³³

presented significance. Although the role of these factors in TMD is not fully understood⁶⁶ and it has been broadly studied^{67,68}. The findings goes on the way of the high prevalence of depressive symptoms and somatization in patients with TMD^{69,70} while symptoms of anxiety presented a stronger link with myofascial pain⁷¹. However, only one included study comprised a great variety of psychosocial issues³³. Thus, more cohort studies are recommended in order to investigate which of them may contribute to TMD and reinforcing the findings from this study. In addition, psychosocial categories may impact differently for the different TMD diagnostics and mostly of included studies did not present results differentiating it⁷².

Limitations

The distinction between muscle and articular disorders were not possible due to the general assessment of TMD by the included studies. The variables were greatly heterogeneous and a reliable comparison between different samples and studies were impaired. Thus, a risk of over generalization of results is recognized due to type of this review, and the results presented should be concluded with caution.

Knowledge gaps

Most of the variables were assessed by one or two studies. Thus, future studies must comprise similar variables already assessed to enable a reliable comparison between samples and studies. In addition, some important variables assessed have subdivision, such as bruxism. The difference between awake bruxism and sleep bruxism can lead to different results, essential to better understand the role of this issue in temporomandibular disorder.

Similarly, TMD diagnoses were evaluated in a general form by the majority of the included studies. It is necessary indicates if it has a muscle or articular involvement because the risk factors may variate to each of them, as well as painful and non-painful TMD.

In addition, the role of most psychosocial characteristics is unclear. Hence, it is suggested that future studies also comprise these characteristics in order to better understand its role in TMD.

Further, many articles were excluded due to not using an international tool such as RDC/TMD, DC/TMD or AAOP guidelines. The standardization of studies is crucial to increase the possibility of results comparison regarding TMD etiology, comorbidities or treatment, and fully understand this process.

Moreover, considering the multifactorial nature of TMD, more multivariate analyses are indicated in order to contemplate relevant cofounders of this complex disorder.

CONCLUSIONS

The significant variables were greatly heterogeneous. In general, female gender and age were the characteristics most assessed. Back pain, trauma, headache, sleep-related variables, somatization, facial symptoms, parafunctional habits and occlusal-related variables were also significantly related to TMD in all studies that contemplated these variables. Due to the multifactorial etiology of TMD, the risk factors related as significant by the included studies are intercorrelated and must be appraised in a conjunctive form. Thus, through this ScR, it is possible to infer that more studies, mainly comprising multivariable analysis, are necessary in order to fully understand which are the potentially factors to increase the likelihood of TMD.

Authors' contribution: C.D.C. and L.F.V. conducted the study, designed the protocol and search strategy, executed the study selection and data extraction. C.D.C. performed the synthesis and prepared the manuscript. L.F.V., L.P.N., A.C.S.D. and B.D.M.S. participated in interpretation of the results and helped to write the manuscript. B.D.M.S. coordinated and helped to write the manuscript. The final manuscript was revised by all authors.

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Figure 1 - Flow Diagram of Literature Search and Selection Criteria (adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analysis)

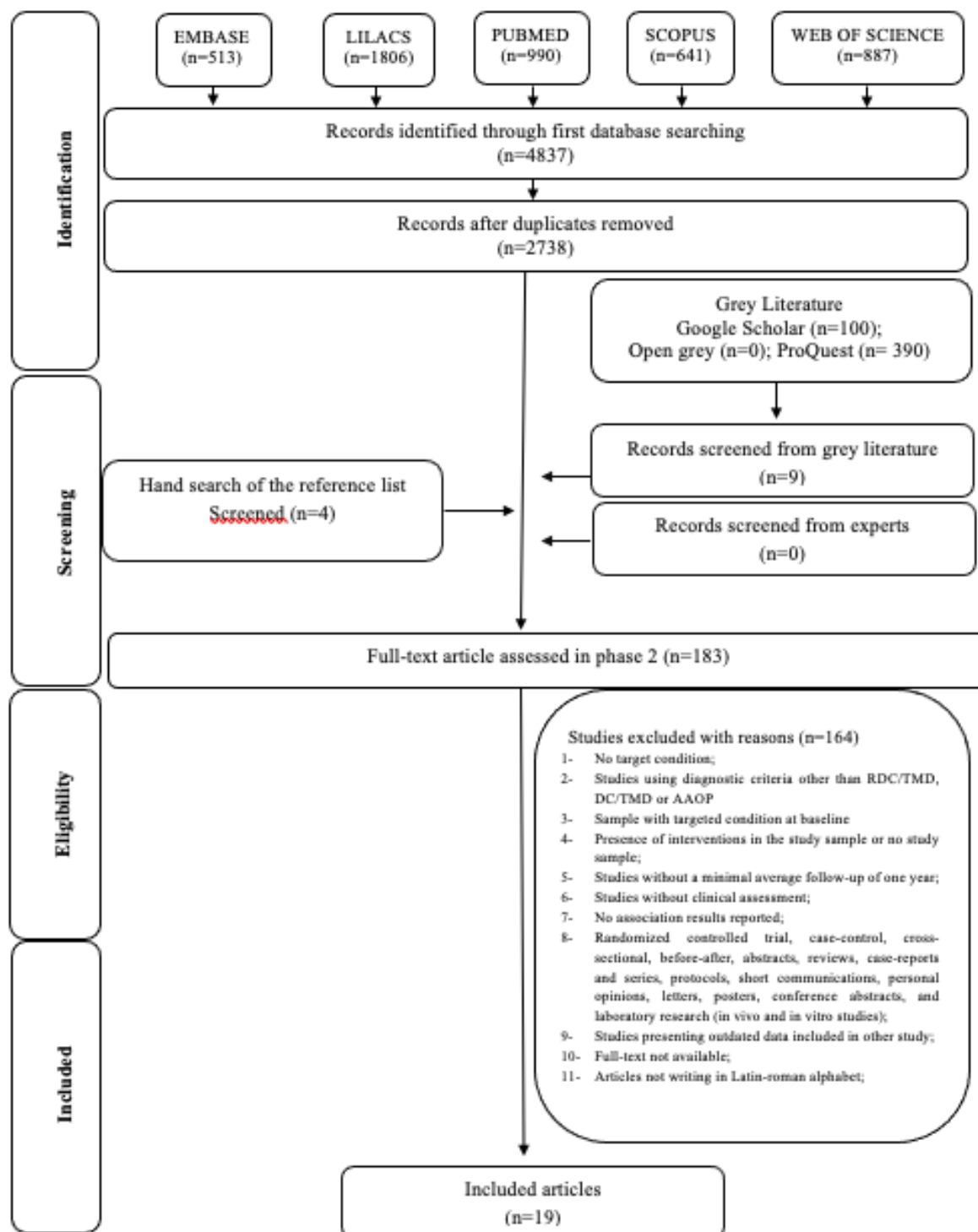


Table 1 – Summary of main evidence and significant results of included studies (n=19)

Study Characteristics			Results	
Author, Country (year)	Sample Size/ Mean Age at baseline	Follow-up time/ TMD diagnostic criteria	Variables Assessed	Statistically Significant Results
Diatchenko et al., USA (2005)	170 females/ 18-34 years	9 months - 3 years/ RDC/TMD	Outcome: myogenous temporomandibular mandibular joint disorder Trimonthly interviews and annual physical examination. Catecholamine-O-methyltransferase LPS =low pain sensitivity (G_C_C_G) APS = Average pain sensitivity (A_T_C_A) HPS= High pain sensitivity (A_C_C_G) 58 subjects: Low COMT activity (HPS and/or APS) 112 subjects: at least one “high activity” haplotype (LPS)	HPS and/or APS: IDR 2.3 [1.1-4.8]
Marklund et al., Sweden (2007)	Final Sample: 191/ 23y.o (18-48y.o)	1 year/ RDC/TMD	Outcome: TMJ disorders Symptom Report Questionnaire (SRQ): Age, gender, presence, location, and frequency of clicking sounds, locking, pain and difficulties in opening the mouth wide, perception of tooth contact pattern at jaw closing, awareness of tooth-grinding, tooth-clenching, cheek and/or tongue-biting, and frequent use of chewing gum; Clinical examination: Morphologic Occlusion (angle classification, crossbite, scissors bite, frontal open bite; Edge-to-Edge bite, deep bite) Functional occlusion: Contact patten in centric relation; horizontal, vertical, and lateral distances between centric relation and centric occlusion; Mandibular stability in centric occlusion; Mediotrusive side interferences Temporomandibular Joint (TMJ): TMJ clicking sounds; TMJ locking; TMJ tenderness; TMJ pain during movements; TMJ pain on joint loading.	Univariate Analysis: Female gender [OR:2.0]; Bruxism [OR:1.6]; Any deviation of morphological occlusion [OR:1.7]; Crossbite [OR:2.9]; Unilateral contact in centric relation [OR:2.0]; Mandibular instability in the intercuspal position [OR:3.5]; Reported TMJ sounds [OR: 3.6];
Marklund et al., Sweden (2008)	Final Sample: 191/ 23y.o (18-48y.o)	1 year/ RDC/TMD	Outcome: Myofascial pain Symptom Report Questionnaire (SRQ): Age, gender, Tooth-presence and frequency of fatigue, stiffness, or pain in jaw muscle region, difficulties in opening or closing the jaw, presence and location of headaches, neck pain, and shoulder or back pain, awareness of parafunction (tooth clenching, tooth-grinding) and of tooth contact at jaw closing. Clinical examination: number of teeth, overbite and overjet, morphological dental occlusion, Sagittal occlusion, vertical occlusion, transversal occlusion, overjet, contact patterns in the retruded contact position (RCP) and intercuspal position (ICP), mandibular stability in the ICP, contact in eccentric positions (3mm and 9mm lateral excursion), Perceived occlusal stability. Pain palpation (the tendon, the anterior and posterior part of the temporal	Univariate Analysis: Female gender [OR:4.9]; Tooth-clenching [OR:2.1]; Tooth-grinding [OR:2.1]; Unilateral contact in the RCP [OR:2.5]; Mandibular instability in the ICP [OR:3.2];

			muscles, superficial and deep masseter, lateral and medial pterygoid.	
Slade et al., USA (2007)	Final Sample: 171/23y.o (SD: 4.9/18-48y.o)	Average 30 months (8-42 months)/ RDC/TMD	Genotyping of 4 COMT SNPs: rs6269, rs4633, rs4818 and val ¹⁵⁸ met: Pain Sensitivity haplotypes (PSH) = participating carrying haplotypes ACCG or ATCA for 4 SNPs (rs6269, rs4633, rs4818, and val ¹⁵⁸ met respectively); Pain Resistant Haplotypes (PRH)= at least 1 haplotype (GCGG); Psychological aspects: The Brief Symptom Inventory (BSI): 53 items designed to assess 9 subscales of psychological function The Perceived Stress Scale (PSS): 14 sources of stress, to yield a single, overall rating The Profile of Mood States-Bi-Polar (POMS-Bi): 72 mood-related items yielding 6 subscales measuring affective dimensions of mood The State-Trait Anxiety Inventory (STAI): 20 statements evaluating levels of state and trait anxiety separately Pain phenotype: 13 pain perceptions assessment at baseline - threshold and tolerance to thermal pain, sensitivity to ischemic pain, pressure pain threshold in 4 sites (temporalis and masseter muscles, temporomandibular joint, ventral surfaces of the wrists), global measure of temporal perceptual responses to heat pain.	Univariate Analysis: BSI depression [IDR:3.2]; POMS confident-unsure [IDR:3.7]; Perceived Stress [IDR: 2.6]; Multivariate Analysis: High BSI depression (adjusted for COMT haplotype): [IDR:3.1]; <i>Independent effects:</i> BSI depression (p=0.0004); COMT haplotype (p=0.046)
Lim et al., (N/A) (2010)	First year: 186 females Second years: 147 Third year: 189 / 18-34 y.o	3 year/ RDC/TMD	Symptom Report Questionnaire (SRQ): Headaches, muscle soreness or pain, joint soreness or pain, back pain, chest pain, pelvic pain, abdominal pain, menstrual pain, other pain.	Univariate Analysis: Headaches (p=0.0089); Muscle soreness or pain (p=0.005); Joint soreness or pain (p=0.0012); Back pain (p=0.0001); Chest pain (p=0.0004); Abdominal pain (p=0.0021); Menstrual pain (p=0.0036).
Marklund et al., Sweden (2010)	Final sample: 280 (98 M, 182 F)/ 23y.o (18-43y.o)	2 year/ RDC/TMD	Sex, presence of symptoms of TMD, signs of TMD and spinal pain.	Univariate Analysis: Female gender [OR: 4.9]; Spinal pain [OR: 2.9]; Female with spinal pain vs Male with spinal pain [OR:5.6]; Female with spinal pain vs. Male without spinal pain [OR:14.9]
Kindler et al., Germany (2012)	Final Sample: Analysis of joint pain (n=3,600); Analysis of muscle pain (n=3,034) / 49 y.o (20-81y.o)	5 years/ AAOP	Depressive and Anxiety symptoms: Composite International Diagnostic-Screener (CID-S) - self-reported questionnaire	Multivariate Analysis: <i>Main analysis:</i> JOINT PAIN: Anxiety symptoms: Model 1 [RR: 2.01]; Model 2 [RR: 1.79]; Model 3 [RR: 1.78]; Model 4 [RR: 1.75]; Model 5 [RR: 1.74]; Model 6 [RR: 1.58]; Depressive Symptoms: Model 1 [RR: 2.37]; Model 2 [RR: 2.13]; Model 3 [RR: 2.13]; Model 4 [RR: 2.09]; Model 5 [RR: 2.08]; Model 6 [RR: 1.86]; Model 7 [RR: 1.97]; JOINT PAIN OR DISCOMFORT: Anxiety symptoms: Model 1 [RR: 1.62]; Model 2 [RR: 1.55]; Model 3 [RR: 1.52]; Model 4 [RR: 1.49]; Model 5 [RR: 1.47]; Model 6 [RR: 1.28]; Model 7 [RR: 1.40];

				<p>Depressive Symptoms: Model 1 [RR: 1.91]; Model 2 [RR: 1.80]; Model 3 [RR: 1.77]; Model 4 [RR: 1.72]; Model 5 [RR: 1.69]; Model 6 [RR: 1.58]; Model 7 [RR: 1.62]</p> <p>MUSCLE PAIN: Anxiety symptoms: Model 1 [RR: 3.89]; Model 2 [RR: 3.46] Model 3[RR: 3.49]; Model 4 [RR: 3.37]; Model 5 [RR: 3.18]; Model 6 [RR: 3.18]; Model 7 [RR: 3.19]; Depressive symptoms: Model 1 [RR: 2.07]; Model 2 [RR: 1.83]; Model 3 [RR: 1.82];</p> <p>MUSCLE PAIN OR DISCOMFORT: Anxiety symptoms: Model 1 [RR: 2.35]; Model 2 [RR: 2.04]; Model 3 [RR: 2.03]; Model 4 [RR: 1.95]; Model 5 [RR: 1.92]; Model 6 [RR: 1.71]; Model 7 [RR: 1.74] Depressive Symptoms: Model 1 [RR: 2.25]; Model 2 [RR: 1.93]; Model 3 [RR: 1.90]; Model 4 [RR: 1.79]; Model 5 [RR: 1.75]; Model 6 [RR: 1.50]; Model 7 [RR: 1.58];</p> <p><i>Sensitivity Analysis (excluding patients taking pain medications):</i> JOINT PAIN: Depressive symptoms: Model 4 [RR:1.95]; Model 6 [RR:1.88] Anxiety symptoms: Model 4 [RR:1.56];</p> <p>MUSCLE PAIN: Anxiety symptoms: Model 4 [RR: 5.19]; Model 6 [RR: 5.22];</p> <p>Successive Adjustments for confounders: Model 1 (Unadjusted) Model 2 (Age and sex) Model 3 (School Education) Model 4 (Arthritis and degenerative disc disease - final model) Model 5 (Migraine) Model 6 (Treatment for Depression/Anxiety) Model 7 (Pain Conditions - headache, neck and shoulder pain, pain in suboccipital muscles, pain in sternocleidomastoid muscles, and migraine)</p>
<p>Filligim et al., USA (2013)</p>	<p>Final Sample: 2,737/ 18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years)/ RDC/TMD</p>	<p>Measures of Global Psychological and Somatic Function, Stress, and Mood: Psychological Function: Symptom Checklist 90-Revised (SCL90R): Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. Eysenck Personality Questionnaire-Revised (Short-Form, EPO-R): Extraversion, Neuroticism, and Psychoticism. Affective Distress: State-Trait Anxiety Inventory (STAI): State Anxiety Inventory (“feel right now”) and Trait Anxiety Inventory (“generally feel”) The Profile of Mood States-Bipolar (POMS-Bi): Positive and Negative affective Psychosocial Stress:</p>	<p>Univariate Analysis <i>Findings from measures of Global Psychological and Somatic Function, Stress, and Mood:</i> High levels of somatic symptoms (PILL Global Score) [HR:1.55][‡] [HR:1.44][§]; Depression [HR:1.35][‡][HR:1.31][§]; Somatization FULL [HR:1.42][‡][HR:1.38][§]; Anxiety [HR:1.31][‡][HR:1.29][§]; Obsessive Compulsive [HR:1.36][‡][HR:1.32][§]; Interpersonal sensitivity [HR: 1.28][‡][HR:1.25][§]; Hostility [HR:1.25][‡][HR:1.23][§]; Phobia [HR:1.22][‡][HR:1.19][§];</p>

			<p><u>The Perceived Stress Scale (PSS)</u>: Stressful level of variety of situations</p> <p><u>The Life Experiences Survey (LES)</u>: Life events that occurred over the past year and impact of this events</p> <p><u>The Lifetime Stressor List/Post Traumatic Stress Disorder Checklist-Civilian Version (LSL/PCL-C)</u>: Which of 15 described events the participants have experienced, identification of the most stressor event and the extent of these to which they experience PTSD symptoms (e.g., repeated, disturbing memories)</p> <p>Somatic Symptoms and Reactivity:</p> <p><u>Pennebaker Inventory of Limbic Languidness (PILL)</u>: Frequency with which individual experience of 54 common physical symptoms and sensations on a five-category scale</p> <p><u>The Kohn Reactivity Scale</u>: Assess an individual's level of reactivity or central nervous system arousability to sensory stimuli.</p> <p>Coping/Catastrophizing:</p> <p><u>The Coping Strategies Questionnaire-Revised (CSQ-R)</u>: How individuals cope with pain</p> <p><u>The Pain Catastrophizing Scale (PCS)</u>: degree of thoughts and feeling when experiencing pain. Three dimensions: Rumination, Magnification, and Helplessness.</p> <p>Principal Component Analysis (PCA):</p> <p><u>Global Psychological and Somatic Symptoms</u> (loadings from all SCL-90-R scales, the PILL, and the LSL/PCL-C PTSD symptom scale);</p> <p><u>Stress and Negative Affectivity</u> (loadings from both State and Trait Anxiety, Perceived Stress, POMS Negative Affect, and EPQ-R Neuroticism; negative loadings for POMS Positive Affect and EPQ-R Extraversion);</p> <p><u>Passive Pain Coping</u> (positive loading from all three PCS subscales, the Praying and Hoping subscale of the CSQ-R, and the Kohn score);</p> <p><u>Active Pain Coping</u> (positive loadings from the remaining CSQ-R subscales).</p> <p>Interactions: Age groups, race/ethnicity, gender</p>	<p>Paranoid [HR:1.31][‡][HR:1.28][§];</p> <p>Psychotic [HR:1.21][‡][HR:1.31][§];</p> <p>PTSD (Checklist for civilians) [HR:1.34][‡][HR:1.34][§];</p> <p>Personality (EPQ-R Neuroticism) [HR:1.29][‡][HR:1.24][§];</p> <p>Perceived Stress Scale [HR:1.35][‡][HR:1.31][§];</p> <p>LES Negative Events [HR:1.30][‡];</p> <p>LES Negative Impact [HR:1.27][‡];</p> <p>State Anxiety [HR:1.23][‡][HR:1.23][§]</p> <p>Trait anxiety [HR:1.42][‡][HR:1.35][§];</p> <p>Negative Affect (POMS-Bi) [HR: 1.26][‡][HR:1.22][§];</p> <p>Positive affect (POMS-Bi) [HR: 0.80][‡][HR:0.80][§];</p> <p>Helplessness (PCS Helplessness) [HR:1.12][§];</p> <p>PCA:</p> <p>High levels of Global Psychological and Somatic Symptoms [HR:1.41][‡] [HR:1.37][§];</p> <p>High levels of Stress and Negative Affectivity [HR:1.35][‡][HR:1.31][§];</p> <p>Passive Coping [HR: 1.16][§];</p> <p>Multivariate Analyses</p> <p>PCA:</p> <p>Global Psychological and Somatic Symptoms [HR:1.37][‡][HR:1.33][§];</p> <p>Stress and Negative Affectivity [HR:1.17][‡]</p> <p>Stress and Negative Affectivity when Global Psychological and Somatic Symptoms were low [HR=1.30]</p> <p>Global Psychological and age (ref. 35-44): 18-24 years group [HR:1.45]; 25-34 years group [HR:1.65];</p> <p>Global Psychological and Lifetime US residency : (No/Not stated) [HR: 1.37]; Yes [HR:2.28]</p> <p>[‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p>
Greenspan et al., USA (2013)	Final Sample: 2,737/ 18-44y.o	5.2 years (median follow-up=2.8 years)/ RDC/TMD	<p>Quantitative Sensitivity Test (QST):</p> <ol style="list-style-type: none"> 1) Pressure pain threshold (PPTs): temporalis muscle, masseter muscle, TMJ, trapezius muscle and lateral epicondyle 2) Cutaneous mechanical pain sensitivity: threshold, ratings of suprathreshold stimuli, temporal summation, and aftersensation 3) Heat pain sensitivity: threshold, tolerance, ratings of suprathreshold stimuli, temporal summation, and aftersensation, assessed on the forearm. 	<p>Univariate Analysis</p> <p>Lower PPTs measured at cranial sites:</p> <p>Temporalis [HR: 1.20][†][HR: 1.20][‡][HR: 1.17][§];</p> <p>Masseter [HR: 1.18][†][HR: 1.18][‡][HR: 1.16][§];</p> <p>TM joint [HR: 1.16][§];</p> <p>Greater pain rating for a series of mechanical stimuli and heat stimuli:</p> <p>Overall ratings of 10 stimuli with 512mN probe [HR: 1.13][§];</p>

			<p>Autonomic measures: arterial blood pressure, heart rate, heart rate variability, under rest and during two provocative conditions: orthostatic challenge and Stroop protocol</p>	<p>Ratings of 10 heat stimuli – area under curve (rating 0-1,000) on 46°C [HR:1.16][§], 48°C [HR:1.22][§], 50°C [HR:1.23][§]; Greater maximum pain ratings of heat stimuli: Maximum pain rating from among 10 stimuli (Rating 0-1,000) on 46°C [HR:1.16][§], 48°C [HR:1.22][†][HR:1.23][‡][HR: 1.23][§], 50°C [HR: 1.21][†][HR:1.21][‡][HR: 1.24][§]; Greater temporal summation of heat pain at 50 °C: Highest minus first rating [HR:1.24][†][HR:1.25][‡][HR: 1.14][§]; Slope of line for first 3 heat pulses (β coefficient) [HR:1.12][§]; Temporal summation – highest minus first rating (subjects with a first-pulse rating of 0-19): 48°C [HR:1.25][†][HR:1.23][‡]; 50°C [HR:1.35][†][HR:1.33][‡] [HR: 1.27][§] Greater aftersensation rating associated with either mechanical cutaneous or heat pain stimuli: Aftersensation ratings of 30s with 512mN probe (ratings 0-100) [HR:1.15][†][HR:1.16][‡][HR: 1.16][§]; Thermal aftersensation: 30s 46°C [HR:1.14][†][HR:1.15][‡]; 15s 48°C [HR: 1.17][†][HR:1.20][‡][HR: 1.17][§]; 30s 50°C [HR: 1.16][†][HR:1.17][‡]; Higher resting hearth rate: Electrocardiograph-derived heart rate (beat-by-beat basis during 20-minute rest) [HR: 1.02][†][HR: 1.02][‡][HR: 1.01][§]</p> <p><i>Multivariate Analyses</i> Greater heat pain temporal summation among people with relatively low ratings of single-heat stimuli [HR: 1.54].</p> <p>[†]Adjusted rate for study site; [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p>
<p>Sanders et al. (a) USA (2013)</p>	<p>Final Sample: 2,604/ 18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years)/ RDC/TMD</p>	<p>Signs/Symptoms of Obstructive Sleep Apnea (OSA): Pittsburgh Sleep Quality Index (PSQI) - Three questions about loud snoring, trouble staying awake, and witnessed apnea; Medical history about hypertension = 4-item OSA screening questionnaire; Autonomic Parameters: arterial blood pressure, heart rate during 20 min of rest (by blood pressure cuff), average resting heart rate variability (3-lead electrocardiogram); Covariates: Gender, age, race and ethnicity (White, African American, Asian, Hispanic). Body mass index (BMI= Height/Weight); Smoking history (Never smoked, former smoker, or current smoker); Subjective sleep quality (PSQI-item #6: During the past month, how would you rate your sleep quality overall?)</p>	<p><i>Univariate Analysis:</i> Female [HR: 1.32]; Age groups (ref.=18-24 y.o): 25-34 y.o [HR: 1.55]; 35-44 y.o [HR: 1.81]; Race/Ethnicity (ref.=White): African American [HR: 1.58] Hispanic [HR: 0.35]; Mean arterial pressure (>85 mmHg) [HR: 1.62]; Heart rating (>69 beats per min) [HR: 1.54]; Obesity (Body Mass Index $\geq 30\text{kg/m}^2$) [HR: 1.68]; High Likelihood of OSA [HR: 2.29]; Smoking history (ref.: Never): Former Smoking history [HR: 2.33]; Current Smoking [HR: 2.15]; Fairly bad and very bad subjective sleep quality (PSQI) [HR: 2.11];</p> <p><i>Multivariate Analysis:</i></p>

				<p>High likelihood of OSA: Model 1: [HR: 1.90] Model 2: [HR: 1.85] Model 3: [HR: 1.73];</p> <p>Age in years/decades: Model 1: [HR: 1.21];</p> <p>Race/Ethnicity (ref.: White):</p> <p>African American: Model 1 [HR: 1.38];</p> <p>Hispanic: Model 1: [HR: 0.37] Model 2: [HR: 0.37] Model 3:[HR: 0.39]</p> <p>Smoking History (ref.: Never):</p> <p>Current: Model 3: [HR: 1.81];</p> <p>Former: Model 3: [HR: 2.20];</p> <p>Model 1: Adjusted for study site and demographic characteristics; Model 2: adds autonomic parameters; Model 3: adds BMI and smoking history</p>
<p>Sanders et al. (b), USA (2013)</p>	<p>Final Sample: 2,722/ 18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years) / RDC/TMD</p>	<p>Pain disorders:</p> <p>Headache (International Headache Society – ICHD-2): probable tension-type, tension-type and migraine headache,</p> <p>Past or current low back pain (constancy of pain symptoms, frequency of episodes in the last 12 months, duration of episodes)</p> <p>Irritable Bowel Syndrome (IBS): assessment based on Rome III criteria - questions about bowel movements and the experience of discomfort or pain in the abdomen that lasted at least 1 day a week during previous 3 weeks</p> <p>Genital symptoms: presence of genital pain on contact but absence of genital itching during the last 3 months</p> <p>Health status:</p> <p>Overall health (excellent, good, fair or poor): Short Form 12 Health Survey (SF-12v2)</p> <p>Conditions: Endocrine (diabetes, hypothyroid disease, hyperthyroid disease); Cardiovascular (mitral valve prolapse; high blood pressure; angina; heart attack; heart failure; pacemaker/defibrillator; stroke), Hematologic (anemia; bleeding disorder; leukemia), Neural and sensory (earache; ringing in ears; hearing loss; fainting or dizzy spells; epilepsy; seizures; or convulsion; psychiatric treatment); Respiratory (sinus trouble; allergies or hives; asthma; tuberculosis; breathing difficulties); Sleep apnea; history of being hospitalized for any surgical operation or serious illness.</p> <p>Cigarette smoking: Nonsmokers (fewer than 100 cigarettes in their lives), current or former smoker</p> <p>Pittsburgh Sleep Quality Index (PSQI): sleep quality and disturbances over a 1-month reference period</p> <p>Anthropometric Status:</p> <p>Body Mass Index (BMI= weight/height²)</p> <p>2D:4D ratio: Length of the second digit [2D] and the fourth digit [4D]. High 2D:4D is a marker of greater estrogen relative to testosterone exposure toward the end of the first trimester in utero</p>	<p>Univariate analysis</p> <p>Current low back pain [HR: 2.02][†][HR: 1.91][‡][HR: 1.89][§];</p> <p>Number of low back pain episodes in last year:</p> <p>5-10 episodes [HR: 2.40][†][HR: 2.33][‡][HR: 2.20][§];</p> <p>≥11 episodes: [HR: 2.04][†][HR: 1.92][‡][HR: 2.01][§];</p> <p>Positive ROME classification to IBS [HR: 3.00][†][HR: 2.84][‡][HR: 2.27][§];</p> <p>Number IBS symptoms:</p> <p>3-5 [HR: 1.89][†][HR: 1.77][‡][HR: 1.68][§];</p> <p>≥6 [HR: 2.95][†][HR: 2.66][‡][HR: 2.35][§];</p> <p>Tension-type headache [HR: 1.75][†][HR: 1.74][‡][HR: 1.69][§];</p> <p>≥3 headaches types in last year [HR: 2.23][†][HR: 2.05][‡][HR: 1.94][§]</p> <p>Mostly severe headache intensity at baseline [HR: 2.33][†][HR: 2.07][‡][HR: 2.13][§];</p> <p>Genital pain symptoms [HR: 3.06][†][HR: 2.78][‡][HR: 2.31][§];</p> <p>Higher number of comorbid conditions (≥2) [HR: 3.20][†][HR: 2.87][‡][HR: 2.70][§];</p> <p>History of neurosensory conditions [HR: 1.52][†][HR: 1.51][‡][HR: 1.52][§];</p> <p>History of respiratory condition [HR: 1.50][†][HR: 1.50][‡][HR: 1.44][§];</p> <p>Usage of three or more medications [HR: 1.41][†][HR: 1.35][‡][HR: 1.52][§];</p> <p>Former cigarette smoking [HR: 2.26][†][HR: 2.12][‡][HR: 1.86][§];</p> <p>Current cigarette smoking [HR: 2.07][†][HR: 1.74][‡][HR: 1.61][§];</p> <p>Self-rating of general health status (ref.: Excellent):</p> <p>Good [HR: 1.40][†][HR: 1.35][‡][HR: 1.37][§];</p> <p>Poor/Fair [HR: 2.93][†][HR: 2.55][‡][HR: 2.60][§];</p> <p>Lower testosterone and higher estrogen exposure in utero (Average of RD2:RD4 ratio left and right hands) [HR: 1.18][†][HR: 1.21][‡][HR: 1.15][§];</p> <p>BMI (Kg/m²) [HR: 1.23][†][HR: 1.13][‡]</p> <p>PSQI Global Score: [HR: 1.47][†][HR: 1.40][‡][HR: 1.32][§]</p>

				<p>Higher summary scores on physical and Mental component: SF-12v2 Physical [HR: 0.83][†][HR: 0.86][‡][HR: 0.85][§] and Mental [HR: 0.71][†][HR: 0.71][‡][HR: 0.74][§]</p> <p>[†]Adjusted rate for study site; [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p>Multivariable Analysis Female gender: Model 1 [HR:1.37]; Age (decades): Model 1 [HR:1.20]; Current low back pain (ref.: no): Model 2 [HR:1.80] Model 3 [HR:1.50]; Rome IBS classification (ref.: no): Model 2 [HR:1.92]; Genital symptoms (ref.: no): Model 2 [HR:1.92] Model 3 [HR:1.75]; Genital symptoms not stated (ref.: no): Model 2 [HR:1.84]; Tension-Type headache (ref.: no): Model 2 [HR: 1.57]; Black race (ref.: white): Model 3 [HR:1.47]; RD2:RD4 ratio average both hands: Model 3 [HR:1.15] Current smoker (ref.: never smoked): Model 3[HR:1.55] Former smoker (ref.: never smoked): Model 3 [HR:1.84]; PSQI: Model 3 [HR:1.18] No-lifetime U.S residence (ref.: lifetime): Model 1 [HR:0.46]; Model 2 [HR:0.47]; Model 3 [HR:0.51] Model 1: Adjusted for study site + demographics; Model 2: Adjusted for study site + Pain Disorders; Model 3: Adjusted for study site + other health conditions;</p>
Slade et al, USA (2013)	Final sample:2,737/18-44y.o	5.2 years (median follow-up=2.8 years)/ RDC/TMD	<p>Sociodemographic characteristics: Age, gender, race/ethnicity, Lifetime U.S Residence (yes or not); Health Insurance Coverage, first language spoken (English or not English), Marital status (never married, married/cohabiting or separated/divorced/widowed);</p> <p>Socioeconomic status: Level of schooling (high school or less, some college, college graduate, postgraduate), Family annual household income in USD (≤USD 20,000; USD 20,000 to 39,999; USD 40,000 to 79,999; ≥80,000), Rating of satisfaction with financial situation, Ratings of satisfaction with material standards in life (Low, Mid, Not stated, High);</p>	<p>Univariate analysis Age: 25-34 [HR: 1.54][†][HR: 1.61][‡][HR: 1.38][§]; 35-44 [HR: 1.87][†][HR: 1.66][‡][HR: 1.46][§]; Race/Ethnicity (ref.: White): Black race [HR: 1.37][§]; Self-report rating of satisfaction with materials standards of life (ref.: High 9-10): Low (0-5) [HR: 2.09][†][HR: 1.98][‡][HR: 1.71][§]; Mid (6-8) [HR: 1.68][†][HR: 1.69][‡][HR: 1.45][§]; Not stated [HR: 3.20][†][HR: 2.96][§]; Level of schooling (ref.: postgraduate): Not stated [HR: 3.40][§] Lifetime U.S residence (ref.: Yes): No [HR: 0.34][†]; [HR: 0.37][‡]; [HR: 0.44][§] [†]Adjusted rate for study site; [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p>Multivariable Analysis:</p>

				<p>Greater age (as continuous variables) [HR:1.18]; Female gender [HR: 1.34]; Rating of satisfaction with material standards of life (ref.= high 9-10): Mid (6-8) [HR: 1.45]; Low (0-5) [HR: 1.71]; Not stated [HR: 2.96] Lifetime U.S residence (ref.=yes): No [HR: 0.49];</p>
Smith et al., USA (2013)	Final sample: 2,737/ 18-44y.o	5.2 years (median follow-up=2.8 years)/ RDC/TMD	3295 single nucleotide polymorphisms (SNPs) representing 358 genes involved in systems relevant to pain perception such as nociceptive transmission, inflammation, and mood and affect. Twenty-three genes were chosen a priori as “first tier” candidate genes	None significant SNP was found.
Orbach et al., USA (2014)	Final sample:2,737/18-44y.o	5.2 years (median follow-up=2.8 years)/ RDC/TMD	<p>Self-reported putative etiologic factors: Lifetime history of regional trauma: Check-list of five potentially traumatic experiences, injury by yawning and history of orthodontic procedures Parafunctional behaviors: Oral Behaviors Checklist = 21 activities such as clenching, chewing gum and holding objects between the teeth Clinical Status by Self-Report: Pain and Disability: Grade Chronic Pain Scale (GCPS); Modifying Factors (5-item checklist and ordinal summary measure): Limitations in using the jaw: Jaw Functional Limitation Scale - JFLS; Checklist of six “non-specific orofacial symptoms” in the preceding month (jaw stiffness, cramping, fatigue, pressure, soreness, and ache); TMJ clicking and locking: past month and period prior to the past month Clinical Status by Examination: Jaw mobility: pain-free opening, maximum unassisted opening, maximum assisted opening, left lateral excursion, right lateral excursion and protrusion; TMJ noises (crepitus, click during opening and closing), Palpation Pain: positive and negative report of pain Tooth wear: visual signs of facets representing at least 2mm in length of surface wear at opposing tooth edges were recorded bilaterally from the incisor, cuspid, and pre-molar teeth</p>	<p>Univariate Associations Lifetime history of jaw injury due to prolonged opening [HR:1.94][‡]; Parafunctional oral behavior summary score (ref.: 0-16): 25-62 [HR: 1.71][‡][HR: 1.75][‡][HR: 1.75][§]; Non-specific orofacial symptoms: 1-2 [HR: 2.01][‡][HR: 1.98][‡][HR: 1.96][§]; 3 or more [HR: 2.97][‡][HR: 2.89][‡][HR: 2.43][§]; Pain intensity at baseline: [HR: 1.20][‡][HR: 1.18][‡][HR: 1.15][§]; Facial pain in the 6-months before baseline: [HR: 1.11][‡][HR: 1.09][‡] Facial GCPS (ref.:0): (1) [HR: 1.73][‡][HR: 1.74][‡][HR: 1.68][§]; (2-4) [HR: 4.40][‡][HR: 4.05][‡][HR: 3.43][§] # days when efficiency dropped below 50%: [HR: 1.21][‡][HR: 1.23][‡][HR: 1.24][§]; Self-report of TMJ noises in last month [HR: 1.47][‡][HR: 1.58][‡][HR: 1.61][§]; TMJ noises at baseline [HR: 1.56][‡][HR: 1.69][‡][HR: 1.66][§]; History of inability of open jaw widely [HR: 1.61][‡][HR: 1.67][‡][HR: 1.59][§]; Great numbers of palpation tenderpoints in neck [HR: 1.14][‡][HR: 1.14][‡][HR: 1.13][§]; Great numbers of palpation tenderpoints in body [HR: 1.17][‡][HR: 1.16][‡][HR: 1.17][§]; Impossibility of open mouth wide for any reason in last month [HR: 2.71][‡][HR: 2.66][‡][HR: 2.46][§] Pain on unassisted opening [HR: 1.43][‡][HR: 1.51][‡][HR: 1.56][§]; Pain on assisted opening (un-terminated) [HR: 1.40][‡][HR: 1.47][‡]; Pain on palpation (right side): Temporalis [HR: 1.64][‡][HR: 1.61][‡][HR: 1.55][§]; Masseter [HR: 1.68][‡][HR: 1.68][‡][HR: 1.63][§]; Posterior mandibular and submandibular [HR: 1.44][‡][HR: 1.46][‡]; Lateral pterygoid area [HR: 1.51][‡][HR: 1.50][‡][HR: 1.50][§];</p>

				<p>Temporomandibular joint [HR: 1.56][†][HR: 1.57][‡]; Pain on palpation (left side): Temporalis [HR: 1.59][†][HR: 1.56][‡][HR: 1.49][§]; Masseter [HR: 1.59][†][HR: 1.59][‡][HR: 1.53][§]; Posterior mandibular and submandibular [HR: 1.41][†][HR: 1.41][‡]; Lateral pterygoid area [HR: 1.40][†][HR: 1.39][‡][HR: 1.38][§]; Temporomandibular joint [HR: 1.43][†][HR: 1.48][‡]; [†]Adjusted rate for study site; [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p>Multivariate Analysis: Age (decades): Model 1 [HR:1.28] Model 2 [HR: 1.27] Model 3 [HR: 1.25] Model 4 [HR: 1.29]; Black race (ref. White): Model 2 [HR: 1.45] No or unstated Lifetime U.S residence: Model 1 [HR:0.48] Model 2 [HR: 0.48] Model 3 [HR: 0.47] Model 4 [HR: 0.49]; Jaw Mobility pain: Model 1 [HR:1.23] Model 2 [HR: 1.20] Model 3 [HR: 1.19] Model 4 [HR: 1.20]; Pain from palpation: Model 1 [HR:1.19] 1-2 number of non-specific orofacial symptoms Model 2 [HR: 1.63] Model 3 [HR: 1.63] Model 4 [HR: 1.55]; ≥3 number of non-specific orofacial symptoms: Model 2 [HR: 1.92] Model 3 [HR: 1.93] Model 4 [HR: 1.77]; Ps.: All models are adjusted for study site, Model 1 adds Pain during examination, Model 2 adds other symptoms, Model 3 adds trauma history, model 4 adds oral behavior</p>
Sanders et al., USA (2016)	Final sample: 2,410/18-44y.o	5.2 years (median follow-up=2.8 years)/ RDC/TMD	<p>Subjective sleep: Habitual sleep quality and sleep disturbance (19-item Pittsburgh Sleep Quality Index (PSQI), Quarterly Health Update (QHUs) with Sleep Quality Numeric Rating Scale (NRS), Covariates: study site, age, sex, race and ethnicity, non-painful facial symptoms, score for the Pennebaker Inventory of Limbic Languidness (PILL), Score for the Perceived Stress Scale (PSS) and a checklist of 20 comorbid health conditions)</p>	<p>Univariate Analysis Any non-pain facial symptom at baseline (ref.: none) [HR:1.74]; Any comorbid health condition at baseline (ref.: none) [HR:1.64]; Baseline PILL score per 21.0 units [HR:1.16]; Time-varying covariate per 2.0 units [HR:1.23].</p> <p>Multivariate Analysis Baseline poor sleep quality (PSQI score >5): Model 1 [HR:2.04] Model 2 [HR:1.39]; Any non-pain facial symptom at baseline: Model 2 [HR:1.67] Model 3 [HR:1.69]; Any comorbid health condition at baseline: Model 2 [HR:1.65] Model 3 [HR:1.63]; Baseline PILL score per 21.0 units: Model 2 [HR:1.16] Time-varying covariate of sleep quality rating >6: Model 3 [HR:1.73] All models adjusted for study site+ demographics + race/ethnicity Ps.: Model 1: PSQI at baseline; Model 2: adds four covariates (perceived stress, somatic awareness, comorbid conditions, non-pain facial symptoms); Model 3: adds time-varying sleep quality</p>

<p>Sanders et al., USA (2017)</p>	<p>Final sample: 2,722/18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years)/ RDC/TMD</p>	<p>Habitual sleep quality and disturbance: 19-item Pittsburgh Sleep Quality Index (PSQI) at baseline Sleep quality over the preceding 3 months: Sleep Quality Numeric Rating Scale (SQ-NRS) in each quarterly follow-up, Perceived stress: 10-item Perceived Stress Scale (PSS) and Quarterly Health Update questionnaires *Poor sleep quality (PSQI global score at baseline) was dichotomized at ≤ 5 = good sleep quality versus >5 = poor sleep quality.</p>	<p>Univariate Analysis: Age: 25-34 years [HR:1.54]; 35-44 years [HR:1.86]; Race/Ethnicity: African American (ref.: White) [HR:1.54] Asian race [HR: 0.39] High levels of perceived stress [HR:1.69]; Poor sleep (PSQI >5) [HR:2.22]</p> <p>Multivariate analysis: Perceived stress (predictor)/SQ-NRS (mediator): Total effect [HR:1.70]; Direct effect [HR:1.49] SQ-NRS (predictor)/Perceived stress (mediator): Total effect [HR:2.10]; Direct effect [HR:1.62]; Indirect effect [HR:1.29]</p>
<p>Tchivileva et al., USA (2017)</p>	<p>Final Sample: 2,410/18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years)/ RDC/TMD</p>	<p>Comprehensive Pain Symptom Questionnaire (CSPQ): details of up to three different types of headaches (location, intensity, characteristics, duration, frequency, and aggravating factors associated with each type of headache) Classification: International Classification of Headache Disorders (ICDH-3) Self-report Headaches: No headaches: no headache in preceding year Unclassified headache: reported headache in the last year but did not provide a complete set of data necessary for classification in the other types or did not meet the minimum ICDH criteria for even probable TTH or migraine Probable tension-type headache (TTH): all but one ICDH for TTH were satisfied Definite TTH: all ICDH criteria for TTH were met Probable migraine: all but one ICHD criterion for migraine without aura were fulfilled Definite migraine: all ICHD criteria for migraine without aura were met Mixed headache: definite migraine and definite TTH</p>	<p>Multivariate Analysis Migraine [HR: 1.67]; Mixed headache [HR:4.11]; Headache frequency per month: 2 [HR: 1.57] 3 [HR: 1.80] 4 [HR:3.09]; Headache frequency at baseline + time-varying (increase of 3 headaches per month) headache frequency: 4 headaches [HR: 1.78]; Time-varying headache frequency [HR:1.53]; Headache frequency at baseline + time-varying (increase of 3 headaches per month) lagged headache frequency: 4 headaches [HR: 2.13] Time-varying lagged headache frequency [HR:1.36]</p>
<p>Sharma et al., USA (2019)</p>	<p>Final Sample: 1,729/ 18-44y.o</p>	<p>5.2 years (median follow-up=2.8 years)/ RDC/TMD</p>	<p>Exposure Assessment: <i>Quarterly health update questionnaire (QHU)</i> First jaw injury: First positive record of any jaw injury Experience of extrinsic events: tooth extraction or dental treatments, oral intubation, sports injury (including falls, bumps, and blows), motor vehicle accidents, accidents resulting in whiplash, and injuries to the shoulder, neck, and head region. Experience of intrinsic injury: jaw injury attributed to yawning or prolonged mouth opening <i>Type of jaw injury:</i> Extrinsic or intrinsic <i>Number of jaw injuries:</i> injury reported in subsequent QHU</p> <p>Confounders: Demographic variables (study site, age, education, annual household income, marital status, satisfaction with material standards of life and satisfaction with financial situation), Symptom</p>	<p>Multivariate Analysis: First injury: Model 1 [HR:4.00] Model 2 [HR: 3.98] Model 3 [HR:3.67]; Extrinsic Injury only: Model 1 [HR:3.95] Model 2 [HR: 4.26] Model 3 [HR:4.04]; Intrinsic Injury only: Model 1 [HR:3.85] Model 2 [HR: 3.80] Model 3 [HR:3.47]; Two or more injuries: Model 1 [HR:2.65] Model 2 [HR: 2.34] Model 3 [HR:1.94]; Only one injury: Model 1 [HR:5.27] Model 2 [HR: 5.93] Model 3 [HR:6.01];</p> <p>Model 1: Unadjusted; Model 2: Adjusted for study site, age, sex, and race; Model 3: Adjusted for study site, age, sex, race, depression, anxiety, physical symptoms, positive and negative mood, coping, oral behaviors, previous pain, financial and material satisfaction, and smoking</p>

			Check List-90 revised (SCL 90R), The profile of mood States-Bipolar (PMOS-Bi), Comprehensive Pain and Symptom Questionnaire (CPQ-R), Oral Behavior Checklist Summary score and questions about previous injuries, smoking, health insurance, US lifetime residency.	
Lee et al., Taiwan (2020)	Final sample= 65,121 with low back pain and 195,363 without low back pain/ 20-70y.o	15 years/ RDC/TMD	Retrospective Cohort study Sex; Age groups; Insured premium (IP) in New Taiwan dollars (NTD); Level of Care; Comorbidities: Hypertension (HTN), Congestive heart failure (CHF), Stroke, Chronic kidney disease (CKD), Migraine, Osteoporosis, Hyperlipidemia, Nonpsychotic mental disorders (NMD), Psychoses, Coronary artery disease (CAD), Insomnia, Rheumatoid arthritis (RA), Charlson comorbidity index revised (CCI_R), Chronic obstructive pulmonary disease (COPD), Low back pain (LBP).	Low back pain (LPB) [HR:1.56]; Osteoporosis [HR:1.8]; Age (ref.=60-70): 20-29 years [HR:5.6]; 30-39 years [HR:2.4]; Insured premium (ref.:<18,000 NTD): 18,000-34,999 [HR:12.74], ≥35,000 [HR:33.68]

Abbrev.: y.o: years old; TMD: Temporomandibular Disorder; RDC/TMD: Research Diagnostic Criteria; AAOP: American Academy of Orofacial Pain; IDR: Incidence Density Ratio; HR: Hazard Ratio; OR: Odds Ratio; RR: Risk Ratio;

Table 2 - Most assessed significant variables and number of studies (n)

Variable	Assessed (n)	Positive Association (n)	No Association (n)
Gender-related	13	7	6
Age-related	11	6	5
Race-related	9	4	5
Back Pain	5	5	0
Parafunctional Habits	4	4	0
Facial Symptoms	4	4	0
Headaches	4	4	0
Perceived Stress	4	3	1
Depression	4	3	1
Current and Former Smoking	4	2	2
Anxiety	3	2	1
Genetic Factors	3	2	1
Trauma	2	2	0
Occlusal-related	2	2	0
Obstructive Sleep Apnea	2	1	1

Supplementary Table (S1) - Fulfilled data from included studies

STUDY AND POPULATION CHARACTERISTICS					RESULTS
Author, Country (Year)	Follow-up time	Sample Size/Mean age at baseline	TMD Diagnostic	Risk Factors Assessed	Hazard Ratio (HR) / Incidence density ratio (IDR) / Risk Ratio (RR) / Odds Ratio (OR)- 95% Confidence Interval (CI)
Diatchenko et al., USA (2005)	9month – 3 years	170 females with the five most common haplotype combinations	RDC/TMD	Outcome: myogenous temporomandibular joint disorder Trimonthly interviews and annual physical examination. Catecholamine-O-methyltransferase LPS =low pain sensitivity (G_C_C_G) APS = Average pain sensitivity (A_T_C_A) HPS= High pain sensitivity (A_C_C_G) 58 subjects: Low COMT activity (HPS and/or APS) 112 subjects: at least one “high activity” haplotype (LPS)	At baseline: HPS and/or APS subjects = more sensitivity (p=0.02) HPS and/or APS: IDR: 2.3 (1.1-4.8)
Marklund et al., Sweden (2007)	1 year	Initial sample: 371 1y follow-up: 308 (114 M/ 194 F) Drop-out: 63 (interruption of their study)/ 23 years (SD 4.9/18-48y.o)	RDC/TMD	Outcome: TMJ disorders Symptom Report Questionnaire (SRQ): Age, gender, presence, location, and frequency of clicking sounds, locking, pain and difficulties in opening the mouth wide, perception of tooth contact pattern at jaw closing, awareness of tooth-grinding, tooth-clenching, cheek and/or tongue-biting, and frequent use of chewing gum; Clinical examination:	LOGISTIC REGRESSION ANALYSIS OF BASELINE FACTORS AS INDEPENDENT VARIABLES AND PRESENCE OF 1-YEAR TMJ PAIN AS DEPENDENT VARIABLE: Age: ≤21 years [n=173; OR: 1.0]; >21 years [n=135; OR: 1.0 (0.6-1.6)]; Gender: Male [n=112; OR: 1.0]; Female [n=196; OR: 2.0 (1.2-3.4)]; Bruxism: No [n=158; OR: 1.0]; Yes [n=150; OR: 1.6 (1.04-2.6)]; Morphological occlusion: Normal occlusion [n=199; OR: 1.0]; Any Deviation [n=109; OR: 1.7 (1.04-2.7)]; Sagittal occlusion: Neutro-occlusion [n=270; OR: 1.0]; Mesio-occlusion [n=7; OR: 1.2 (0.3-5.6)]; Dist-occlusion [n=31; OR: 1.0 (0.5-2.2)] Vertical occlusion: Normal [n=232; OR: 1.0]; Open or edge- to edge [n=32; OR: 1.2 (0.6-2.3)]; Deep bite [n=44; OR: 1.6 (0.9-3.2)] Transversal occlusion: Normal [n=277; OR: 1.0]; Crossbite [n=29; OR: 2.9 (1.3-6.5)]; Overjet: <5mm [n=271; OR: 1.0]; ≥5mm [n=37; OR: 1.5 (0.7-2.9)]; Contact in RP: Bilateral [n=117; OR: 1.0]; Unilateral [n=191; OR: 2.0 (1.2-3.3)]; Lateral slide in centric: <1mm [n=284; OR: 1.0]; ≥1mm [n=24; OR: 2.0 (0.9-4.7)]; Mandibular stability in IP: Stable [n=274; OR: 1.0]; Instability [n=34; OR: 3.5 (1.6-7.3)];

				<p>Morphologic Occlusion (angle classification, crossbite, scissors bite, frontal open bite; Edge-to-Edge bite, deep bite)</p> <p>Functional occlusion: Contact patten in centric relation; horizontal, vertical, and lateral distances between centric relation and centric occlusion; Mandibular stability in centric occlusion; Mediotrusive side interferences</p> <p>Temporomandibular Joint (TMJ): TMJ clicking sounds; TMJ locking; TMJ tenderness; TMJ pain during movements; TMJ pain on joint loading,</p>	<p>Perceived occlusal stability: Equal [n=223; OR: 1.0]; Unequal [n=85; OR: 1.3 (0.8-2.1)];</p> <p>Mediotrusive side interferences (MI): No [n=209; OR: 1.0]; Yes [n=99; OR: 0.9 (0.6-1.5)];</p> <p>MI at 3mm lateral excursion: No [n=280; OR: 1.0]; Yes [n=28; OR: 0.9 (0.4-2.0)];</p> <p>MI at 9mm lateral excursion: No [n=219; OR: 1.0]; Yes [n=89; OR: 0.9 (0.6-1.6)];</p> <p>Reported TMJ sounds: Yes: [OR: 3.6 (1.4-9.2)]</p>
<p>Marklund et al., Sweden (2008)</p>	<p>1 year</p>	<p>Initial sample: 371</p> <p>1y follow-up: 308 (112 M/ 196 F)</p> <p>Drop-out: 63 (interruption of their study)/ 23 years (SD 4.9/18-48y.o)</p>	<p>RDC/TMD</p>	<p>Outcome: Myofascial pain</p> <p>Symptom Report Questionnaire (SRQ): Age, gender, Tooth-presence and frequency of fatigue, stiffness, or pain in jaw muscle region, difficulties in opening or closing the jaw, presence and location of headaches, neck pain, and shoulder or back pain, awareness of parafunction (tooth clenching, tooth-grinding) and of tooth contact at jaw closing.</p> <p>Clinical examination: number of teeth, overbite and overjet, morphological dental occlusion, Sagittal occlusion, vertical occlusion, transversal occlusion, overjet, contact patterns in the retruded contact position (RCP) and Intercuspal position (ICP), mandibular stability in the ICP, contact in eccentric positions (3mm and 9mm lateral excursion), Perceived</p>	<p>LOGISTIC REGRESSION ANALYSIS OF BASELINE FACTORS AS INDEPENDENT VARIABLES AND PRESENCE OF 1-YEAR PERIOD PREVALENCE OF JAW MUSCLE SIGNS AND SYMPTOMS OR MYOFASCIAL PAIN ACCORDING RESEARCH DIAGNOSTIC CRITERIA FOR TEMPOROMANDIBULAR DISORDERS (RDC/TMD) AS DEPENDENT VARIABLE.</p> <p>Age: ≤21 years [n=108; OR: 1.0]; >21 years [n=88; OR: 0.8 (0.4-1.5)];</p> <p>Gender: Male [n=82; OR: 1.0]; Female [n=114; OR: 4.9 (2.3-10.4)];</p> <p>Tooth-clenching: No [n=80; OR: 1.0]; Yes [n=116; OR: 2.1 (1.1-3.9)];</p> <p>Tooth-grinding: No [n=144; OR: 1.0]; Yes [n=52; OR: 2.1 (1.1-4.1)];</p> <p>Morphological occlusion: Normal occlusion [n=123; OR: 1.0]; Any Deviation [n=73; OR: 0.7 (0.4-1.4)];</p> <p>Sagittal occlusion: Neutro-occlusion [n=174; OR: 1.0]; Mesio-occlusion [n=5; OR: N/A]; Dist-occlusion [n=17; OR: 0.7 (0.2-2.3)]</p> <p>Vertical occlusion: Normal [n=142; OR: 1.0]; Open or edge- to edge [n=21; OR: 0.6 (0.2-1.8)]; Deep bite [n=33; OR: 1.2 (0.5-2.8)]</p> <p>Transversal occlusion: Normal [n=176; OR: 1.0]; Crossbite [n=18; OR: 0.5 (0.1-1.7)];</p> <p>Overjet: <5mm [n=170; OR: 1.0]; ≥5mm [n=20; OR: 0.6 (0.2-1.8)];</p> <p>Contact in RCP: Bilateral [n=77; OR: 1.0]; Unilateral [n=119; OR: 2.5 (1.2-4.9)];</p> <p>Lateral slide in centric: <1mm [n=181; OR: 1.0]; ≥1mm [n=15; OR: 1.7 (0.6-5.2)];</p> <p>Mandibular stability in ICP: Stable [n=181; OR: 1.0]; Instability [n=15; OR: 3.2 (1.1-9.2)];</p> <p>Perceived occlusal stability: Equal [n=145; OR: 1.0]; Unequal [n=51; OR: 1.2 (0.6-2.4)];</p> <p>Mediotrusive side interferences (MI): No [n=135; OR: 1.0]; Yes [n=61; OR: 0.8 (0.4-1.7)];</p> <p>MI at 3mm lateral excursion: No [n=179; OR: 1.0]; Yes [n=17; OR: 1.9 (0.7-5.2)];</p> <p>MI at 9mm lateral excursion: No [n=139; OR: 1.0]; Yes [n=57; OR: 0.9 (0.4-1.7)];</p>

<p>Slade et al., USA (2007)</p>	<p>3 years</p>	<p>Aimed: 254 F Blood sample and written consent for genotyping: 212 F Follow-up Data: 171 F/18-34.y.o</p>	<p>RDC/TMD</p>	<p>occlusal stability. Pain palpation (the tendon, the anterior and posterior part of the temporal muscles, superficial and deep masseter, lateral and medial pterygoid. Genotyping of 4 COMT SNPs: rs6269, rs4633, rs4818 and val¹⁵⁸ met: Pain Sensitivity haplotypes (HPS) = participating carrying haplotypes ACCG or ATCA for 4 SNPs (rs6269, rs4633, rs4818, and val¹⁵⁸met respectively); Pain Resistant Haplotypes (PRH)= at least 1 haplotype (GCGG); The Brief Symptom Inventory (BSI), The Perceived Stress Scale (PSS), The Profile of Mood States-Bi-Polar (POMS-Bi), The State-Trait Anxiety Inventory (STAI), Pain phenotype score (13 pain perceptions assessment at baseline).</p>	<p>Univariate Poisson Regression: Pain phenotype score (ref.: <3); ≥ 3 [IDR: 2.5 (1.2-5.2)]</p> <p>Bivariate Analysis: TMD ANNUAL INCIDENCE RATE (PER 100 PERSON-YEARS\pm 95%CI) AND % of people with PSH (p<0.0028, equivalent to Bonferroni's correction of the conventional p<0.05):</p> <p>BSI depression: Incidence density ratio: [3.2 (1.5-6.7)] Prevalence ratio: [1.2 (0.8- 1.8)]</p> <p>POMS confident-unsure: Incidence density ratio: [3.7 (1.7-8.1)] Prevalence ratio: [1.4 (0.9-2.1)]</p> <p>Perceived Stress Scale: Incidence density ratio: [2.6 (1.2-5.5)] Prevalence ratio: [1.3 (0.8-1.9)] The threshold of p < 0.0028, equivalent to Bonferroni's correction of the conventional P < 0.05</p> <p>Multivariate Analysis: Independent effects on TMD risk: BSI depression [likelihood ratio statistic, 1 df, = 8.75, P = 0.004] COMT haplotype [likelihood ratio statistic, 1 df, = 4.03, P = 0.046] BSI depression (adjusted for COMT haplotype for high BSI depression- subscale scores>60): IDR: 3.1 (1.5-6.4)</p>
<p>Lim et al, (2010)</p>	<p>3 years</p>	<p>Baseline: 266 females First year: 186 (69.9%) Second years: 147 (55.3%) Third year: 189 (71.1%)/18-34 years</p>	<p>RDC/TMD</p>	<p>Symptom Report Questionnaire: Headaches, muscle soreness or pain, joint soreness or pain, back pain, chest pain, pelvic pain, abdominal pain, menstrual pain, other pain.</p>	<p>Univariate Analysis: Participants who developed TMD reported: more headaches (p=0.0089), muscle soreness or pain (p=0.005), joint soreness or pain (p=0.0012), back pain (p=0.0001), chest pain (p=0.0004), abdominal pain (p=0.0021), and menstrual pain (p=0.0036) than participants who did not develop TMD at baseline and final visits.</p>
<p>Marklund et al., Sweden (2010)</p>	<p>2 years</p>	<p>Invited: 372 Drop-out: 91education interrupted Final sample: 280 (98 M, 182 F)/ 23 y.o (18-43)</p>	<p>RDC/TMD</p>	<p>Sex, presence of signs and symptoms of TMD, headaches and spinal pain.</p>	<p>BINARY LOGISTIC REGRESSION: Risk Factors to TMD pain (Axis I: group 1a and 3a - myofascial pain and arthralgia): Spinal pain [OR: 2.9 (1.3– 6.2)]; Female with spinal pain vs. Male with spinal pain [OR 5.6 (1.6–19.7); p<0.05]; Female with spinal pain vs. Male without Spinal pain [OR: 14.9 (3.3-67.9); p<0.001]. Female without spinal pain vs. Male without spinal pain [OR: 4.9 (1.1-22.3); p<0.05] Male without Spinal pain vs. Male with Spinal pain: [OR: 1.8 (0.2-20.9); p>0.05]</p>

<p>Kindler et al., Germany (2012)</p>	<p>5 year Data Collection: 1997-2001 Follow-up examination: 2002-2006</p>	<p>Invited: 7,008 Eligible: 6,265 Final sample: 4,308 Joint Pain: 3006 Muscle: 3034 Follow-up drop-outs: 1008 (231 died, 129 moved away, 541 refused, 107 other reasons) Final Sample after 5y: 3300 (1711 females and 1589 males)/ 49 y.o (20-81y.o)</p>	<p>American Academy of Orofacial Pain</p>	<p>Depressive and Anxiety symptoms: Composite International Diagnostic Screener (CID-S) – self-reported questionnaire</p>	<p>DEPRESSIVE SYMPTOMS: JOINT PAIN (n=3,006): Model 1 [RR: 2.37 (1.67-3.35); p<0.001]; Model 2 [RR: 2.13 (1.50-3.01); p<0.001]; Model 3 [RR: 2.13 (1.51-3.01); p<0.001]; Model 4 [RR: 2.09 (1.47-2.98); p<0.001]; Model 5 [RR: 2.08 (1.46-2.96); p<0.001]; Model 6 [RR: 1.86 (1.28-2.69); p<0.01]; Model 7 [RR: 1.97 (1.37-2.83); p<0.001]; MUSCLE PAIN (n=3,034): Model 1 [RR: 2.07 (1.19-3.59); p<0.01]; Model 2 [RR: 1.83 (1.05-3.19); p<0.05]; Model 3 [RR: 1.82 (1.03-3.19); p<0.05]; Model 4 [RR: 1.70 (0.96-3.00)]; Model 5 [RR: 1.57 (0.87-2.86)]; Model 6 [RR: 1.21 (0.69-2.12)]; Model 7 [RR: 1.51 (0.85-2.71)]; JOINT PAIN OR DISCOMFORT (n=2,872): Model 1 [RR: 1.91 (1.55-2.35); p<0.001]; Model 2 [RR: 1.80 (1.46-2.22); p<0.001]; Model 3 [RR: 1.77 (1.43-2.18); p<0.001]; Model 4 [RR: 1.72 (1.39-2.13); p<0.001]; Model 5 [RR: 1.69 (1.37-2.10); p<0.001]; Model 6 [RR: 1.58 (1.26-1.98); p<0.01]; Model 7 [RR: 1.62 (1.31-2.02); p<0.001]; MUSCLE PAIN OR DISCOMFORT (n=2,909): Model 1 [RR: 2.25 (1.60-3.18); p<0.001]; Model 2 [RR: 1.93 (1.37-2.73); p<0.001]; Model 3 [RR: 1.90 (1.34-2.69); p<0.001]; Model 4 [RR: 1.79 (1.26-2.54); p<0.01]; Model 5 [RR: 1.75 (1.32-2.79); p<0.01]; Model 6 [RR: 1.50 (1.03-2.18); p<0.05]; Model 7 [RR: 1.58 (1.10-2.27); p<0.05]</p> <p>ANXIETY SYMPTOMS: JOINT PAIN (n=3,006): Successive Adjustments for confounders Model 1 [RR: 2.01 (1.40-2.90); p<0.001]; Model 2 [RR: 1.79 (1.24-2.58); p<0.01]; Model 3 [RR: 1.78 (1.24-2.57); p<0.01]; Model 4 [RR: 1.75 (1.21-2.52); p<0.01]; Model 5 [RR: 1.74 (1.20-2.52); p<0.01]; Model 6 [RR: 1.42 (0.97-2.10)]; Model 7 [RR: 1.58 (1.10-2.29); p<0.05] MUSCLE PAIN (n=3,034): Model 1 [RR: 3.89 (2.00-7.57); p<0.001]; Model 2 [RR: 3.46 (1.75-6.78); p<0.001]; Model 3 [RR: 3.49 (1.78-6.82); p<0.001]; Model 4 [RR: 3.37 (1.70-6.66); p<0.001]; Model 5 [RR: 3.18 (1.59-6.38)]; Model 6 [RR: 3.18 (1.61-6.27); p<0.001]; Model 7 [RR: 3.19 (1.65-6.13); p<0.001] JOINT PAIN OR DISCOMFORT (n=2,872): Model 1 [RR: 1.62 (1.32-2.01); p<0.001]; Model 2 [RR: 1.55 (1.25-1.92); p<0.001]; Model 3 [RR: 1.52 (1.23-1.88); p<0.001]; Model 4 [RR: 1.49 (1.20-1.84); p<0.001]; Model 5 [RR: 1.47 (1.19-1.83); p<0.001]; Model 6 [RR: 1.28 (1.02-1.61); p<0.05]; Model 7 [RR: 1.40 (1.12-1.75); p<0.001] MUSCLE PAIN OR DISCOMFORT (n=2,909): Model 1 [RR: 2.35 (1.63-3.41); p<0.001]; Model 2 [RR: 2.04 (1.41-2.97); p<0.001]; Model 3 [RR: 2.03 (1.40-2.94); p<0.001]; Model 4 [RR: 1.95 (1.34-2.83); p<0.001]; Model 5 [RR: 1.92 (1.32-2.79); p<0.001]; Model 6 [RR: 1.71 (1.15-2.55); p<0.01]; Model 7 [RR: 1.74 (1.19-2.54); p<0.01]</p> <p>SENSITIVITY ANALYSIS (Excluding subjects taking pain medication - Rate ratio 95% CI)</p> <p>Depressive symptoms (85 events; n=2,279): Joint pain: Model 4 [RR: 1.95 (1.29-2.96); p=0.002]; Model 6 [RR: 1.88 (1.23 -2.86); p=0.003]; Muscle Pain: Model 4 [RR: 1.95 (0.95-4.00); p=0.068]; Model 6 [RR: 2.01 (0.99-4.08); p=0.054]; Anxiety symptoms (28 events; n=2,301): Joint pain: Model 4 [RR: 1.56 (1.02-2.38); p=0.039]; Model 6 [RR: 1.51 (0.99 -2.31); p=0.056]; Muscle Pain: Model 4 [RR: 5.19 (1.95-13.80); p=0.001]; Model 6 [RR: 5.22 (1.96-13.9); p=0.001];</p> <p>Successive Adjustments for confounders: Model 1= Unadjusted; Model 2= adds age and sex; Model 3= adds school education; Model 4= adds arthritis and degenerative disc disease (final model); Model 5= adds migraine as confounder;</p>
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<p>Fillingim et al., USA (2013)</p>	<p>5.2 years (median follow-up=2.8 years)</p>	<p>Screened: 3,263 Drop-outs: 526 returned no quarterly screening questionnaire. Final sample: 2,737 Data Imputed: 243 who reported TMD symptoms but did not receive follow-up examination/18 to 44 y.o</p>	<p>RDC/TMD</p>	<p>Measures of Global Psychological and Somatic Function, Stress, and Mood: Psychological Function: <u>Symptom Checklist 90-Revised (SCL90R):</u> Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. <u>Eysenck Personality Questionnaire-Revised (Short-Form, EPQ-R):</u> Extraversion, Neuroticism, and Psychoticism. Affective Distress: <u>State-Trait Anxiety Inventory (STAI):</u> State Anxiety Inventory (“feel right now”) and Trait Anxiety Inventory (“generally feel”) The Profile of Mood States-Bipolar (POMS-Bi): Positive and Negative affective Psychosocial Stress: <u>The Perceived Stress Scale (PSS):</u> Stressful level of variety of situations <u>The Life Experiences Survey (LES):</u> Life events that occurred over the past year and impact of these events <u>The Lifetime Stressor List/PTSD Checklist-Civilian Version (LSL/PCL-C):</u> Which of 15 described events the participants have experienced, identification of the most stressor event and the extent of these to which they experience PTSD symptoms (e.g., repeated, disturbing memories)</p>	<p>Model 6= adds Depression/Anxiety as confounders; Model 7= adds Pain Conditions (headache, neck and shoulder pain, pain in suboccipital muscles, pain in sternocleidomastoid muscles, and migraine) as confounder</p> <p>UNIVARIATE ASSOCIATIONS OF PSYCHOLOGICAL CHARACTERISTICS AND INCIDENCE RATE OF FIRST-ONSET TMD</p> <p>PILL GLOBAL SCORE (1-270 scale): [n=2,597; HR: 1.52 (1.36-1.68)][†]; [n=2,597; HR: 1.55 (1.39-1.72); p<0.001][‡]; [n=2,733; HR: 1.44 (1.29-1.60); p<0.001][§]</p> <p>SCL 90R DEPRESSION (0-4 scale): [n=2,693; HR: 1.35 (1.23-1.47)][†]; [n=2,693; HR: 1.35 (1.23-1.46); p<0.001][‡]; [n=2,729; HR: 1.31 (1.19-1.42); p<0.001][§]</p> <p>SCL 90R SOMATIZATION FULL (0-4 scale): [n=2,699; HR: 1.44 (1.32-1.55)][†]; [n=2,699; HR: 1.42 (1.30-1.53); p<0.001][‡]; [n=2,729; HR: 1.38 (1.27-1.49); p<0.001][§]</p> <p>SCL 90R ANXIETY (0-4 scale): [n=2,699; HR: 1.33 (1.22-1.43)][†]; [n=2,699; HR: 1.31 (1.20-1.41); p<0.001][‡]; [n=2,729; HR: 1.29 (1.19-1.39); p<0.001][§]</p> <p>SCL 90R OBS COMPULS (0-4 scale): [n=2,705; HR: 1.35 (1.23-1.48)][†]; [n=2,705; HR: 1.36 (1.24-1.49); p<0.001][‡]; [n=2,729; HR: 1.32 (1.20-1.44); p<0.001][§]</p> <p>SCL 90R INTERPERS SENSITIVITY (0-4 scale): [n=2,703; HR: 1.26 (1.14-1.38)][†]; [n=2,703; HR: 1.28 (1.16-1.40); p<0.001][‡]; [n=2,729; HR: 1.25 (1.14-1.37); p<0.001][§]</p> <p>SCL 90R HOSTILITY (0-4 scale): [n=2,719; HR: 1.25 (1.14-1.35)][†]; [n=2,719; HR: 1.25 (1.15-1.36); p<0.001][‡]; [n=2,729; HR: 1.23 (1.13-1.33); p<0.001][§]</p> <p>SCL 90R PHOBIA (0-4 scale): [n=2,702; HR: 1.22 (1.14-1.30)][†]; [n=2,702; HR: 1.22 (1.13-1.30); p<0.001][‡]; [n=2,729; HR: 1.19 (1.11-1.27); p<0.001][§]</p> <p>SCL 90R PARANOID (0-4 scale): [n=2,716; HR: 1.32 (1.20-1.43)][†]; [n=2,716; HR: 1.31 (1.19-1.42); p<0.001][‡]; [n=2,729; HR: 1.28 (1.16-1.39); p<0.001][§]</p> <p>SCL 90R PSYCHOTIC (0-4 scale): [n=2,704; HR: 1.22 (1.12-1.33)][†]; [n=2,704; HR: 1.21 (1.10-1.31); p<0.001][‡]; [n=2,729; HR: 1.31 (1.19-1.42); p<0.001][§]</p> <p>PTSD CHECKLIST FOR CIVILIANS (17-85 scale): [n=2,631; HR: 1.38 (1.25-1.50)][†]; [n=2,631; HR: 1.34 (1.21-1.46); p=0.000][‡]; [n=2,669; HR: 1.34 (1.21-1.46); p=0.000][§]</p> <p>EPQ-R EXTRAVERSIONS (0-12 scale): [n=2,695; HR: 0.97 (0.85-1.09)][†]; [n=2,695; HR: 1.00 (0.88-1.12); p=0.970][‡]; [n=2,726; HR: 1.02 (0.89-1.15); p=0.790][§]</p> <p>EPQ-R NEUROTICISM (0-12 scale): [n=2,704; HR: 1.28 (1.13-1.43)][†]; [n=2,704; HR: 1.29 (1.14-1.45); p<0.001][‡]; [n=2,726; HR: 1.24 (1.09-1.39); p=0.001][§]</p> <p>PERCEIVED STRESS SCALE (0-40 scale): [n=2,690; HR: 1.34 (1.18-1.51)][†]; [n=2,690; HR: 1.35 (1.19-1.51); p<0.001][‡]; [n=2,734; HR: 1.31 (1.16-1.48); p<0.001][§]</p> <p>LES # NEGATIVE EVENTS (0-50 scale): [n=2,394; HR: 1.32 (1.19-1.45)][†]; [n=2,394; HR: 1.30 (1.17-1.43); p<0.001][‡];</p> <p>LES NEGATIVE IMPACTS (0-150 scale): [n=2,394; HR: 1.30 (1.19-1.41)][†]; [n=2,394; HR: 1.27 (1.16-1.39); p<0.001][‡];</p> <p>STATE ANXIETY INVENTORY (20-80 scale): [n=2,679; HR: 1.22 (1.09-1.36)][†]; [n=2,679; HR: 1.23 (1.10-1.37); p<0.001][‡]; [n=2,725; HR: 1.23 (1.09-1.37); p<0.001][§]</p> <p>TRAIT ANXIETY INVENTORY (20-80 scale): [n=2,674; HR: 1.40 (1.25-1.57)][†]; [n=2,674; HR: 1.42 (1.26-1.59); p<0.001][‡]; [n=2,733; HR: 1.35 (1.20-1.51); p<0.001][§]</p> <p>POMS-Bi POSITIVE AFFECT (30-120 scale): [n=2,604; HR: 0.80 (0.70-0.89)][†]; [n=2,604; HR: 0.80 (0.71-0.89); p<0.001][‡]; [n=2,720; HR: 0.80 (0.71-0.90); p<0.001][§]</p> <p>POMS-Bi NEGATIVE AFFECT (30-120 scale): [n=2,645; HR: 1.24 (1.10-1.38)][†]; [n=2,645; HR: 1.26 (1.12-1.41); p<0.001][‡]; [n=2,720; HR: 1.22 (1.08-1.36); p=0.001][§]</p> <p>PCS HELPLESSNESS (0-24 scale): [n=2,716; HR: 1.11 (0.99-1.24)][†]; [n=2,716; HR: 1.10 (0.98-1.23); p=0.086][‡]; [n=2,734; HR: 1.12 (1.00-1.25); p=0.036][§]</p> <p>PCS MAGNIFICATION (0-12 scale): [n=2,727; HR: 1.06 (0.94-1.19)][†]; [n=2,727; HR: 1.06 (0.94-1.18); p=0.340][‡]; [n=2,734; HR: 1.09 (0.97-1.22); p=0.140][§]</p>
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			<p>Somatic Symptoms and Reactivity: <u>Pennebaker Inventory of Limbic Languidness (PILL):</u> Frequency with which individual experience of 54 common physical symptoms and sensations on a five-category scale <u>The Kohn Reactivity Scale:</u> Assess an individual's level of reactivity or central nervous system arousability to sensory stimuli. Coping/Catastrophizing: <u>The Coping Strategies Questionnaire-Revised (CSQ-R):</u> How individuals cope with pain <u>The Pain Catastrophizing Scale (PCS):</u> degree of thoughts and feeling when experiencing pain. Three dimensions: Rumination, Magnification, and Helplessness. Principal Component Analysis (PCA): <u>Global Psychological and Somatic Symptoms</u> (high loadings from all SCL-90-R scales, the PILL, and the LSL/PCL-C PTSD symptom scale); <u>Stress and Negative Affectivity</u> (high loadings from both State and Trait Anxiety, Perceived Stress, POMS Negative Affect, and EPQ-R Neuroticism; negative loadings for POMS Positive Affect and EPQ-R Extraversion); <u>Passive Pain Coping</u> (positive loading from all three PCS subscales, the Praying and Hoping subscale of the CSQ-R, and the Kohn score);</p>	<p>PCS RUMINATION (0-16 scale): [n=2,722; HR: 1.07 (0.95-1.20)][†]; [n=2,722; HR: 1.05 (0.93-1.18); p=0.390][‡]; [n=2,734; HR: 1.07 (0.94-1.20); p=0.270][§] CSQ COPING STATEMENTS (0-6 scale): [n=2,715; HR: 0.98 (0.86-1.10)][†]; [n=2,715; HR: 1.00 (0.88-1.12); p=1.000][‡]; [n=2,734; HR: 0.98 (0.86-1.10); p=0.750][§] CSQ REINTERPRETING PAIN (0-6 scale): [n=2,727; HR: 1.00 (0.88-1.13)][†]; [n=2,727; HR: 1.02 (0.89-1.15); p=0.810][‡]; [n=2,734; HR: 1.04 (0.91-1.17); p=0.550][§] CSQ DISTRACTION (0-6 scale): [n=2,715; HR: 1.01 (0.89-1.13)][†]; [n=2,715; HR: 0.99 (0.87-1.12); p=0.890][‡]; [n=2,734; HR: 1.01 (0.88-1.14); p=0.940][§] CSQ IGNORING PAIN (0-6 scale): [n=2,714; HR: 0.93 (0.82-1.05)][†]; [n=2,714; HR: 0.96 (0.84-1.08); p=0.530][‡]; [n=2,734; HR: 0.94 (0.82-1.06); p=0.300][§] CSQ PRAYING & HOPING (0-6 scale): [n=2,723; HR: 1.07 (0.94-1.20)][†]; [n=2,723; HR: 0.98 (0.85-1.11); p=0.720][‡]; [n=2,734; HR: 1.03 (0.90-1.18); p=0.630][§] KOHN GLOBAL SCORE (24-120 scale): [n=2,643; HR: 1.15 (1.02-1.30)][†]; [n=2,643; HR: 1.09 (0.94-1.24); p=0.240][‡]; [n=2,727; HR: 1.12 (0.97-1.28); p=0.120][§] UNIVARIATE ASSOCIATIONS OF PRINCIPAL COMPONENT SCORES AND INCIDENCE RATE OF FIRST-ONSET TMD (n= 2737) STRESS AND NEGATIVE AFFECTIVITY: [HR: 1.34 (1.19-1.50)][†]; [HR:1.35 (1.20-1.52); p<0.001][‡]; [HR: 1.31 (1.16-1.47); p<0.001][§] GLOBAL PSYCHOLOGICAL SYMPTOMS: [HR: 1.42 (1.30-1.55)][†]; [HR:1.41 (1.29-1.53); p<0.001][‡]; [HR: 1.37 (1.25-1.49); p<0.001][§] PASSIVE PAIN COPING: [HR: 1.16 (1.02-1.30)][†]; [HR:1.12 (0.98-1.26); p=0.084][‡]; [HR:1.16 (1.02-1.31); p=0.018][§] ACTIVE PAIN COPING: [HR: 0.99 (0.87-1.11)][†]; [HR:1.00 (0.88-1.13); p=0.960][‡]; [HR: 0.99 (0.87-1.12); p=0.890][§] MULTIVARIABLE ASSOCIATION OF PRINCIPAL COMPONENT SCORES AND INCIDENCE RATE OF FIRST-ONSET TMD: STRESS AND NEGATIVE AFFECTIVITY: [HR: 1.17 (1.01-1.35); p=0.040][‡]; [HR:1.12 (0.97-1.30); p=0.1333][§]; GLOBAL PSYCHOLOGICAL SYMPTOMS: [HR: 1.37 (1.22-1.55); p<0.001][‡]; [HR:1.33 (1.18-1.50); p<0.001][§]; PASSIVE PAIN COPING: [HR: 0.89 (0.77-1.02); p=0.096][‡]; [HR:0.96 (0.83-1.11); p=0.56][§]; ACTIVE PAIN COPING: [HR: 0.97 (0.86-1.10); p=0.659][‡]; [HR:0.95 (0.84-1.08); p=0.428][§]; [†] Adjusted for study site [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were not examined as intended. MULTIVARIABLE PROPORTIONAL HAZARDS MODEL: DEMOGRAPHICALLY STRATIFIED ASSOCIATIONS OF PRINCIPAL COMPONENT SCORES AND INCIDENCE RATE OF FIRST-ONSET TMD GLOBAL PSYCHOLOGICAL SYMPTOMS: Age (p=0.030): 18-24 years [1.45 (1.26-1.67)]; 25-34 years [1.65 (1.42-1.92)]; 35-44 years [1.23 (1.04-1.44)] Gender (p=0.706): Female [1.39 (1.26-1.54)]; Male [1.45 (1.23-1.71)]; Race/ Ethnicity (p=0.135): White [1.51 (0.99-2.30)]; Black/African American [1.27 (1.11-1.45)]; Asian [2.02 (1.24-3.30)]; Hispanic [1.96 (0.94-4.11)]; Other [1.54 (1.36-1.75)] Lifetime US residency (p=0.003): Yes [2.28 (1.65-3.14)]; No/Not stated [1.37 (1.25-1.51)]; STRESS AND NEGATIVE AFFECTIVITY: Age (p=0.070): 18-24 years [1.33 (1.11-1.60)]; 25-34 years [1.66 (1.34-2.06)]; 35-44 years [1.16 (0.93-1.45)] Gender (p=0.383): Female [1.42 (1.22-1.64)]; Male [1.27 (1.05-1.55)];</p>
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				<p><u>Active Pain Coping</u> (positive loadings from the remaining CSQ-R subscales). Interactions: Age groups, race/ethnicity, gender</p>	<p>Race/Ethnicity (p=0.568): White [1.77 (0.95-3.32)]; Black/African American [1.20 (0.97-1.48)]; Asian [1.66 (1.02-2.73)]; Hispanic [1.37 (0.68-2.77)]; Other [1.41 (1.21-1.65)] Lifetime US Residency (p=0.057): Yes [1.99 (1.32-2.98)]; No/Not stated [1.32 (1.16-1.49)];</p> <p>PASSIVE COPING Age (p=0.374): 18-24 years [1.04 (0.83-1.29)]; 25-34 years [1.26 (1.02-1.56)]; 35-44 years [1.08 (0.88-1.33)] Gender (p=0.593): Female [1.10 (0.94-1.27)]; Male [1.17 (0.95-1.44)]; Race/Ethnicity (p=0.845): White [1.30 (0.71-2.37)]; Black/African American [1.11 (0.93-1.33)]; Asian [0.85 (0.50-1.47)]; Hispanic [1.31 (0.56-3.09)]; Other [1.15 (0.95-1.39)] Lifetime US Residency (p=0.522): Yes [0.97 (0.62-1.53)]; No/Not stated [1.13 (1.00-1.29)];</p> <p>ACTIVE COPING Age (p=0.224): 18-24 years [1.01 (0.82-1.25)]; 25-34 years [0.86 (0.69-1.08)]; 35-44 years [1.12 (0.92-1.37)] Gender (p=0.105): Female [1.08 (0.93-1.26)]; Male [0.87 (0.71-1.07)]; Race/ethnicity (p=0.422): White [0.60 (0.30-1.20)]; Black/African American [1.10 (0.92-1.32)]; Asian [1.00 (0.61-1.65)]; Hispanic [0.75 (0.35-1.60)]; Other [0.96 (0.80-1.16)] Lifetime us residency (p=0.160): Yes [0.74 (0.47-1.15)]; No/Not stated [1.03 (0.90-1.17)];</p>
Greenspan, USA (2013)	5.2 years (median follow-up=2.8 years)	Screened: 3,263 Drop-outs: 526 returned no quarterly screening questionnaire. Final sample: 2,737 Data Imputed: 243 who reported TMD symptoms but did not receive follow-up examination/18 to 44 y.o	RDC/TMD	<p>Quantitative Sensitivity Test (QST): 1) Pressure pain threshold (PPTs): temporalis muscle, masseter muscle, temporomandibular (TM) joint, trapezius muscle and lateral epicondyle 2) Cutaneous mechanical pain sensitivity: threshold, ratings of suprathreshold stimuli, temporal summation, and aftersensation 3) Heat pain sensitivity: threshold, tolerance, ratings of suprathreshold stimuli, temporal summation, and aftersensation, assessed on the forearm. Autonomic measures: arterial blood pressure, heart rate, heart rate variability, under rest and during two provocative conditions: orthostatic challenge and Stroop protocol</p>	<p>UNIVARIATE ASSOCIATION OF MECHANICAL PAIN MEASURES AND INCIDENCE OF TMD <u>Pressure pain threshold:</u> Temporalis (kPa, 50-600): [n= 2,692; HR: 1.20 (1.05 - 1.37)][†]; [n= 2,692; HR: 1.20 (1.04-1.37); p=0.012][‡]; [n= 2,714; HR: 1.17 (1.01 - 1.34) p=0.27][§]; Masseter (kPa, 50-600): [n= 2,691; HR: 1.18 (1.03 - 1.34)][†]; [n= 2,691; HR: 1.18 (1.02 - 1.35); p= 0.021][‡]; [n= 2,714; HR: 1.16 (1.01 - 1.33); p= 0.034][§]; TM joint (kPa, 50-600): [n= 2,657; HR: 1.15 (1.00-1.30)][†]; [n= 2,657; HR: 1.14 (0.99-1.31); p =0.57][‡]; [n= 2,714; HR: 1.16 (1.00-1.32); p =0.037][§]; Trapezius (kPa, 100-600): [n= 2,637; HR: 1.13 (0.99 - 1.28)][†]; [n= 2,637; HR: 1.12 (0.97 - 1.29); p= 0.100][‡]; [n= 2,714; HR: 1.11 (0.96 - 1.27); p= 0.160][§]; Lateral epicondyle (kPa, 100-600) [n= 2,643; HR: 1.04 (0.90 - 1.19)][†]; [n= 2,643; HR: 1.02 (0.88 - 1.17); p= 0.800][‡]; [n= 2,714; HR: 1.05 (0.90 - 1.21); p= 0.500][§]; <u>Mechanical cutaneous pain:</u> Threshold (mN, 8-512): [n= 2,621; HR: 1.02 (0.89 - 1.16)][†]; [n= 2,621; HR: 1.06 (0.92 - 1.20); p=0.400][‡]; [n= 2,621; HR: 1.12 (0.96 - 1.28); p=0.130][§]; Single stimulus ratings: 256-mN probe (ratings, 0-100) [n= 2,650; HR: 0.99 (0.86 - 1.12)][†]; [n= 2,650; HR: 1.05 (0.92 - 1.19); p= 0.460][‡]; [n= 2,657; HR: 1.07 (0.93 - 1.21); p= 0.310][§]; 512mN probe (ratings, 0-100) [n= 2,488; HR: 1.07 (0.94-1.21)][†]; [n= 2,488; HR: 1.11 (0.98-1.25); p= 0.97][‡]; [n= 2,657; HR: 1.13 (0.99-1.27); p= 0.59][§]; Overall rating of 10 stimuli: 256mN probe (ratings, 0-100) [n= 2,648; HR: 0.95 (0.83- 1.08)][†]; [n= 2,648; HR: 1.01 (0.88- 1.15); p= 0.840][‡]; [n= 2,657; HR: 1.05 (0.91- 1.19); p= 0.470][§]; 512 mN probe (ratings, 0-100) [n= 2,487; HR: 1.04 (0.91 - 1.17)][†]; [n= 2,487; HR: 1.08 (0.95 - 1.23); p= 0.230][‡]; [n= 2,657; HR: 1.13 (1.00 - 1.28); p= 0.048][§]; Aftersensation ratings: 15s, 256mN probe (ratings, 0-100): [n=2,649; HR: 1.04 (0.91 - 1.18)][†]; [n=2,649; HR: 1.08 (0.95 - 1.23); p= 0.220][‡]; [n=2,658; HR: 1.12 (0.97 - 1.27); p= 0.100][§];</p>

				<p>30s, 256mN probe (ratings, 0-100): [n=2,650; HR: 1.07 (0.94 – 1.21)][†]; [n=2,650; HR: 1.10 (0.97 – 1.24); p=0.140][‡]; [n=2,658; HR: 1.10 (0.96 – 1.24); p=0.170][§];</p> <p>15s, 512mN probe (ratings, 0-100) [n=2,482; HR: 1.09 (0.95 – 1.25)][†]; [n=2,482; HR: 1.12 (0.97 – 1.29); p=0.110][‡]; [n=2,658; HR: 1.14 (0.99 – 1.30); p=0.061][§];</p> <p>30s, 512mN probe (ratings, 0-100): [n=2,475; HR: 1.15 (1.00 – 1.31)][†]; [n=2,475; HR: 1.16 (1.01 – 1.32); p=0.035][‡]; [n=2,658; HR: 1.16 (1.01 – 1.32); p=0.032][§];</p> <p>Temporal Summation:</p> <p>256mN probe (Δ Ratings, ± 100): [n=2,645; HR: 0.93 (0.81- 1.06)][†]; [n=2,645; HR: 0.97 (0.84- 1.11); p=0.670][‡]; [n=2,657; HR: 1.01 (0.88- 1.15); p=0.880][§];</p> <p>512mN probe (Δ Ratings, ± 100): [n=2,485; HR: 0.98 (0.86- 1.11)][†]; [n=2,485; HR: 1.01 (0.88- 1.15); p=0.840][‡]; [n=2,657; HR: 1.08 (0.95- 1.21); p=0.230][§];</p> <p style="text-align: center;">UNIVARIATE ASSOCIATIONS OF THERMAL PAIN MEASURES:</p> <p>Heat pain threshold (C,32-52): [n= 2,103; HR: 1.00 (0.86- 1.15)][†]; [n= 2,103; HR: 1.00 (0.86- 1.16); p = 0.97][‡]; [n= 2,103; HR: 1.03 (0.88- 1.20); p = 0.720][§];</p> <p>Heat pain tolerance (C, 32-52): [n= 2,455; HR: 1.05 (0.92- 1.18)][†]; [n= 2,455; HR: 1.03 (0.91- 1.16); p = 0.620][‡]; [n= 2,567; HR: 1.06 (0.92- 1.21); p = 0.410][§];</p> <p>Single stimulus ratings (Rating, 0-100):</p> <p>46°C [n= 2,429; HR: 1.12 (0.99- 1.27)][†]; [n= 2,429; HR: 1.11 (0.98- 1.25); p = 0.094][‡]; [n= 2,539; HR: 1.11 (0.97- 1.27); p = 0.120][§];</p> <p>48°C [n= 2,400; HR: 1.05 (0.92- 1.19)][†]; [n= 2,400; HR: 1.04 (0.91- 1.17); p = 0.590][‡]; [n= 2,539; HR: 1.14 (0.99- 1.30); p = 0.062][§];</p> <p>50°C [n= 2,322; HR: 1.05 (0.92- 1.19)][†]; [n= 2,322; HR: 1.04 (0.91- 1.18); p = 0.550][‡]; [n= 2,539; HR: 1.07 (0.93- 1.23); p = 0.320][§];</p> <p>Ratings of 10 stimuli - area under curve (Rating, 0-1,000):</p> <p>46°C [n= 2,030; HR: 1.00 (0.86- 1.16)][†]; [n= 2,030; HR: 1.05 (0.90- 1.21); p = 0.530][‡]; [n= 2,539; HR: 1.16 (1.01- 1.32); p = 0.033][§];</p> <p>48°C [n= 1,701; HR: 1.10 (0.92- 1.29)][†]; [n= 1,701; HR: 1.14 (0.96- 1.34); p = 0.130][‡]; [n= 2,539; HR: 1.22 (1.06- 1.41); p = 0.006][§];</p> <p>50°C [n= 1,258; HR: 1.16 (0.94- 1.40)][†]; [n= 1,258; HR: 1.20 (0.98- 1.46); p = 0.076][‡]; [n= 2,539; HR: 1.23 (1.05- 1.41); p = 0.006][§];</p> <p>Maximum rating from among 10 stimuli (Rating, 0-1,000):</p> <p>46°C [n= 2,534; HR: 1.11 (0.97- 1.26)][†]; [n= 2,534; HR: 1.12 (0.97- 1.28); p = 0.099][‡]; [n= 2,539; HR: 1.16 (1.01- 1.32); p = 0.032][§];</p> <p>48°C [n= 2,509; HR: 1.22 (1.06- 1.39)][†]; [n= 2,509; HR: 1.23 (1.06- 1.41); p = 0.004][‡]; [n= 2,539; HR: 1.23 (1.06- 1.42); p = 0.005][§];</p> <p>50°C [n= 2,420; HR: 1.21 (1.05- 1.39)][†]; [n= 2,420; HR: 1.21 (1.04- 1.40); p = 0.009][‡]; [n= 2,539; HR: 1.24 (1.06- 1.44); p = 0.005][§];</p> <p>Thermal aftersensation (Rating, 0-100):</p> <p>15s, 46°C [n= 2,498; HR: 1.08 (0.94- 1.22)][†]; [n= 2,498; HR: 1.09 (0.95- 1.24); p = 0.190][‡]; [n= 2,504; HR: 1.07 (0.93- 1.22); p = 0.320][§];</p> <p>30s, 46°C [n= 2,500; HR: 1.14 (1.00- 1.28)][†]; [n= 2,500; HR: 1.15 (1.00- 1.30); p = 0.036][‡]; [n= 2,504; HR: 1.12 (0.98- 1.27); p = 0.095][§];</p> <p>15s, 48°C [n= 2,501; HR: 1.17 (1.01- 1.33)][†]; [n= 2,501; HR: 1.20 (1.04- 1.37); p = 0.011][‡]; [n= 2,504; HR: 1.17 (1.01- 1.34); p = 0.026][§];</p> <p>30s, 48°C [n= 2,502; HR: 1.12 (0.97- 1.27)][†]; [n= 2,502; HR: 1.12 (0.98- 1.28); p = 0.088][‡]; [n= 2,504; HR: 1.11 (0.96- 1.26); p = 0.140][§];</p>
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				<p>15s, 50°C [n= 2,405; HR: 1.13 (0.98- 1.29)][†]; [n= 2,405; HR: 1.14 (0.99- 1.31); p = 0.067][‡]; [n= 2,504; HR: 1.13 (0.98- 1.30); p = 0.081][§]; 30s, 50°C [n= 2,401; HR: 1.16 (1.01- 1.33)][†]; [n= 2,401; HR: 1.17 (1.02- 1.34); p = 0.023][‡]; [n= 2,504; HR: 1.14 (0.99- 1.30); p = 0.063][§]; Temporal summation - highest minus first rating (Δ Ratings, 0-100): 46°C [n= 2,302; HR: 0.99 (0.86 - 1.12)][†]; [n= 2,302; HR: 1.00 (0.87 - 1.14); p = 0.980][‡]; [n= 2,539; HR: 1.07 (0.94 - 1.20); p = 0.310][§]; 48°C [n= 2,207; HR: 1.12 (0.98 - 1.28)][†]; [n= 2,207; HR: 1.11 (0.96 - 1.26); p = 0.130][‡]; [n= 2,539; HR: 1.07 (0.94 - 1.20); p = 0.300][§]; 50°C [n= 1,922; HR: 1.24 (1.07 - 1.43)][†]; [n= 1,922; HR: 1.25 (1.07 - 1.44); p = 0.003][‡]; [n= 2,539; HR: 1.14 (1.00 - 1.28); p = 0.039][§]; Temporal summation - slope of line for first 3 ratings (β coefficient): 46°C [n= 2,304; HR: 0.99 (0.86 - 1.13)][†]; [n= 2,304; HR: 0.99 (0.86 - 1.13); p = 0.860][‡]; [n= 2,539; HR: 1.04 (0.91 - 1.17); p = 0.570][§]; 48°C [n= 2,211; HR: 1.12 (0.99 - 1.26)][†]; [n= 2,211; HR: 1.09 (0.97 - 1.22); p = 0.140][‡]; [n= 2,539; HR: 1.08 (0.96 - 1.20); p = 0.180][§]; 50°C [n= 1,922; HR: 1.15 (1.01 - 1.31)][†]; [n= 1,922; HR: 1.14 (1.00 - 1.29); p = 0.050][‡]; [n= 2,539; HR: 1.12 (1.00 - 1.26); p = 0.044][§];</p> <p style="text-align: center;">UNIVARIATE ASSOCIATIONS OF THERMAL PAIN TEMPORAL SUMMATION AND INCIDENCE RATES OF FIRST-ONSET TMD, STRATIFIED ACCORDING TO FIRST PULSE RESPONSE</p> <p>Temporal summation- highest minus first rating: Subjects with a first-pulse rating of 0-19: 46°C (Δ Ratings, 0-100): [n=963; 1.14 (0.93-1.39)][†]; [n=963; 1.14 (0.92-1.38); p=0.210][‡]; [n=964; 1.18 (0.96-1.42); p=0.100][§]; 48°C (Δ Ratings, 0-100): [n=938; 1.25 (1.03-1.50)][†]; [n=938; 1.23 (1.01-1.48); p=0.039][‡]; [n=964; 1.15 (0.94-1.38); p=0.170][§]; 50°C (Δ Ratings, 0-100): [n=870; 1.35 (1.11-1.63)][†]; [n=870; 1.33 (1.10-1.61); p=0.003][‡]; [n=964; 1.27 (1.06-1.52); p=0.009][§]; Subjects with a first-pulse rating of 20-59: 46°C (Δ Ratings, 0-100): [n=928; 1.04 (0.82-1.30)][†]; [n=928; 1.07 (0.84-1.34); p=0.580][‡]; [n=934; 1.15 (0.90-1.46); p=0.240][§]; 48°C (Δ Ratings, 0-100): [n=890; 1.15 (0.90-1.47)][†]; [n=890; 1.16 (0.90-1.47); p=0.230][‡]; [n=934; 1.13 (0.90-1.40); p=0.300][§]; 50°C (Δ Ratings, 0-100): [n=786; 1.19 (0.91-1.54)][†]; [n=786; 1.24 (0.94-1.61); p=0.120][‡]; [n=934; 1.21 (0.96-1.51); p=0.096][§]; Subjects with a first-pulse rating of 60-100: 46°C (Δ Ratings, 0-100): [n=411; 0.83 (0.63-1.08)][†]; [n=411; 0.89 (0.68-1.16); p=0.420][‡]; [n=641; 0.96 (0.72-1.27); p=0.770][§]; 48°C (Δ Ratings, 0-100): [n=379; 0.91 (0.63-1.30)][†]; [n=379; 0.90 (0.62-1.28); p=0.560][‡]; [n=641; 1.05 (0.78-1.40); p=0.740][§]; 50°C (Δ Ratings, 0-100): [n=266; 0.94 (0.55-1.58)][†]; [n=266; 0.94 (0.56-1.55); p=0.800][‡]; [n=641; 1.00 (0.68-1.44); p=0.990][§];</p> <p style="text-align: center;">UNIVARIATE ASSOCIATIONS OF AUTONOMIC MEASURES AT REST AND AFTER ORTHOSTATIC CHALLENGE WITH INCIDENCE RATE OF FIRST-ONSET TMD</p> <p>BASELINE RESTING -RECLINED (20min):</p>
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				<p> Mean SBP (mmHg): [n=2,673; 1.15 (1.02-1.30)][†]; [n=2673; 1.07 (0.93-1.21); p=0.330][‡]; [n=2692; 1.09 (0.96-1.24); p=0.170][§]; Mean DBP (mmHg): [n=2,666; 1.23 (1.09-1.38)][†]; [n=2666; 1.10 (0.96-1.25); p=0.160][‡]; [n=2692; 1.11 (0.97-1.26); p=0.130][§]; Mean MAP (mmHg): [n=2,669; 1.20 (1.07-1.35)][†]; [n=2669; 1.09 (0.95-1.23); p=0.190][‡]; [n=2690; 1.12 (0.98-1.26); p=0.084][§]; Mean HR- cuff (bpm): [n=2,655; 1.12 (0.98-1.25)][†]; [n=2655; 1.08 (0.95-1.21); p=0.250]; [n=2687; 1.07 (0.94-1.21); p=0.300][§]; HR/MAP Index (bpm/mmHg): [n=2,650; 1.00 (0.88-1.13)][†]; [n=2650; 1.03 (0.90-1.16); p=0.680][‡]; [n=2685; 1.00 (0.88-1.13); p=0.980][§]; Mean HR - ECG (bpm): [n=2,566; 1.02 (1.00-1.03)][†]; [n=2566; 1.02 (1.00-1.02); p=0.005][‡]; [n=2566; 1.01 (1.00-1.02); p=0.023][§]; SDNN (ms): [n=2,560; 1.00 (0.99-1.00)][†]; [n=2560; 1.00 (0.99-1.00); p=0.690][‡]; [n=2560; 1.00 (0.99-1.00); p=0.860][§]; RMSSD (ms): [n=2,540; 1.00 (0.99-1.00)][†]; [n=2540; 1.00 (0.99-1.00); p=0.870][‡]; [n=2540; 1.00 (0.99-1.00); p=0.830][§]; Log TP (ms²): [n=2,548; 0.88 (0.75-1.01)][†]; [n=2548; 0.94 (0.81-1.09); p=0.460][‡]; [n=2548; 0.95 (0.82-1.10); p=0.530][§]; Log VLF (ms²): [n=2,558; 0.92 (0.79-1.06)][†]; [n=2558; 1.00 (0.85-1.16); p=0.990][‡]; [n=2558; 0.99 (0.85-1.15); p=0.930][§]; Log LF (ms²): [n=2,547; 0.90 (0.78-1.01)][†]; [n=2547; 0.96 (0.84-1.09); p=0.540][‡]; [n=2547; 0.96 (0.83-1.09); p=0.530][§]; Log HF (ms²): [n=2,530; 0.90 (0.80-1.00)][†]; [n=2530; 0.93 (0.82-1.04); p=0.220][‡]; [n=2530; 0.94 (0.83-1.05); p=0.300][§]; ORTHOSTATIC CHALLENGE (5 min): Δ SBP (mmHg): [n=2,547; 0.98 (0.86-1.11)][†]; [n=2547; 0.98 (0.86-1.11); p=0.800][‡]; [n=2563; 1.00 (0.87-1.13); p=0.950][§]; Δ DBP (mmHg): [n=2,527; 1.05 (0.92-1.19)][†]; [n=2527; 1.10 (0.96-1.26); p=0.150][‡]; [n=2550; 1.05 (0.91-1.21); p=0.450][§]; Δ MAP (mmHg): [n=2,538; 0.98 (0.86-1.11)][†]; [n=2538; 1.02 (0.89-1.16); p=0.730][‡]; [n=2555; 1.02 (0.88-1.16); p=0.830][§]; Δ HR - cuff (bpm): [n=2,531; 0.88 (0.77-1.00)][†]; [n=2531; 0.96 (0.84-1.10); p=0.600][‡]; [n=2560; 0.95 (0.82-1.09); p=0.470][§]; Mean HR - ECG (bpm): [n=2,534; 1.00 (0.99-1.01)][†]; [n=2534; 1.01 (0.99-1.01); p=0.250][‡]; [n=2534; 1.00 (0.99-1.01); p=0.380][§]; SDNN (ms): [n=2,531; 1.00 (0.99-1.00)][†]; [n=2531; 1.00 (0.99-1.00); p=0.800][‡]; [n=2531; 1.00 (0.99-1.00); p=0.940][§]; RMSSD (ms): [n=2,460; 1.00 (0.99-1.00)][†]; [n=2460; 1.00 (0.99-1.00); p=0.250][‡]; [n=2460; 1.00 (0.99-1.00); p=0.230][§]; Log TP (ms²): [n=2,526; 0.86 (0.73-1.00)][†]; [n=2526; 0.94 (0.79-1.10); p=0.450][‡]; [n=2526; 0.98 (0.83-1.16); p=0.830][§]; Log VLF (ms²): [n=2,527; 0.86 (0.74-0.99)][†]; [n=2527; 0.92 (0.78-1.06); p=0.260][‡]; [n=2527; 0.96 (0.81-1.11); p=0.580][§]; Log LF (ms²): [n=2,522; 0.86 (0.75-0.99)][†]; [n=2522; 0.95 (0.81-1.10); p=0.490][‡]; [n=2522; 0.98 (0.84-1.14); p=0.830][§]; Log HF (ms²): [n=2,435; 0.97 (0.85-1.10)][†]; [n=2435; 0.98 (0.86-1.11); p=0.740][‡]; [n=2435; 1.02 (0.89-1.15); p=0.770][§]; </p>
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				<p>UNIVARIATE ASSOCIATIONS OF AUTONOMIC DURING STROOP CHALLENGE WITH INCIDENCE RATE OF FIRST-ONSET TMD</p> <p>COLOR-WORD STROOP:</p> <p>Mean Resting SBP (mmHg): [n=2,660; 1.12 (0.99-1.26)][†]; [n=2660; 1.08 (0.94-1.22); p=0.280][‡]; [n=2707; 1.09 (0.95-1.24); p=0.200][§];</p> <p>Mean Resting DBP (mmHg): [n=2,648; 1.18 (1.04-1.32)][†]; [n=2660; 1.08 (0.94-1.22); p=0.270][‡]; [n=2707; 1.11 (0.97-1.26); p=0.130][§];</p> <p>Mean Resting MAP (mmHg): [n=2,659; 1.16 (1.03-1.31)][†]; [n=2659; 1.09 (0.95-1.23); p=0.210][‡]; [n=2706; 1.11 (0.97-1.26); p=0.110][§];</p> <p>Mean Resting HR (mmHg): [n=2,656; 1.05 (0.93-1.18)][†]; [n=2656; 1.06 (0.94-1.20); p=0.310][‡]; [n=2707; 1.07 (0.94-1.20); p=0.300][§];</p> <p>Mean Color SBP (mmHg): [n=2,320; 1.07 (0.93-1.21)][†]; [n=2320; 1.01 (0.87-1.16); p=0.890][‡]; [n=2695; 1.02 (0.89-1.16); p=0.710][§];</p> <p>Mean Color DBP (mmHg): [n=2,308; 1.22 (1.07-1.38)][†]; [n=2308; 1.16 (1.00-1.33); p=0.040][‡]; [n=2692; 1.13 (0.99-1.28); p=0.057][§];</p> <p>Mean Color MAP (mmHg): [n=2,313; 1.14 (1.00-1.29)][†]; [n=2313; 1.07 (0.93-1.23); p=0.320][‡]; [n=2694; 1.07 (0.94-1.21); p=0.290][§];</p> <p>Mean Color HR (bpm): [n=2,321; 1.05 (0.92-1.19)][†]; [n=2321; 1.05 (0.91-1.19); p=0.490][‡]; [n=2695; 1.02 (0.90-1.15); p=0.770][§];</p> <p>Mean Δ SBP (mmHg): [n=2,286; 0.92 (0.80-1.05)][†]; [n=2286; 0.91 (0.79-1.04); p=0.170][‡]; [n=2694; 0.92 (0.80-1.04); p=0.190][§];</p> <p>Mean Δ DBP (mmHg): [n=2,267; 1.09 (0.94-1.24)][†]; [n=2267; 1.11 (0.96-1.27); p=0.130][‡]; [n=2691; 1.05 (0.91-1.19); p=0.480][§];</p> <p>Mean Δ MAP (mmHg): [n=2,280; 0.97 (0.84-1.10)][†]; [n=2280; 0.97 (0.84-1.11); p=0.690][‡]; [n=2693; 0.96 (0.83-1.09); p=0.540][§];</p> <p>Mean Δ HR (bpm): [n=2,283; 0.92 (0.80-1.05)][†]; [n=2283; 0.89 (0.77-1.02); p=0.110][‡]; [n=2694; 0.93 (0.81-1.05); p=0.230][§];</p> <p>HR/MAP Ratio (bpm/mmHg): [n=2,312; 0.96 (0.83-1.09)][†]; [n=2312; 0.99 (0.86-1.14); p=0.930][‡]; [n=2694; 0.96 (0.84-1.09); p=0.580][§];</p> <p>Mean HR - HRV (bpm): [n=2,550; 1.01 (0.99-1.01)][†]; [n=2550; 1.01 (0.99-1.01); p=0.350][‡]; [n=2550; 1.00 (0.99-1.01); p=0.450][§];</p> <p>SDNN (ms): [n=2,550; 0.99 (0.98-0.99)][†]; [n=2550; 1.00 (0.99-0.99); p=0.049][‡]; [n=2550; 1.00 (0.99-1.00); p=0.120][§];</p> <p>RMSSD (ms): [n=2,515; 1.00 (0.99-1.00)][†]; [n=2515; 1.00 (0.99-1.00); p=0.350][‡]; [n=2515; 1.00 (0.99-1.00); p=0.430][§];</p> <p>Log TP (ms²): [n=2,544; 0.81 (0.70-0.93)][†]; [n=2544; 0.86 (0.74-0.99); p=0.050][‡]; [n=2544; 0.91 (0.78-1.05); p=0.210][§];</p> <p>Log VLF (ms²): [n=2,547; 0.83 (0.72-0.94)][†]; [n=2547; 0.88 (0.76-1.00); p=0.067][‡]; [n=2547; 0.91 (0.79-1.05); p=0.210][§];</p> <p>Log LF (ms²): [n=2,540; 0.85 (0.73-0.96)][†]; [n=2540; 0.90 (0.78-1.03); p=0.140][‡]; [n=2540; 0.95 (0.82-1.08); p=0.450][§];</p> <p>Log HF (ms²): [n=2,500; 0.90 (0.80-1.01)][†]; [n=2500; 0.94 (0.83-1.05); p=0.310][‡]; [n=2500; 0.96 (0.84-1.07); p=0.450][§];</p> <p>PAIN-AFFECT STROOP:</p>
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				<p> Mean SBP (mmHg): [n=2,249; 1.04 (0.91-1.17)][†]; [n=2249; 0.96 (0.83-1.10); p=0.610][‡]; [n=2691; 1.04 (0.91-1.18); p=0.560][§]; Mean DBP (mmHg): [n=2,237; 1.08 (0.94-1.22)][†]; [n=2237; 0.98 (0.84-1.12); p=0.730][‡]; [n=2688; 1.03 (0.89-1.17); p=0.700][§]; Mean MAP (bpm): [n=2,242; 1.07 (0.94-1.21)][†]; [n=2242; 0.98 (0.85-1.12); p=0.740][‡]; [n=2690; 1.04 (0.91-1.18); p=0.570][§]; Mean HR – cuff (mmHg): [n=2,646; 1.00 (0.88-1.13)][†]; [n=2646; 1.01 (0.88-1.14); p=0.910][‡]; [n=2691; 1.05 (0.92-1.18); p=0.480][§]; Mean Δ SBP (mmHg): [n=2,221; 0.93 (0.81-1.06)][†]; [n=2221; 0.93 (0.81-1.05); p=0.260][‡]; [n=2687; 0.94 (0.82-1.06); p=0.330][§]; Mean Δ DBP (mmHg): [n=2,201; 0.94 (0.82-1.08)][†]; [n=2201; 0.94 (0.81-1.07); p=0.370][‡]; [n=2684; 0.90 (0.78-1.02); p=0.120][§]; Mean Δ MAP (bpm): [n=2,213; 0.91 (0.79-1.04)][†]; [n=2213; 0.90 (0.78-1.03); p=0.150][‡]; [n=2686; 0.89 (0.77-1.01); p=0.085][§]; Mean Δ HR - cuff (bpm/mmHg): [n=2,213; 0.96 (0.84-1.09)][†]; [n=2213; 0.93 (0.81-1.06); p=0.320][‡]; [n=2687; 0.94 (0.82-1.06); p=0.350][§]; HR/MAP Ratio (bpm): [n=2,236; 0.96 (0.84-1.09)][†]; [n=2236; 1.02 (0.88-1.17); p=0.780][‡]; [n=2690; 1.02 (0.89-1.15); p=0.820][§]; Mean HR - ECG (ms): [n=2,545; 1.01 (0.99-1.01)][†]; [n=2545; 1.01 (0.99-1.01); p=0.230][‡]; [n=2545; 1.01 (0.99-1.01); p=0.310][§]; SDNN (ms): [n=2,545; 1.00 (0.99-0.99)][†]; [n=2545; 1.00 (0.99-1.00); p=0.120][‡]; [n=2545; 1.00 (0.99-1.00); p=0.160][§]; RMSSD (ms²): [n=2,506; 1.00 (0.99-1.00)][†]; [n=2506; 1.00 (0.99-1.00); p=0.092][‡]; [n=2506; 1.00 (0.99-1.00); p=0.110][§]; Log TP (ms²): [n=2,541; 0.88 (0.76-1.00)][†]; [n=2541; 0.94 (0.81-1.08); p=0.420][‡]; [n=2541; 0.97 (0.83-1.11); p=0.640][§]; Log VLF (ms²): [n=2,536; 0.94 (0.82-1.07)][†]; [n=2536; 1.00 (0.86-1.14); p=0.970][‡]; [n=2536; 1.00 (0.86-1.14); p=0.960][§]; Log LF (ms²): [n=2,535; 0.87 (0.76-0.99)][†]; [n=2535; 0.94 (0.81-1.07); p=0.360][‡]; [n=2535; 0.97 (0.84-1.10); p=0.650][§]; Log HF (ms²): [n=2,495; 0.92 (0.81-1.02)][†]; [n=2495; 0.94 (0.83-1.06); p=0.330][‡]; [n=2495; 0.96 (0.85-1.08); p=0.510][§]; [†] Adjusted rate for study site; [‡] Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended. STANDARDIZED HAZARD RATIOS FOR RATE OF FIRST-ONSET TMD FROM UNIVARIATE MODELS OF AUTONOMIC PRINCIPAL COMPONENTS Blood Pressure: [n=2,731; HR:1.10 (0.96-1.24); p= 0.160] Stroop heart rate variability: [n=2,731; HR:0.94 (0.82-1.07); p= 0.400] Heart rate: [n=2,731; HR:1.05 (0.92-1.18); p= 0.440] Resting heart rate variability: [n=2,731; HR:0.97 (0.85-1.10); p= 0.670] Orthostatic heart rate variability: [n=2,731; HR:1.05 (0.93-1.18); p= 0.440] TWO-WAY INTERACTIONS BETWEEN AUTONOMIC PRINCIPAL COMPONENTS AND DEMOGRAPHIC CHARACTERISTICS BLOOD PRESSURE: </p>
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				<p>Age (p=0.422): 18-24y [HR:0.98 (0.78-1.22)]; 25-34y [HR: 1.20 (0.95-1.51)]; 35-44y [HR: 1.12 (0.93-1.35)] Gender (p=0.161): Female [HR:1.16 (1.00-1.35)]; Male [HR: 0.97 (0.78-1.20)] Race/Ethnicity (p=0.553): White [HR:1.13 (0.95-1.35)]; Black/African American [HR: 1.05 (0.86-1.28)]; Asian [HR: 1.41 (0.72-2.72)]; Hispanic [HR: 1.23 (0.78-1.93)]; Other [HR: 0.66 (0.31-1.37)]; Lifetime US residency (p=0.904): Yes [HR:1.10 (0.96-1.25)]; No [HR: 1.06 (0.66-1.71)]</p> <p>STROOP HEART RATE VARIABILITY: Age (p=0.645): 18-24y [HR:0.98 (0.80-1.21)]; 25-34y [HR: 0.95 (0.74-1.22)]; 35-44y [HR: 0.85 (0.68-1.07)] Gender (p=0.482): Female [HR:0.89 (0.76-1.05)]; Male [HR: 0.98 (0.79-1.22)] Race/Ethnicity (p=0.693): White [HR:0.99 (0.82-1.18)]; Black/African American [HR: 0.86 (0.71-1.05)]; Asian [HR: 0.64 (0.25-1.63)]; Hispanic [HR: 0.87 (0.50-1.52)]; Other [HR: 1.13 (0.68-1.88)]; Lifetime US residency (p=0.707): Yes [HR:0.92 (0.80-1.05)]; No [HR: 1.01 (0.63-1.63)]</p> <p>HEART RATE: Age (p=0.716): 18-24y [HR:1.01 (0.84-1.23)]; 25-34y [HR: 1.06 (0.85-1.31)]; 35-44y [HR: 1.14 (0.92-1.42)] Gender (p=0.950): Female [HR:1.06 (0.91-1.24)]; Male [HR: 1.07 (0.88-1.30)] Race/Ethnicity (p=0.414): White [HR:1.09 (0.93-1.29)]; Black/African American [HR: 1.00 (0.82-1.23)]; Asian [HR: 1.73 (0.97-3.06)]; Hispanic [HR: 0.93 (0.57-1.49)]; Other [HR: 0.78 (0.31-1.95)]; Lifetime US residency (p=0.435): Yes [HR:1.05 (0.92-1.19)]; No [HR: 1.24 (0.83-1.86)]</p> <p>RESTING HEART RATE VARIABILITY: Age (p=0.217): 18-24y [HR:1.07 (0.87-1.32)]; 25-34y [HR: 0.99 (0.78-1.27)]; 35-44y [HR: 0.82 (0.66-1.02)] Gender (p=0.677): Female [HR:0.94 (0.81-1.10)]; Male [HR: 0.99 (0.80-1.24)] Race/Ethnicity (p=0.407): White [HR:1.04 (0.87-1.24)]; Black/African American [HR: 0.88 (0.71-1.08)]; Asian [HR: 0.61 (0.33-1.14)]; Hispanic [HR: 0.96 (0.58-1.59)]; Other [HR: 1.30 (0.49-3.44)]; Lifetime US residency (p=0.341): Yes [HR:0.94 (0.82-1.08)]; No [HR: 1.18 (0.75-1.87)]</p> <p>ORTHOSTATIC HEART RATE VARIABILITY: Age (p=0.276): 18-24y [HR:0.86 (0.66-1.12)]; 25-34y [HR: 1.04 (0.77-1.41)]; 35-44y [HR: 1.11 (0.95-1.29)] Gender (p=0.357): Female [HR:0.98 (0.81-1.17)]; Male [HR: 1.10 (0.92-1.33)] Race/Ethnicity (p=0.287): White [HR:0.94 (0.75-1.17)]; Black/African American [HR: 1.08 (0.91-1.29)]; Asian [HR: 0.55 (0.23-1.33)]; Hispanic [HR: 1.53 (0.86-2.74)]; Other [HR: 1.31 (0.50-3.46)]; Lifetime US residency (p=0.925): Yes [HR:1.03 (0.89-1.18)]; No [HR: 1.06 (0.62-1.79)]</p> <p>MULTIVARIABLE PROPORTIONAL HAZARDS MODELS OF TIME-TO-EVENT FOR FIRST-ONSET TMD (separate models for each principal component that includes interaction between stratum variable and principal component)</p> <p>HEAT PAIN RATING Age (p=0.791): 18-24 years [1.12 (0.92-1.36)]; 25-34 years [1.03 (0.82-1.30)]; 35-44 years [1.15 (0.92-1.43)] Gender (p=0.544): Female [1.13 (0.97-1.33)]; Male [1.05 (0.85-1.29)]; Race/ethnicity (p=0.746): White [1.18 (0.99-1.42)]; Black/African American [1.03 (0.83-1.27)]; Asian [1.31 (0.66-2.61)]; Hispanic [0.94 (0.59-1.48)]; Other [0.95 (0.46-1.98)] Lifetime us residency (p=0.450): Yes [1.12 (0.98-1.28)]; No/Not stated [0.94 (0.60-1.46)];</p> <p>HEAT PAIN AFTERSENSATIONS AND TOLERANCE Age (p=0.745): 18-24 years [1.02 (0.86-1.21)]; 25-34 years [1.04 (0.85-1.27)]; 35-44 years [1.12 (0.94-1.33)] Gender (p=0.525): Female [1.04 (0.92-1.17)]; Male [1.13 (0.90-1.41)];</p>
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				<p>Race/ethnicity (p=0.880): White [1.07 (0.90-1.27)]; Black/African American [1.08 (0.94-1.25)]; Asian [1.10 (0.67-1.82)]; Hispanic [0.86 (0.56-1.31)]; Other [0.91 (0.35-2.39)]</p> <p>Lifetime us residency (p=0.541): Yes [1.05 (0.94-1.17)]; No/Not stated [1.17 (0.84-1.62)];</p> <p>MECHANICAL CUTANEOUS PAIN SENSITIVITY</p> <p>Age (p=0.493): 18-24 years [0.95 (0.78-1.16)]; 25-34 years [1.13 (0.91-1.40)]; 35-44 years [1.05 (0.83-1.32)]</p> <p>Gender (p=0.427): Female [1.00 (0.86-1.16)]; Male [1.11 (0.89-1.39)];</p> <p>Race/ethnicity (p=0.347): White [1.08 (0.90-1.31)]; Black/African American [0.92 (0.74-1.14)]; Asian [1.22 (0.86-1.72)]; Hispanic [0.95 (0.64-1.40)]; Other [1.54 (0.90-2.64)]</p> <p>Lifetime us residency (p=0.744): Yes [1.02 (0.89-1.17)]; No/Not stated [1.08 (0.79-1.48)];</p> <p>PRESSURE PAIN THRESHOLD (REVERSE CODED)</p> <p>Age (p=0.353): 18-24 years [1.11 (0.91-1.36)]; 25-34 years [1.29 (1.02-1.63)]; 35-44 years [1.02 (0.82-1.28)]</p> <p>Gender (p=0.093): Female [1.03 (0.87-1.22)]; Male [1.29 (1.05-1.59)];</p> <p>Race/ethnicity (p=0.883): White [1.11 (0.92-1.33)]; Black/African American [1.12 (0.92-1.37)]; Asian [1.28 (0.64-2.56)]; Hispanic [1.19 (0.73-1.93)]; Other [1.84 (0.68-4.93)]</p> <p>Lifetime us residency (p=0.314): Yes [1.11 (0.97-1.27)]; No/Not stated [1.42 (0.90-2.24)];</p> <p>HEAT PAIN TEMPORAL SUMMATION</p> <p>Age (p=0.265): 18-24 years [1.18 (0.98-1.43)]; 25-34 years [0.91 (0.72-1.17)]; 35-44 years [1.08 (0.88-1.32)]</p> <p>Gender (p=0.243): Female [1.12 (0.97-1.30)]; Male [0.96 (0.77-1.20)];</p> <p>Race/ethnicity (p=0.092): White [1.15 (0.97-1.36)]; Black/African American [1.08 (0.89-1.32)]; Asian [0.51 (0.25-1.02)]; Hispanic [0.72 (0.43-1.20)]; Other [1.37 (0.72-2.61)]</p> <p>Lifetime us residency (p=0.067): Yes [1.11 (0.98-1.26)]; No/Not stated [0.72 (0.46-1.12)];</p> <p>MULTIVARIABLE PROPORTIONAL HAZARDS MODELS OF TIME-TO-EVENT FOR FIRST-ONSET TMD (separate models for each principal component that includes interaction between stratum variable and principal component)</p> <p>HEAT PAIN RATING</p> <p>Heat pain aftersensations and tolerance (p=0.543): Low [1.01 (0.80-1.28)]; Mid [1.04 (0.82-1.32)]; High [1.18 (0.93-1.51)]</p> <p>Mechanical cutaneous pain sensitivity (p=0.472): Low [1.04 (0.84-1.30)]; Mid [1.18 (0.95-1.47)]; High [0.97 (0.76-1.22)]</p> <p>Pressure pain thresholds – reverse coded (p=0.058): Low [0.89 (0.71-1.11)]; Mid [1.26 (1.03-1.54)]; High [1.14 (0.91-1.43)]</p> <p>Heat pain temporal summation (p=0.281): Low [1.18 (0.98-1.41)]; Mid [1.07 (0.84-1.37)]; High [0.92 (0.70-1.19)]</p> <p>HEAT PAIN AFTERSENSATIONS AND TOLERANCE</p> <p>Heat pain ratings (p=0.676): Low [1.14 (0.89-1.48)]; Mid [1.09 (0.93-1.27)]; High [1.01 (0.85-1.19)]</p> <p>Mechanical cutaneous pain sensitivity (p=0.077): Low [0.92 (0.76-1.13)]; Mid [1.29 (1.04-1.59)]; High [1.07 (0.91-1.25)]</p> <p>Pressure pain thresholds – reverse coded (p=0.663): Low [1.13 (0.96-1.32)]; Mid [1.02 (0.83-1.24)]; High [1.04 (0.86-1.26)]</p> <p>Heat pain temporal summation (p=0.291): Low [1.14 (0.99-1.31)]; Mid [0.92 (0.71-1.19)]; High [1.03 (0.86-1.24)]</p> <p>MECHANICAL CUTANEOUS PAIN SENSITIVITY</p> <p>Heat pain ratings (p=0.736): Low [0.95 (0.71-1.27)]; Mid [1.07 (0.90-1.27)]; High [0.96 (0.77-1.21)]</p>
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					<p>Heat pain aftersensations and tolerance (p=0.744): Low [0.89 (0.66-1.20)]; Mid [1.02 (0.70-1.49)]; High [1.03 (0.89-1.19)]</p> <p>Pressure pain thresholds – reverse coded (p=0.674): Low [1.08 (0.91-1.29)]; Mid [0.96 (0.76-1.22)]; High [0.96 (0.75-1.22)]</p> <p>Heat pain temporal summation (p=0.930): Low [1.04 (0.86-1.26)]; Mid [1.02 (0.82-1.28)]; High [0.96 (0.76-1.21)]</p> <p>PRESSURE PAIN THRESHOLD (REVERSE CODED)</p> <p>Heat pain ratings (p=0.403): Low [1.00 (0.80-1.24)]; Mid [1.14 (0.92-1.41)]; High [1.21 (0.98-1.50)]</p> <p>Heat pain aftersensations and tolerance (p=0.344): Low [1.30 (1.00-1.68)]; Mid [1.09 (0.88-1.35)]; High [1.03 (0.84-1.25)]</p> <p>Mechanical cutaneous pain sensitivity (p=0.445): Low [1.18 (0.96-1.46)]; Mid [1.17 (0.94-1.46)]; High [0.99 (0.79-1.23)]</p> <p>Heat pain temporal summation (p=0.308): Low [1.20 (0.96-1.50)]; Mid [1.18 (0.95-1.47)]; High [0.97 (0.79-1.19)]</p> <p>HEAT PAIN TEMPORAL SUMMATION</p> <p>Heat pain ratings (p=0.002): Low [1.54 (1.21-1.94)]; Mid [0.96 (0.79-1.17)]; High [0.95 (0.77-1.17)]</p> <p>Heat pain aftersensations and tolerance (p=0.342): Low [0.94 (0.76-1.15)]; Mid [1.15 (0.90-1.46)]; High [1.11 (0.92-1.34)]</p> <p>Mechanical cutaneous pain sensitivity (p=0.821): Low [1.10 (0.91-1.33)]; Mid [1.07 (0.84-1.35)]; High [1.00 (0.82-1.23)]</p> <p>Pressure pain thresholds – reverse coded (p=0.279): Low [1.22 (0.99-1.50)]; Mid [0.98 (0.79-1.20)]; High [1.03 (0.84-1.27)]</p> <p>STANDARDIZED HAZARD RATIOS FOR RATE OF FIRST-ONSET TMD FROM UNIVARIATE AND MULTIVARIABLE MODELS OF QST PRINCIPAL COMPONENTS:</p> <p>UNIVARIATE ASSOCIATIONS:</p> <p>Heat pain ratings [n= 2737; HR: 1.09 (0.95- 1.24); p= 0.180];</p> <p>Heat pain aftersensation and tolerance [n= 2737; HR: 1.06 (0.95- 1.18); p= 0.290];</p> <p>Mechanical cutaneous pain sensitivity [n= 2737; HR: 1.06 (0.93- 1.20); p= 0.370];</p> <p>Pressure pain thresholds (reverse coded) [n= 2737; HR: 1.09 (0.95- 1.24); p= 0.180];</p> <p>Heat pain temporal summation [n= 2737; HR: 1.11 (0.98- 1.25); p= 0.088]</p> <p>MULTIVARIABLE ASSOCIATIONS:</p> <p>Heat pain ratings [n= 2737; HR: 1.12 (0.98- 1.28); p= 0.101];</p> <p>Heat pain aftersensation and tolerance [n= 2737; HR: 1.06 (0.95- 1.18); p= 0.292];</p> <p>Mechanical cutaneous pain sensitivity [n= 2737; HR: 1.02 (0.90- 1.16); p= 0.736];</p> <p>Pressure pain thresholds (reverse coded) [n= 2737; HR: 1.14 (1.00- 1.31); p= 0.051];</p> <p>Heat pain temporal summation [n= 2737; HR: 1.06 (0.94- 1.19); p= 0.357]</p> <p>COX REGRESSION MODEL OF BASELINE CHARACTERISTICS OF PARTICIPANTS WITH SIGNS/SYMPTOMS OF OBSTRUCTIVE SLEEP APNEA (OSA) AND HAZARD RATIOS FOR FIRST-ONSET TMD</p> <p>Likelihood of OSA: Low: [n=2,445; ref.]; High [n=159; HR: 2.29 (1.54-3.42)]</p> <p>Gender: Male: [n=1,057; ref.]; Female [n=1,547; HR: 1.32 (1.02-1.72)]</p> <p>Age group (years): 18-24: [n=1,370; ref.]; 25-34 [n=702; HR: 1.55 (1.14-2.09)]; 35-44 [n=532; HR: 1.81 (1.29-2.54)]</p> <p>Race/Ethnicity: White: [n=1,397; ref.]; African American [n=700; HR: 1.58 (1.16-2.15)]; Hispanic: [n=249; HR: 0.35 (0.17-0.71)]; Asian [n=172; HR: 0.96 (0.59-1.57)]; Other/Multiple/not stated: [n=86; HR:0.65 (0.27-1.60)]</p>
Sanders et al. (a), USA (2013)	5.2 years (median follow-up=2.8 years)	Enrolled: 3,258 Excluded: missing follow-up data (n=521), missing OSA classification (n=1), or	RDC/TMD	Signs/Symptoms of Obstructive Sleep Apnea (OSA): - Pittsburgh Sleep Quality Index (PSQI); Three questions from PSQI about loud snoring, trouble staying awake, and witnessed apnea. In addition, the medical	

		<p>missing covariates (n=132) Final Sample: 2,604/ 18-44 y.o</p>		<p>history about hypertension was noted. Together, these 4-item about OSA screening questionnaire called STOP. Autonomic Parameters: arterial blood pressure, heart rate during 20 min of rest (by blood pressure cuff), average resting heart rate variability (3-lead electrocardiogram); Covariates: Gender, age, race and ethnicity (White, African American, Asian, Hispanic). Body mass index (BMI= Height/Weight); Smoking history (Never smoked, former smoker, or current smoker); Subjective sleep quality (PSQI-item #6: During the past month, how would you rate your sleep quality overall?)</p>	<p>Mean Arterial Pressure (mmHg): < 75: [n=435; ref.]; 75 - <80: [n=597; HR: 1.18 (0.73-1.58)]; 80- <85: [n=672; HR: 1.39 (0.93-1.98)]; >85: [n=900; HR: 1.62 (1.07-2.21)]; Heart Rate (beats per min): < 55: [n=609; ref.]; 55 - 61.9: [n=675; HR: 1.07 (0.75-1.83)]; 62- 68.9: [n=628; HR: 1.36 (0.91-2.13)]; >69: [n=692; HR: 1.54 (1.09-2.42)]; Body Mass Index (kg/m²) Underweight/Normal (< 25): [n=1,409; ref.]; Overweight (25- <30): [n=712; HR: 0.87 (0.64-1.20)]; Obese (≥ 30): [n=483; HR: 1.68 (1.24-2.27)]; Smoking History: Never: [n=1,973; ref.]; Former: [n=224; HR: 2.33 (1.62-3.34)]; Current: [n=407; HR: 2.15 (1.54-2.99)]; PSQI subjective sleep quality: Very good: [n=759; ref.]; Fairly good: [n=1,444; HR: 1.07 (0.79-1.46)]; Fairly bad and very bad: [n=401; HR: 2.11 (1.49-3.00)];</p> <p>MULTIVARIABLE MODEL SHOWING HAZARD RATIOS FOR INCIDENT FIRST-ONSET TMD High Likelihood of OSA: Model 1 [1.90 (1.26 - 2.87)]; Model 2 [1.85 (1.22-2.79)]; Model 3 [1.73 (1.14 - 2.62)]; Gender, Female (ref.= Male): Model 1 [1.30 (1.00 - 1.69)]; Model 2 [1.29 (0.99-1.69)]; Model 3 [1.31 (1.00 - 1.72)]; Age in Years (decades): Model 1 [1.21 (1.01 - 1.44)]; Model 2 [1.17 (0.98-1.41)]; [1.05 (0.86 - 1.27)]; Race/ethnicity African American (ref.= White): Model 1 [1.38 (1.01 - 1.90)]; Model 2 [1.29 (0.93-1.79)]; Model 3 [1.32 (0.94 - 1.85)]; Race/ethnicity Hispanic (ref.= White): Model 1 [0.37 (0.18 - 0.76)]; Model 2 [0.37 (0.18-0.76)]; Model 3 [0.39 (0.19 - 0.80)]; Race/ethnicity Asian (ref.= White): Model 1 [0.99 (0.61 - 1.62)]; Model 2 [0.98 (0.60-1.60)]; Model 3 [0.96 (0.59 - 1.57)]; Race/ethnicity Other (ref.= White): Model 1 [0.62 (0.25 - 1.52)]; Model 2 [0.61 (0.25-1.50)]; Model 3 [0.66 (0.27 - 1.62)]; Average resting hearth rate (bpm/10): Model 2 [1.07 (0.94-1.21)]; Model 3 [1.04 (0.92 - 1.18)]; Average resting mean arterial blood pressure(mmHg/10): Model 2 [1.11 (0.95-1.29)]; Model 3 [1.08 (0.92 - 1.25)]; BMI overweight (ref. = underweight/normal): Model 3 [0.78 (0.56 - 1.08)]; BMI obese (ref. = underweight/normal): Model 3 [1.21 (0.87 - 1.70)]; Smoking history - Former (ref.= Never): Model 3 [2.20 (1.51 - 3.21)]; Smoking history - Current (ref.= Never): Model 3 [1.81 (1.27 - 2.57)];</p> <p>Model 1: Adjusted for study site and demographic characteristics; Model 2: adds autonomic parameters; Model 3: adds BMI and smoking history</p>
<p>Sanders et al. (b), USA (2013)</p>	<p>5.2 years (median follow-up=2.8 years)</p>	<p>Enrolled: 3,200 Final Sample: 2,722/18-44 y.o</p>	<p>RDC/TMD</p>	<p>Pain disorders: Headache (International Headache Society - ICHD-2): probable tension-type, tension-type and migraine headache, Past or current low back pain (constancy of pain symptoms, frequency of episodes in the last 12 months, duration of episodes) Irritable bowel syndrome (IBS): assessment based on</p>	<p>UNIVARIATE ASSOCIATIONS BETWEEN BASELINE PAIN DISORDERS AS ETIOLOGIC RISK FACTORS MEASURED CATEGORICALLY</p> <p>Current low back pain (p<0.001): No (ref.; n=2,379); Yes [n=341; 2.02 (1.49-2.72)][†]; [n=341; 1.91 (1.41-2.58)][‡]; [n=341; 1.89 (1.38-2.57)][§]; Low back pain episodes in last year (p<0.001): ≥11: [n=236; 2.04 (1.38-2.99)][†]; [n=236; 1.92 (1.30-2.83)][‡]; [n=236; 2.01 (1.35-3.00)][§]; 5-10: [n=293; 2.40 (1.71-3.36)][†]; [n=293; 2.33 (1.65-3.27)][‡]; [n=293; 2.20 (1.54-3.14)][§]; 2-4: [n=592; 1.20 (0.85-1.67)][†]; [n=592; 1.16 (0.82-1.61)][‡]; [n=592; 1.24 (0.87-1.74)][§]; 1: [n=237; 1.04 (0.63-1.69)][†]; [n=237; 0.98 (0.59-1.59)][‡]; [n=237; 0.99 (0.60-1.63)][§]; ROME IBS Classification (p<0.001): No (ref.; n=2,632); Yes: [n=74; 3.00 (1.85-4.84)][†]; [n=74; 2.84 (1.75-4.62)][‡]; [n=74; 2.27 (1.35-3.79)][§]; Count of 10 IBS symptoms (p<0.001):</p>

			<p>Rome III criteria - questions about bowel movements and the experience of discomfort or pain in the abdomen that lasted at least 1 day a week during previous 3 weeks</p> <p>Genital symptoms: presence of genital pain on contact but absence of genital itching during the last 3 months</p> <p>Health status:</p> <p>Overall health (excellent, good, fair or poor): Short Form 12 Health Survey (SF-12v2)</p> <p>Conditions: Endocrine (diabetes, hypothyroid disease, hyperthyroid disease); Cardiovascular (mitral valve prolapse; high blood pressure; angina; heart attack; heart failure; pacemaker/defibrillator; stroke), Hematologic (anemia; bleeding disorder; leukemia), Neural and sensory (earache; ringing in ears; hearing loss; fainting or dizzy spells; epilepsy; seizures; or convulsion; psychiatric treatment); Respiratory (sinus trouble; allergies or hives; asthma; tuberculosis; breathing difficulties); Sleep apnea; history of being hospitalized for any surgical operation or serious illness.</p> <p>Cigarette smoking:</p> <p>Nonsmokers (fewer than 100 cigarettes in their lives), current or former smoker</p> <p>Pittsburgh Sleep Quality Index (PSQI): sleep quality and disturbances over a 1-month reference period</p> <p>Anthropometric Status:</p>	<p>0 (ref.; n=1,507); ≥ 6: [n=182; 2.95 (2.00-4.34)][†]; [n=182; 2.66 (1.79-3.93)][‡]; [n=182; 2.35 (1.57-3.50)][§]; 3-5: [n=446; 1.89 (1.37-2.60)][†]; [n=446; 1.77 (1.28-2.44)][‡]; [n=446; 1.68 (1.20-2.33)][§]; 1-2: [n=574; 1.37 (0.98-1.89)][†]; [n=574; 1.26 (0.90-1.74)][‡]; [n=574; 1.15 (0.81-1.62)][§];</p> <p>Genital pain symptoms(p<0.001):</p> <p>No (ref.; n=2,570); Yes: [n=84; 3.06 (1.93-4.84)][†]; [n=84; 2.78 (1.74-4.44)][‡]; [n=84; 2.31 (1.41-3.77)][§];</p> <p>Number of headache types in last year(p<0.001):</p> <p>0 (ref.; n=696); ≥ 3: [n=496; 2.23 (1.55-3.19)][†]; [n=496; 2.05 (1.42-2.95)][‡]; [n=496; 1.94 (1.33-2.81)][§]; 2: [n=681; 1.37 (0.94-1.98)][†]; [n=681; 1.25 (0.85-1.82)][‡]; [n=681; 1.29 (0.88-1.89)][§]; 1: [n=836; 0.98 (0.67-1.43)][†]; [n=836; 1.00 (0.68-1.47)][‡]; [n=836; 0.97 (0.66-1.42)][§];</p> <p>Headache intensity at baseline (p=0.004):</p> <p>None (ref. n= 696); Mostly severe: [n=218; 2.33 (1.51-3.57)][†]; [n=218; 2.07 (1.34-3.18)][‡]; [n=218; 2.13 (1.37-3.28)][§]; Mostly Mild: [n=1,732; 1.37 (0.99-1.88)][†]; [n=1,732; 1.32 (0.95-1.82)][‡]; [n=1,732; 1.26 (0.90-1.75)][§];</p> <p>Migraine headache(s) (p=0.57):</p> <p>No (ref.; n=1,827); Yes: [n=894; 1.32 (1.03-1.70)][†]; [n=894; 1.28 (0.99-1.64)][‡]; [n=894; 1.26 (0.97-1.62)][§];</p> <p>Tension-type headache(s) (p=0.004):</p> <p>No (ref.; n=2,515); Yes: [n=206; 1.75 (1.20-2.53)][†]; [n=206; 1.74 (1.18-2.53)][‡]; [n=206; 1.69 (1.12-2.53)][§];</p> <p>Probable tension-type headache(s) (p=0.860):</p> <p>No (ref.; n=1,450); Yes: [n=1,271; 1.00 (0.77-1.27)][†]; [n=1,271; 0.98 (0.76-1.25)][‡]; [n=1,271; 1.01 (0.77-1.29)][§];</p> <p>UNIVARIATE ASSOCIATIONS BETWEEN BASELINE CLINICAL CONDITIONS AND CONDITIONS AS ETIOLOGIC RISK FACTORS MEASURED CATEGORICALLY</p> <p>Count of 20 comorbidities (p<0.001):</p> <p>Zero (ref.; n=1,773); ≥ 2: [n=424; 3.20 (2.41-4.23)][†]; [n=424; 2.87 (2.15-3.81)]; p<0.001[‡]; [n=424; 2.70 (2.02-3.59)][§]; 1: [n=505; 1.40 (0.99-1.95)][†]; [n=505; 1.39 (0.98-1.94)][‡]; [n=505; 1.42 (1.00-2.01)][§];</p> <p>History of 3 endocrine conditions (p=0.56):</p> <p>Zero (ref.; n=2,659) ≥ 1: [n= 78; 1.82 (1.01-3.25)][†]; [n= 78; 1.78 (0.98-3.20)][‡]; [n=78; 1.41 (0.75-2.64)][§];</p> <p>History of 7 cardiovascular conditions (p=0.710):</p> <p>Zero (ref.; n=2,598) ≥ 1: [n= 139; 1.47 (0.90-2.37)][†]; [n= 139; 1.10 (0.67-1.80)][‡]; [n=139; 1.05 (0.63-1.73)][§];</p> <p>History of 4 hematologic conditions (p=0.520):</p> <p>Zero (ref.; n=2,512) ≥ 1: [n= 225; 1.29 (0.85-1.94)][†]; [n= 225; 1.15 (0.75-1.75)][‡]; [n=225; 1.11 (0.71-1.72)][§];</p> <p>History of 4 neurosensory conditions (p=0.003):</p> <p>Zero (ref.; n=2,110) ≥ 1: [n= 626; 1.52 (1.16-1.98)][†]; [n= 626; 1.51 (1.15-1.97)][‡]; [n=626; 1.52 (1.15-2.00)][§];</p> <p>History of 5 respiratory conditions (p=0.002):</p> <p>Zero (ref.; n=1,805) ≥ 1: [n= 931; 1.50 (1.17-1.92)][†]; [n= 931; 1.50 (1.17-1.92)][‡]; [n=931; 1.44 (1.11-1.85)][§];</p> <p>Sleep apnea (p=0.760):</p>
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			<p>Body Mass Index (BMI= weight/height²) 2D:4D ratio: Length of the second digit [2D] and the fourth digit [4D]. High 2D:4D is a marker of greater estrogen relative to testosterone exposure toward the end of the first trimester in utero</p>	<p>Zero (ref.; n=2,678) ≥1: [n= 47; 1.37 (0.60-3.09)][†]; [n= 47; 1.13 (0.50-2.56)][‡]; [n=47; 1.15 (0.51-2.56)][§]; Past use of 11 medications (p=0.009): Zero (ref.; n=560) ≥3: [n= 427; 1.41 (0.96-2.05)][†]; [n= 427; 1.35 (0.90-2.00)][‡]; [n=427; 1.52 (1.00-2.28)][§]; 2: [n= 954; 0.82 (0.57-1.16)][†]; [n= 954; 0.82 (0.56-1.18)][‡]; [n=954; 0.91 (0.61-1.33)][§]; 1: [n= 790; 0.76 (0.52-1.09)][†]; [n= 790; 0.76 (0.52-0.09)][‡]; [n=790; 0.87 (0.59-1.25)][§]; Cigarette smoking history (p<0.001): Never (ref.; n= 2,058); Current: [n= 415; 2.07 (1.48-2.88)][†]; [n= 415; 1.74 (1.22-2.47)][‡]; [n=415; 1.61 (1.13-2.30)][§]; Former: [n= 210; 2.26 (1.54-3.30)][†]; [n= 210; 2.12 (1.43-3.14)][‡]; [n=210; 1.86 (1.23-2.79)][§]; Ever hospitalized for surgery/serious illness (p=0.720): No (ref.; n=1,714) Yes: [n= 1,010; 1.07 (0.82-1.37)][†]; [n= 1,010; 0.95 (0.73-1.23)][‡]; [n=1,010; 1.07 (0.82-1.39)][§]; Self-rated general health (p=0.000): Excellent (ref.; n= 1,185); Fair or poor: [n= 127; 2.93 (1.86-4.60)][†]; [n= 127; 2.55 (1.60-4.05)][‡]; [n=127; 2.60 (1.64-4.11)][§]; Good: [n= 1,410; 1.40 (1.07-1.82)][†]; [n= 1,410; 1.35 (1.03-1.76)][‡]; [n=1,410; 1.37 (1.04-1.80)][§];</p> <p style="text-align: center;">UNIVARIATE ASSOCIATIONS BETWEEN CONTINUOUS MEASURES OF ETIOLOGIC RISK FACTORS REPORTING AND INCIDENCE OF FIRST-ONSET TMD</p> <p>BMI (kg/m²): [n=2,705; 1.23 (1.11-1.37)][†]; [n= 2,705; 1.13 (1.00-1.26); p=0.038][‡]; [n=2,705; 1.09 (0.97-1.23); p=0.140][§]; AVERAGE OF RD2:RD4 RATIO LEFT AND RIGHT HANDS [n=2,723; 1.18 (1.04-1.33)][†]; [n= 2,723; 1.21 (1.06-1.37); p=0.003][‡]; [n=2,723; 1.15 (1.01-1.30); p=0.026][§]; PSQI GLOBAL SCORE (0-21) [n=2,559; 1.47 (1.32-1.63)][†]; [n= 2,559; 1.40 (1.25-1.55); p<0.001][‡]; [n=2,723; 1.32 (1.18-1.47); p<0.001][§]; SF-12V2 PHYSICAL COMPONENT SUMMARY [n=2,597; 0.83 (0.73-0.93)][†]; [n= 2,597; 0.86 (0.76-0.97); p=0.016][‡]; [n=2,597; 0.85 (0.74-0.95); p=0.008][§]; SF-12V2 MENTAL COMPONENT SUMMARY [n=2,597; 0.71 (0.64-0.79)][†]; [n= 2,597; 0.71 (0.63-0.79); p<0.001][‡]; [n=2,597; 0.74 (0.66-0.82); p<0.001][§];</p> <p>[†]Adjusted rate for study site; [‡]Adjusted rates for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p style="text-align: center;">MULTIVARIABLE-ADJUSTED ASSOCIATIONS IN DEVELOPMENT OF FIRST-ONSET TMD (all adjusted for study site)</p> <p>Female gender (ref.: male): Model 1: 1.37 (1.04-1.80); Model 2: 1.28 (0.96-1.69); Model 3: 1.22 (0.91-1.62); Age (in decades): Model 1: 1.20 (1.01-1.43); Model 2: 1.17 (0.98-1.39); Model 3: 1.07 (0.88-1.28); Asian race (ref.: white): Model 1: 0.66 (0.31-1.40); Model 2: 0.67 (0.32-1.43); Model 3: 0.71 (0.33-1.50); Black race (ref.: white): Model 1: 1.33 (0.97-1.84); Model 2: 1.36 (0.99-1.88); Model 3: 1.47 (1.05-2.05); Hispanic ethnicity (ref.: white): Model 1: 1.17 (0.63-2.14); Model 2: 1.17 (0.63-2.14); Model 3: 1.22 (0.66-2.26); Others race (ref.: white): Model 1: 0.96 (0.45-2.07); Model 2: 1.04 (0.48-2.25); Model 3: 1.08 (0.49-2.34) Nonlife U.S residence (ref.: lifetime): Model 1: 0.46 (0.27-0.78); Model 2: 0.47 (0.28-0.79); Model 3: 0.51 (0.30-0.86) Current low back pain (ref.: no): Model 2: 1.80 (1.30-2.48); Model 3: 1.50 (1.08-2.10)</p>
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<p>Slade et al., USA (2013)</p>	<p>5.2 years (median follow-up=2.8 years)</p>	<p>Screened: 3,258 Drop-outs: 5 ineligibles during post enrollment audits, 521 returned no quarterly screening questionnaire. Final sample: 2,737 Data Imputed: 243 who reported TMD symptoms but did not receive follow-up examination/18 to 44 y.o</p>	<p>RDC/TMD</p>	<p>Sociodemographic characteristics: Age, gender, race/ethnicity, Lifetime U.S Residence (yes or not); Health Insurance Coverage, first language spoken (English or not English), Marital status (never married, married/cohabiting or separated/divorced/widowed);</p> <p>Socioeconomic status: Level of schooling (high school or less, some college, college graduate, postgraduate), Family annual household income in USD (≤USD 20,000; USD 20,000 to 39,999; USD 40,000 to 79,999; ≥80,000), Rating of satisfaction with financial situation, Ratings of satisfaction with material standards in life (Low, Mid, Not stated, High);</p>	<p>Rome IBS classification (ref.: no): Model 2: 1.92 (1.12-3.30); Model 3: 1.62 (0.94-2.81) Genital symptoms (ref.: no): Model 2: 1.92 (1.15-3.19); Model 3: 1.75 (1.04-2.93) Genital symptoms not stated (ref.: no): Model 2: 1.84 (1.04-3.27); Model 3: 1.68 (0.94-3.00) Tension-type headache (ref.: no): Model 2: 1.57 (1.04-2.35); Model 3: 1.46 (0.97-2.20) Neurologic condition (ref.: no): Model 3: 1.25 (0.93-1.68) Respiratory condition (ref.: no): Model 3: 1.28 (0.98-1.67) PSQI (z-score): Model 3: 1.18 (1.05-1.33) RD2:RD4 ratio average both hands (z-score): Model 3: 1.15 (1.00-1.31) Current smoker (ref.: never smoked): Model 3: 1.55 (1.08-2.25) Former smoker (ref.: never smoked): Model 3: 1.84 (1.22-2.78) Smoked status unstated (ref.: never smoked): Model 3: 1.39 (0.63-3.04) Model 1: Adjusted for study site + demographics; Model 2: Adjusted for study site + Pain Disorders; Model 3: Adjusted for study site + other health conditions;</p> <p>UNIVARIATE ASSOCIATIONS: SOCIODEMOGRAPHIC CHARACTERISTICS AND RATE OF FIRST-ONSET TMD</p> <p>Age- years: 18-24 (ref.; n=1,421); 25-34 [n=736; HR: 1.54 (1.14-2.07)][†]; [n=736; HR: 1.61 (1.19-2.18)][‡]; [HR: 1.38 (1.01- 1.88); p=0.040][§]; 35-44 [n=580; HR: 1.87 (1.34-2.59)][†]; [n=580; HR: 1.66 (1.18-2.33); p=0.002][‡]; [HR: 1.46 (1.03-2.04); p=0.030][§];</p> <p>Gender: Male (ref.; n=1107); Female [n=1630; HR: 1.28 (0.99-1.64)][†]; [n=1630; HR: 1.22 (0.94-1.57); p=0.130][‡]; [HR: 1.30 (0.99-1.69); p=0.051][§];</p> <p>Race/ethnicity: White (ref.; n=1448); Black/African American [n=766; HR: 1.52 (1.11- 2.06)][†]; [n=766; HR: 1.42 (1.04-1.93); p=0.089][‡]; [HR: 1.37 (1.00-1.87); p= 0.048][§]; Asian [n= 256; HR: 0.38 (0.19-0.74)][†]; [n= 256; HR: 0.69 (0.33-1.42)][‡]; [HR: 0.64 (0.29-1.35); p=0.240][§]; Hispanic [n= 178; HR: 0.95 (0.58-1.55)][†]; [n= 178; HR: 1.39 (0.83-2.31)][‡]; [HR: 1.15 (0.62-2.11); p=0.650][§]; Other or unstated [n=89; HR: 0.88 (0.41-1.89)][†]; [n=89; HR: 0.99 (0.46-2.13)][‡]; [HR: 0.96 (0.44-2.06); p=0.920][§];</p> <p>Lifetime U.S. Resident: Yes (ref.; n=2236); No [n= 453; HR: 0.34 (0.21-0.55)][†]; [n= 453; HR: 0.37 (0.21-0.62); p=0.001][‡]; [HR: 0.44 (0.25-0.75); p= 0.003][§]; Not stated [n=48; HR: 0.62 (0.19-1.92)][†]; [n=48; HR: 0.66 (0.20-2.07)][‡]; [HR: 0.91 (0.32-2.57); p=0.86][§];</p> <p>First Language spoken: English (ref.; n= 2345); Not English [n=372; HR: 1.62 (0.41-0.94)][†]; [n=372; HR: 1.67 (0.88-3.12); p=260][‡]; [HR: 1.53 (0.77-2.99); p=0.220][§]; Not Stated [n=20; HR: 0.56 (0.7-3.98)][†]; [n=20; HR: 2.05 (0.26-15.74)][‡]; [HR: 2.24 (0.34-14.60); p=0.400][§];</p> <p>Marital Status: Never Married (ref.; n=1963); Married, cohabiting [n= 539; HR: 1.30 (0.96-1.74)][†]; [n= 539; HR: 1.20 (0.86-1.67); p=570][‡]; [HR: 1.13 (0.80-1.58); p=0.470][§]; Separated, divorced, widowed [n= 193; HR: 1.71 (1.13-2.59)][†]; [n= 193; HR: 1.25 (0.78-1.98)][‡]; [HR: 1.33 (0.85-2.08); p= 0.210][§]; Not stated [n= 42; HR: 0.61 (0.15-2.47)][†]; [n= 42; HR: 0.67 (0.16-2.71)][‡]; [HR: 0.74 (0.19-2.81); p=0.660][§];</p> <p>SOCIOECONOMIC CHARACTERISTICS AND TMD INCIDENCE OF FIRST-ONSET TMD</p> <p>Highest level of schooling: Postgraduate (ref.; n=414);</p>
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				<p>High school or less [n=433; HR: 1.68 (1.05-2.65)][†]; [n=433; HR: 1.40 (0.85-2.29); p=0.150][‡]; [HR: 1.36 (0.83-2.22); p=0.220][§]; Some college [n=1105; HR: 1.27 (0.85-1.87)][†]; [n=1105; HR: 1.29 (0.85-1.94)][‡]; [HR: 1.22 (0.80-1.84); p=0.350][§]; College graduate [n= 750; HR: 1.02 (0.66-1.55)][†]; [n= 750; HR: 1.07 (0.69-1.64)][‡]; [HR: 1.08 (0.70-1.66); p=0.710][§]; Not stated [n=35; HR: 2.58 (0.99-6.73)][†]; [n=35; HR: 3.20 (1.19-8.55)][‡]; [HR: 3.40 (1.33-8.65); p=0.10][§]; Family annual household income (USD 1000s): ≥80 (ref.; n=624); ≤20 [n= 421; HR: 1.39 (0.94-2.03)][†]; [n= 421; HR: 1.22 (0.81-1.82); p=660][‡]; [HR: 1.25 (0.82-1.88); p=0.290][§]; 20 -<40 [n= 493; HR: 1.18 (0.79-1.75)][†]; [n= 493; HR: 1.06 (0.70-1.58)][‡]; [HR: 1.04 (0.67-1.58); p =0.870][§]; 40-<80 [n= 583; HR: 1.06 (0.73-1.54)][†]; [n=583; HR: 0.98 (0.67-1.42)][‡]; [HR: 0.91 (0.61-1.36); p= 0.650][§]; Not stated [n=616; HR: 0.86 (0.58-1.27)][†]; [n=616; HR: 0.90 (0.60-1.34)][‡]; [HR: 0.93 (0.61-1.40); p=0.720][§]; Rating of satisfaction with financial situation: High (7-10 ref.; n=838); Low (0-3) [n=825; HR: 1.54 (1.11-2.13)][†]; [n=825; HR: 1.40 (1.00-1.94); p=0.88][‡]; [HR: 1.38 (0.97-1.96); p=0.69][§]; Mid (4-6) [n=1040; HR: 1.22 (0.89-1.67)][†]; [n=1040; HR: 1.18 (0.86-1.61)][‡]; [HR: 1.24 (0.89-1.72); p=0.200][§]; Not stated [n=34; HR: 1.93 (0.69-5.36)][†]; [n=34; HR: 2.85 (1.00-8.05)][‡]; [HR: 3.13 (1.15-8.49); p=0.025][§]; Ratings of satisfaction with material standards in life: High (9-10 ref.; n=692); Low (0-5) [n=751; HR: 2.09 (1.43-3.04)][†]; [n=751; HR: 1.98 (1.35-2.91); p=0.002][‡]; [HR: 1.71 (1.16-2.51); p=0.006][§]; Mid (6-8) [n= 1247; HR: 1.68 (1.18-2.37)][†]; [n= 1247; HR: 1.69 (1.18-2.38)][‡]; [HR: 1.45 (1.02-2.05); p=0.036][§]; Not stated [n= 47; HR: 2.33 (0.91-5.98)][†]; [n= 47; HR: 3.20 (1.22-8.34)][‡]; [HR: 2.96 (1.17-7.40); p=0.021][§]; Covered by health insurance: Yes (ref.; n=2202) No [n=445; HR: 0.96 (0.67-1.37)][†]; [n=445; HR: 0.93 (0.64-1.33); p=0.750][‡]; [HR: 0.97 (0.67-1.39); p= 0.890][§]; Not stated [n=90; HR: 1.18 (0.59-2.33)][†]; [n=90; HR: 1.23 (0.61-2.45)][‡]; [HR: 1.16 (0.56-2.37); p=0.680][§];</p> <p>[†]Adjusted rate using Cox proportional regression controlling for study site; [‡] As footnote [†] with additional adjustment for other demographic characteristics (unless they were already estimated as the risk factor), age, gender, race/ethnicity and lifetime U.S residency; [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p>MULTIVARIABLE ASSOCIATION OF SOCIODEMOGRAPHIC CHARACTERISTICS WITH TMD INCIDENCE (HAZARD RATIO 95% CI): Age (Decades): [HR: 1.18 (1.00-1.40)]; Gender: Male (ref.); Female [HR: 1.34 (1.03-1.75)]; Race: White (ref.); Black/African American [HR: 1.27 (0.92-1.74)]; Asian [HR: 0.59 (0.28-1.26)]; Hispanic [HR: 1.08 (0.59-1.98)]; Other [HR: 0.92 (0.43-1.98)]; Lifetime Residence: Yes (ref.); No [HR: 0.49 (0.30-0.81)]; Rating of satisfaction with material standards of life: High ([9-10]; ref.); Low (0-5) [HR: 1.71 (1.17-2.52)]; Mid (6-8) [HR: 1.45 (1.02-2.06)]; Not stated [HR: 2.96 (1.18-7.41)]</p> <p>MULTIVARIABLE POISSON REGRESSION MODEL BETWEEN PAIRS:</p> <p>Age x Race/Ethnicity (p=0.055):</p>
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					<p>White: [HR: 1.03 (0.81-1.31)]; Black: [HR: 1.43 (1.09-1.87)]; Asian [HR: 2.65 (1.08- 6.50)]; Hispanic [HR: 1.50 (0.52-4.34)]; Other/unstated: [HR: 0.82 (0.32-2.07)]</p> <p>Age x Gender (p=0.79): Female: [HR: 1.17 (0.96-1.43)]; Male: [HR:1.28 (0.98-1.68)]</p> <p>Gender x Race (p=0.76): White: [HR: 1.49 (1.02-2.17)]; Black: [HR:1.01 (0.66-1.56)]; Asian: [HR: 2.07 (0.39-4.94)]; Hispanic: [HR: 1.40 (0.39-4.94)]; Other/unstated [HR:1.40 (0.31-6.26)]</p> <p>Gender x Lifetime U.S residence (p=0.95) Race/Ethnicity x Lifetime U.S residence (p=0.25) Age x Lifetime U.S residence (p=0.88)</p>
Smith et al., USA (2013)	5.2 years (median follow-up=2.8 years)	Recruited = 3,263 Final Sample: 2,737 (1,630 F/1,107 M/ 18-44y.o)	RDC/TMD	3295 single nucleotide polymorphisms (SNPs) representing 358 genes involved in systems relevant to pain perception such as nociceptive transmission, inflammation, and mood and affect. Twenty-three genes were selected as "First tier candidate genes.	<p>MULTIVARIABLE PROPORTIONAL HAZARDS MODELS OF TIME-TO-EVENT FOR FIRST-ONSET TMD WITH RECRUITMENT SITE AND RACE AS COVARIATES (SNP/GENE/Chromosome/Minor Allele):</p> <p>rs12415832/VEGF/6/C: MODE OF INHERITANCE: Additive [HR:0.70; p=n.s.*]; Dominant [HR:0.62; p= n.s.*]; Recessive [HR: 0.68; p= n.s.*]; SEX: Females [HR: 0.79; p= n.s.*]; Males [HR: 0.56; p= n.s.*]; RACE: Whites [HR: 0.78; p= n.s.*]; Blacks [HR:0.60; p= n.s.*];</p> <p>rs1563826/ERBB2/17/G: MODE OF INHERITANCE: Additive [HR:1.38; p= n.s.*]; Dominant [HR:1.57; p= n.s.*]; Recessive [HR: 1.47; p= n.s.*]; SEX: Females [HR: 1.39; p= n.s.*]; Males [HR: 1.34; p= n.s.*]; RACE: Whites [HR: 1.37; p= n.s.*]; Blacks [HR:1.35; p= n.s.*];</p> <p>rs1076292/EPHB2/1/C: MODE OF INHERITANCE: Additive [HR:0.73; p= n.s.*]; Dominant [HR:0.73; p= n.s.*]; Recessive [HR: 0.55; p= n.s.*]; SEX: Females [HR: 0.75; p= n.s.*]; Males [HR: 0.70; p= n.s.*]; RACE: Whites [HR: 0.73; p= n.s.*]; Blacks [HR:0.73; p= n.s.*];</p> <p>rs2072100/CCL5/17/A: MODE OF INHERITANCE: Additive [HR:1.47; p= n.s.*]; Dominant [HR:1.57; p= n.s.*]; Recessive [HR: 1.48; p= n.s.*]; SEX: Females [HR: 1.49; p= n.s.*]; Males [HR: 1.42; p= n.s.*]; RACE: Whites [HR: 1.27; p= n.s.*]; Blacks [HR:1.76; p= n.s.*];</p> <p>rs728273/ERBB2/17/A: MODE OF INHERITANCE: Additive [HR:1.35; p= n.s.*]; Dominant [HR:1.53; p= n.s.*]; Recessive [HR: 1.38; p= n.s.*]; SEX: Females [HR: 1.35; p= n.s.*]; Males [HR: 1.33; p= n.s.*]; RACE: Whites [HR: 1.31; p= n.s.*]; Blacks [HR:1.41; p= n.s.*];</p> <p>rs3782221/MC4R/18/C: MODE OF INHERITANCE: Additive [HR:1.70; p= n.s.*]; Dominant [HR:1.63; p= n.s.*]; Recessive [HR: 4.43; p= n.s.*]; SEX: Females [HR: 1.66; p= n.s.*]; Males [HR: 1.71; p= n.s.*]; RACE: Whites [HR: 1.37; p= n.s.*]; Blacks [HR:1.59; p= n.s.*];</p> <p>rs2367707/DRD2/11/G: MODE OF INHERITANCE: Additive [HR:1.37; p= n.s.*]; Dominant [HR:1.25; p= n.s.*]; Recessive [HR: 1.88; p= n.s.*]; SEX: Females [HR: 1.43; p= n.s.*]; Males [HR: 1.28; p= n.s.*]; RACE: Whites [HR: 1.45; p= n.s.*]; Blacks [HR:1.33; p= n.s.*];</p>

				<p>rs1448239/INADL/1/G: MODE OF INHERITANCE: Additive [HR:1.33; p= n.s.*]; Dominant [HR:1.39; p= n.s.*]; Recessive [HR: 1.54; p= n.s.*]; SEX: Females [HR: 1.32; p= n.s.*]; Males [HR: 1.32; p= n.s.*]; RACE: Whites [HR: 1.18; p= n.s.*]; Blacks [HR:1.49; p= n.s.*];</p> <p>rs255097/ERBB2/17/C: MODE OF INHERITANCE: Additive [HR:1.32; p= n.s.*]; Dominant [HR:1.54; p= n.s.*]; Recessive [HR: 1.30; p= n.s.*]; SEX: Females [HR: 1.32; p= n.s.*]; Males [HR: 1.32; p= n.s.*]; RACE: Whites [HR: 1.32; p= n.s.*]; Blacks [HR:1.31; p= n.s.*];</p> <p>rs6967334/HIF1A/14/T: MODE OF INHERITANCE: Additive [HR:0.69; p= n.s.*]; Dominant [HR:0.65; p= n.s.*]; Recessive [HR: 0.62; p= n.s.*]; SEX: Females [HR: 0.65; p= n.s.*]; Males [HR: 0.78; p= n.s.*]; RACE: Whites [HR: 0.68; p= n.s.*]; Blacks [HR:0.68; p= n.s.*];</p> <p>rs3804452/INADL/1/C: MODE OF INHERITANCE: Additive [HR:0.72; p= n.s.*]; Dominant [HR:0.68; p= n.s.*]; Recessive [HR: 0.59; p= n.s.*]; SEX: Females [HR: 0.76; p= n.s.*]; Males [HR: 0.66; p= n.s.*]; RACE: Whites [HR: 0.77; p= n.s.*]; Blacks [HR:0.64; p= n.s.*];</p> <p>rs3782202/ITGAM/16/T: MODE OF INHERITANCE: Additive [HR:0.72; p= n.s.*]; Dominant [HR: 0.67; p= n.s.*]; Recessive [HR: 0.64; p= n.s.*]; SEX: Females [HR: 0.75; p= n.s.*]; Males [HR: 0.68; p= n.s.*]; RACE: Whites [HR: 0.81; p= n.s.*]; Blacks [HR:0.61; p= n.s.*];</p> <p>Rs4883544/DRD2/11/C: MODE OF INHERITANCE: Additive [HR:1.32; p= n.s.*]; Dominant [HR:1.34; p= n.s.*]; Recessive [HR: 1.62; p= n.s.*]; SEX: Females [HR: 1.38; p= n.s.*]; Males [HR: 1.22; p= n.s.*]; RACE: Whites [HR: 1.50; p= n.s.*]; Blacks [HR:1.25; p= n.s.*];</p> <p>rs1550798/SCN2A/2/G: MODE OF INHERITANCE: Additive [HR:0.72; p= n.s.*]; Dominant [HR:0.69; p= n.s.*]; Recessive [HR: 0.61; p= n.s.*]; SEX: Females [HR: 0.70; p= n.s.*]; Males [HR: 0.77; p= n.s.*]; RACE: Whites [HR: 0.71; p= n.s.*]; Blacks [HR:0.76; p= n.s.*];</p> <p>Rs7800170/P2RY6/11/T: MODE OF INHERITANCE: Additive [HR:0.68; p= n.s.*]; Dominant [HR:0.69; p= n.s.*]; Recessive [HR: 0.31; p= n.s.*]; SEX: Females [HR: 0.66; p= n.s.*]; Males [HR: 0.72; p= n.s.*]; RACE: Whites [HR: 0.73; p= n.s.*]; Blacks [HR:0.64; p= n.s.*];</p> <p>Rs7687621/ITGAM/16/T: MODE OF INHERITANCE: Additive [HR:0.73; p= n.s.*]; Dominant [HR:0.68; p= n.s.*]; Recessive [HR: 0.64; p= n.s.*]; SEX: Females [HR: 0.74; p= n.s.*]; Males [HR: 0.72; p= n.s.*]; RACE: Whites [HR: 0.80; p= n.s.*]; Blacks [HR:0.65; p= n.s.*];</p> <p>Rs2363561/GRIN2B/12/C: MODE OF INHERITANCE: Additive [HR:0.74; p= n.s.*]; Dominant [HR:0.71; p= n.s.*]; Recessive [HR: 0.62; p= n.s.*];</p>
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<p>Orbach et al., USA (2014)</p>	<p>5.2 years (median follow-up=2.8 years)</p>	<p>Recruited = 7,404; Final Sample= 2,737/18-44y.o</p>	<p>RDC/TMD</p>	<p>Self-reported putative etiologic factors: Lifetime history of regional trauma: Check-list of five potentially traumatic experiences, injury by yawning and history of orthodontic procedures Parafunctional behaviors: Oral Behaviors Checklist = 21 activities such as clenching, chewing gum and holding objects between the teeth Clinical Status by Self-Report: Pain and Disability: Grade Chronic Pain Scale (GCPS); Modifying Factors (5-item checklist and ordinal summary measure): Limitations in using the jaw: Jaw Functional Limitation Scale - JFLS; Checklist of six “non-specific orofacial symptoms” in the preceding month (jaw stiffness, cramping, fatigue, pressure, soreness, and ache);</p>	<p>SEX: Females [HR: 0.76; p= n.s.*]; Males [HR: 0.71; p= n.s.*]; RACE: Whites [HR: 0.67; p= n.s.*]; Blacks [HR:0.93; p= n.s.*]; Rs3787535/CCL5/17/C: MODE OF INHERITANCE: Additive [HR:1.38; p= n.s.*]; Dominant [HR:1.46; p= n.s.*]; Recessive [HR: 1.46; p= n.s.*]; SEX: Females [HR: 1.41; p= n.s.*]; Males [HR: 1.36; p= n.s.*]; RACE: Whites [HR: 1.18; p= n.s.*]; Blacks [HR:1.63; p= n.s.*]; Rs1557545/CRHR2/7/A: MODE OF INHERITANCE: Additive [HR:0.76; p= n.s.*]; Dominant [HR:0.70; p= n.s.*]; Recessive [HR: 0.71; p= n.s.*]; SEX: Females [HR: 0.78; p= n.s.*]; Males [HR: 0.75; p= n.s.*]; RACE: Whites [HR: 0.76; p= n.s.*]; Blacks [HR:0.58; p= n.s.*]; Rs6685551/INADL/1/T: MODE OF INHERITANCE: Additive [HR:2.24; p= n.s.*]; Dominant [HR:2.27; p= n.s.*]; Recessive [HR: 6.23; p= n.s.*]; SEX: Females [HR: 3.78; p= n.s.*]; Males [HR: 0.90; p= n.s.*]; RACE: Whites [HR: NA; p=NA]; Blacks [HR:2.21; p= n.s.*]; *not significant considering authors’ statistical corrections UNIVARIATE ASSOCIATIONS: BETWEEN TRAUMA, ORTHODONTICS, AND PARAFUNCTIONS AS ETIOLOGIC RISK FACTORS <u>Lifetime history of external injury to jaw:</u> No (ref.; n= 2363); Yes (n=224): [HR: 1.22 (0.80-1.83)][†]; [HR: 1.29 (0.85-1.95); p=0.23][‡]; [HR: 1.08 (0.68-1.70); p=0.75][§]; <u>Lifetime history of jaw injury due to yawning:</u> No (ref.; n= 2652); Yes (n=75): [HR: 1.07 (0.50-2.31)][†]; [HR: 1.09 (0.51-2.31); p=0.83][‡]; [HR: 1.07 (0.47-2.42); p=0.87][§]; <u>Lifetime history of jaw injury due to prolonged opening:</u> No (ref.; n= 2668); Yes (n=59): [HR: 1.78 (0.94-3.35)][†]; [HR 1.94 (1.02-3.67); p=0.04][‡]; [HR: 1.63 (0.81-3.24); p=0.17][§]; <u>Ever had orthodontic procedures:</u> No (ref.; n= 1489); Yes (n=1227): [HR: 0.79 (0.61-1.02)][†]; [HR: 0.85 (0.64-1.11); p=0.25][‡]; [HR: 0.94 (0.70-1.24); p=0.65][§]; <u>Oral behaviors checklist sum score:</u> 0-16 (ref.; n= 934); 17-24 (n=923): [HR: 1.11 (0.80-1.53)][†]; [HR: 1.13 (0.81-1.56)][‡]; [HR: 1.14 (0.80-1.59)][§]; 25-62 (n=757): [HR: 1.71 (1.25-2.33)][†]; [HR: 1.75 (1.28-2.39); p<0.001][‡]; [HR: 1.75 (1.27-2.40); p<0.001][§]; BETWEEN SELF-REPORTED PAIN-RELATED DISABILITY, FACTORS THAT MODIFY PAIN, AND NON-PAIN CHARACTERISTICS AS ETIOLOGIC RISK FACTORS <u>Facial graded chronic pain status:</u> 0 (ref.; n=2414); 1 (ref.; n=252): [HR: 1.73 (1.23-2.43)][†]; [HR: 1.74 (1.23-2.45)][‡]; [HR: 1.68 (1.18-2.37); p=0.003][§]; 2-4 (ref.; n=20): [HR: 4.40 (1.90-10.14)][†]; [HR: 4.05 (1.74-9.39); p<0.001][‡]; [HR: 3.43 (1.48-7.91); p=0.004][§]; <u>Number of activities that modified facial pain last month:</u> 0-1 (ref.; n=42); 2-3 (ref.; n=29): [HR: 0.47 (0.08-2.60)][†]; [HR: 0.49 (0.08-2.69)][‡]; [HR: 0.30 (0.03-2.71); p=0.280][§]; 4-5 (ref.; n=15): [HR: 1.71 (0.42-6.88)][†]; [HR: 3.75 (0.76-18.24); p=0.890][‡]; [HR: 2.65 (0.59-11.76); p=0.200][§]; <u>Number of non-specific orofacial symptoms:</u></p>
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			<p>TMJ clicking and locking: past month and period prior to the past month</p> <p>Clinical Status by Examination: Jaw mobility: pain-free opening, maximum unassisted opening, maximum assisted opening, left lateral excursion, right lateral excursion and protrusion; TMJ noises (crepitus, click during opening and closing), Palpation Pain: positive and negative report of pain Tooth wear: visual signs of facets representing at least 2mm in length of surface wear at opposing tooth edges were recorded bilaterally from the incisor, cuspid, and pre-molar teeth</p>	<p>0 (ref.; n=2226); 1-2 (ref.; n=383): [HR: 2.01 (1.49-2.71)][†]; [HR: 1.98 (1.46-2.67)][†]; [HR: 1.96 (1.44-2.65); p<0.001][§]; 3 or more (ref.; n=119): [HR: 2.97 (1.96-1.47)][†]; [HR: 2.89 (1.91-4.35); p<0.001][†]; [HR: 2.43 (1.57-3.74); p<0.001][§];</p> <p>SELF-REPORTED PAIN AND FUNCTIONAL LIMITATION OF THE JAW MEASURED AS CONTINUOUS MEASURES OF ETIOLOGIC RISK FACTORS</p> <p>Facial characteristics pain intensity: [n=2708; HR: 1.20 (1.10-1.30)][†]; [n=2708; HR: 1.18 (1.08-1.27); p<0.001][‡]; [n=2708; HR: 1.15 (1.05-1.25); p<0.001][§]; Facial pain interference: [n=2707; HR: 1.11 (1.02-1.20); p=0.043][†]; [n=2707; HR: 1.09 (1.00-1.18); p=0.043][‡]; [n=2707; HR: 1.08 (0.99-1.16); p=0.071][§]; Number Days when efficiency dropped below 50%: [n=398; HR: 1.21 (1.08-1.36)][†]; [n=398; HR: 1.23 (1.08-1.38); p=0.001][‡]; [n=398; HR: 1.24 (1.09-1.40); p=0.008][§]; JFLs: Chewing limitation: [n=2372; HR: 1.06 (0.94-1.18)][†]; [n=2372; HR: 1.05 (0.94-1.18); p=0.320][‡]; [n=2683; HR: 1.04 (0.92-1.16); p=0.560][§]; JFLs: Opening limitation: [n=2591; HR: 1.05 (0.94-1.16)][†]; [n=2591; HR: 1.05 (0.94-1.17); p=0.330][‡]; [n=2678; HR: 1.04 (0.93-1.15); p=0.460][§]; JFLs: Verbal & emotional expression limitation: [n=2531; HR: 1.02 (0.90-1.14)][†]; [n=2531; HR: 1.01 (0.89-1.13); p=0.850][‡]; [n=2678; HR: 1.02 (0.91-1.14); p=0.690][§]; JFLs: Combined global measure: [n=2229; HR: 1.05 (0.94-1.16)][†]; [n=2229; HR: 1.05 (0.94-1.17); p=0.350][‡]; [n=2674; HR: 1.04 (0.92-1.15); p=0.520][§];</p> <p>SELF-REPORTED JAW CLICKING AND LOCKING</p> <p>TMJ noises in last month: 0 (n=2151; ref.); 1 or more: [n=546; HR: 1.47 (1.11-1.93)][†]; [n=546; HR: 1.58 (1.19-2.08); p=0.001][‡]; [n=546; HR: 1.61 (1.21-2.13); p<0.001][§]; Pain with TMJ noises in last month: No (n=2645; ref.); Yes: [n=45; HR: 1.87 (0.91-3.79)][†]; [n=45; HR: 1.97 (0.96-4.00); p=0.062][‡]; [n=45; HR: 1.95 (0.96-3.96); p=0.064][§]; TMJ noises before last month: 0 (n=2099; ref.); 1 or more: [n=599; HR: 1.56 (1.19-2.04)][†]; [n=599; HR: 1.69 (1.28-2.22); p<0.001][‡]; [n=599; HR: 1.66 (1.25-2.19); p<0.001][§]; In last month, could not open mouth wide for any reason: No (n=2648; ref.); Yes: [n=60; HR: 2.71 (1.62-4.51)][†]; [n=60; HR: 2.66 (1.58-4.44); p<0.001][‡]; [n=599; HR: 2.46 (1.42-4.24); p=0.001][§]; Prior to one month ago, could not open mouth wide for any reason: No (n=2533; ref.); Yes: [n=172; HR: 1.61 (1.07-2.42)][†]; [n=172; HR: 1.67 (1.10-2.51); p=0.014][‡]; [n=172; HR: 1.59 (1.03-2.45); p=0.035][§]; In the last month, could not close jaw from wide-open position: No (n=2654; ref.); Yes: [n=51; HR: 1.53 (0.72-3.25)][†]; [n=51; HR: 1.55 (0.72-3.28); p=0.260][‡]; [n=51; HR: 1.52 (0.69-3.32); p=0.290][§]; Prior to one month ago, could not close jaw from wide-open position: No (n=2600; ref.); Yes: [n=115; HR: 1.38 (0.80-2.36)][†]; [n=115; HR: 1.39 (0.81-2.38); p=0.230][‡]; [n=115; HR: 1.40 (0.81-2.41); p=0.220][§];</p>
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					<p>JAW MOBILITY AND BODY PALPATION SCORES MEASURED AS CONTINUOUS MEASURES OF ETIOLOGIC RISK FACTORS REPORTING:</p> <p>Pain-free jaw opening (n=2714): [HR: 0.97 (0.85-1.09)][†]; [HR: 0.96 (0.84-1.09); p=0.560][‡]; [HR:0.96 (0.84-1.10); p=0.560][§];</p> <p>Maximum unassisted jaw opening (n=2714): [HR: 1.00 (0.88-1.13)][†]; [HR: 1.03 (0.90-1.17); p=0.650][‡]; [HR: 1.03 (0.90-1.18); p=0.700][§];</p> <p>Maximum assisted jaw opening (un-terminated) (n=2107): [HR: 1.00 (0.86-1.15)][†]; [HR: 0.99 (0.84-1.15); p=0.870][‡]; [HR: 0.99 (0.84-1.16); p=0.820][§];</p> <p>Maximum assisted jaw opening (terminated) (n=596): [HR: 0.93 (0.73-1.18)][†]; [HR: 1.03 (0.78-1.35); p=0.810][‡]; [HR: 1.10 (0.82-1.46); p=0.540][§];</p> <p>Number of neck sites tender to palpation (n=2736): [HR: 1.14 (1.02-1.25)][†]; [HR: 1.14 (1.02-1.26); p=0.016][‡]; [HR: 1.13 (1.01-1.26); p=0.024][§];</p> <p>Number of body sites tender to palpation (n=2737): [HR: 1.17 (1.04-1.31)][†]; [HR: 1.16 (1.02-1.30); p=0.015][‡]; [HR: 1.17 (1.03-1.33); p=0.011][§];</p> <p>PAIN WITH OPENING, TMJ SOUNDS, AND BRUXOFACETS AS ETIOLOGIC FACTORS</p> <p><u>Pain on unassisted opening:</u> 0 (n=1703; ref.); 1 or more: [n=959; HR: 1.43 (1.10-1.84)][†]; [n=959; HR: 1.51 (1.16-1.96); p=0.002][‡]; [n=959; HR: 1.56 (1.19-2.04); p=0.001][§];</p> <p><u>Pain on assisted opening (un-terminated):</u> 0 (n=1387; ref.); 1 or more: [n=677; HR: 1.28 (0.94-1.73)][†]; [n=677; HR: 1.40 (1.03-1.91); p=0.031][‡]; [n=677; HR: 1.47 (1.07-2.00); p=0.015][§];</p> <p><u>Pain on assisted opening (terminated):</u> 0 (n=121; ref.); 1 or more: [n=469; HR: 1.66 (0.80-3.42)][†]; [n=469; HR: 1.65 (0.80-3.39); p=0.170][‡]; [n=469; HR: 1.58 (0.76-3.26); p=0.220][§];</p> <p><u>TMJ palpation sounds (right):</u> 0 (n=1834; ref.); 1 or more: [n=865; HR: 1.13 (0.86-1.47)][†]; [n=865; HR: 1.13 (0.86-1.47); p=0.360][‡]; [n=865; HR: 1.28 (0.96-1.68); p=0.083][§];</p> <p><u>TMJ palpation sounds (left):</u> 0 (n=1784; ref.); 1 or more: [n=924; HR: 1.00 (0.76-1.30)][†]; [n=924; HR: 0.99 (0.75-1.29); p=0.940][‡]; [n=924; HR: 1.01 (0.75-1.33); p=0.950][§];</p> <p><u>Number of locations with tooth wear (facets):</u> 0 (n=338; ref.); 1 or more: [n=2359; HR: 0.95 (0.66-1.36)][†]; [n=2359; HR: 0.97 (0.67-1.39); p=0.880][‡]; [n=2359; HR: 1.11 (0.75-1.62); p=0.600][§];</p> <p>CLINICAL PALPATION CHARACTERISTICS OF MASTICATORY MUSCLES AS ETIOLOGIC RISK FACTORS</p> <p>RIGHT SIDE:</p> <p>Temporalis: 0 (n=2019; ref.); 1 or more: [n=718; HR: 1.64 (1.26-2.12)][†]; [n=718; HR: 1.61 (1.23-2.08); p<0.001][‡]; [n=718; HR: 1.55 (1.19-2.02); p=0.001][§];</p> <p>Masseter: 0 (n=1918; ref.); 1 or more: [n=819; HR: 1.68 (1.30-2.16)][†]; [n=819; HR: 1.68 (1.30-2.17); p<0.001][‡]; [n=819; HR: 1.63 (1.25-2.10); p<0.001][§];</p> <p>Posterior mandibular and submandibular: 0 (n=2344; ref.); 1 or more: [n=393; HR: 1.44 (1.02-2.05)][†]; [n=393; HR: 1.46 (1.03-2.05); p=0.030][‡]; [n=393; HR: 1.36 (0.97-1.90); p=0.074][§];</p>
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				<p>Lateral pterygoid area: 0 (n=2213; ref.); 1 or more: [n=522; HR: 1.51 (1.13-2.01)][†]; [n=522; HR: 1.50 (1.12-1.99); p=0.030][‡]; [n=522; HR: 1.50 (1.12-2.00); p=0.006][§];</p> <p>TMJ: 0 (n=2457; ref.); 1 or more: [n=280; HR: 1.56 (1.12-2.17)][†]; [n=280; HR: 1.57 (1.12-2.18); p=0.008][‡]; [n=280; HR: 1.36 (0.94-1.94); p=0.094][§];</p> <p>LEFT SIDE:</p> <p>Temporalis: 0 (n=2157; ref.); 1 or more: [n=580; HR: 1.59 (1.21-2.08)][†]; [n=580; HR: 1.56 (1.18-2.04); p=0.002][‡]; [n=580; HR: 1.49 (1.11-1.97); p=0.006][§];</p> <p>Masseter: 0 (n=2029; ref.); 1 or more: [n=708; HR: 1.59 (1.22-2.06)][†]; [n=708; HR: 1.59 (1.22-2.06); p<0.001][‡]; [n=708; HR: 1.53 (1.17-1.99); p=0.002][§];</p> <p>Posterior mandibular and submandibular: 0 (n=2362; ref.); 1 or more: [n=375; HR: 1.41 (1.01-1.97)][†]; [n=375; HR: 1.41 (1.00-1.97); p=0.046][‡]; [n=375; HR: 1.36 (0.96-1.89); p=0.075][§];</p> <p>Lateral pterygoid area: 0 (n=2238; ref.); 1 or more: [n=496; HR: 1.40 (1.04-1.87)][†]; [n=496; HR: 1.39 (1.03-1.86); p=0.027][‡]; [n=496; HR: 1.38 (1.01-1.86); p=0.041][§];</p> <p>TMJ: 0 (n=2429; ref.); 1 or more: [n=308; HR: 1.43 (1.03-1.98)][†]; [n=308; HR: 1.48 (1.06-2.05); p=0.019][‡]; [n=308; HR: 1.36 (0.95-1.93); p=0.087][§];</p> <p>[†]Adjusted rate using Poisson regression controlling for study site; [‡]Adjusted rates using Poisson regression controlling for Study Site+ Demographics (age, gender, race/ethnicity and lifetime); [§]As [‡] with Imputed TMD rates for subjects who were no examined as intended.</p> <p>MULTIVARIATE-ADJUSTED ASSOCIATIONS IN DEVELOPMENT OF FIRST-ONSET TMD</p> <p>Gender (ref.: Male):</p> <p>Female: Model 1 [1.29 (0.98-1.70); p=0.069]; Model 2 [1.29 (0.98-1.71); p=0.067]; Model 3 [1.31 (0.99-1.73); p=0.058]; Model 4 [1.29 (0.97-1.70); p=0.078]</p> <p>Age (Decades):</p> <p>Model 1 [1.28 (1.08-1.53); p=0.005]; Model 2 [1.27 (1.07-1.51); p=0.007]; Model 3 [1.25 (1.05-1.49); p=0.011]; Model 4 [1.29 (1.08-1.54); p=0.005]</p> <p>Race (ref.: White):</p> <p>Asian: Model 1 [0.70 (0.33-1.49); p=0.350]; Model 2 [0.72 (0.34-1.54); p=0.400]; Model 3 [0.70 (0.33-1.50); p=0.360]; Model 4 [0.70 (0.33-1.49); p=0.350];</p> <p>Black: Model 1 [1.37 (1.00-1.89); p=0.053]; Model 2 [1.45 (1.05-2.02); p=0.026]; Model 3 [1.38 (0.97-1.95); p=0.070]; Model 4 [1.37 (0.97-1.93); p=0.078];</p> <p>Hispanic: Model 1 [1.21 (0.66-2.25); p=0.540]; Model 2 [1.34 (0.72-2.48); p=0.360]; Model 3 [1.32 (0.71-2.44); p=0.380]; Model 4 [1.30 (0.70-2.42); p=0.400];</p> <p>Other: Model 1 [1.09 (0.51-2.35); p=0.820]; Model 2 [1.12 (0.52-2.42); p=0.770]; Model 3 [1.10 (0.51-2.38); p=0.810]; Model 4 [1.10 (0.51-2.37); p=0.810];</p> <p>Lifetime U.S residence (ref.: Yes):</p> <p>No or Unstated: Model 1 [0.48 (0.29-0.80); p=0.005]; Model 2 [0.48 (0.29-0.79); p=0.004]; Model 3 [0.47 (0.28-0.78); p=0.003]; Model 4 [0.49 (0.29-0.81); p=0.006]</p> <p>Jaw mobility pain (z-score): Model 1 [1.23 (1.05-1.43); p=0.010]; Model 2 [1.20 (1.02-1.40); p=0.024]; Model 3 [1.19 (1.02-1.40); p=0.025]; Model 4 [1.20 (1.03-1.40); p=0.021]</p> <p>Palpation pain (z-score): Model 1 [1.19 (1.02-1.38); p=0.027]; Model 2 [1.15 (0.98-1.34); p=0.078]; Model 3 [1.15 (0.98-1.35); p=0.078]; Model 4 [1.14 (0.98-1.34); p=0.096]</p> <p>TMJ function by history (z-score): Model 2 [1.09 (0.96-1.23); p=0.170]; Model 3 [1.09 (0.96-1.24); p=0.170]; Model 4 [1.07 (0.94-1.21); p=0.290]</p> <p>Facial pain CPI (ref.: 0):</p>
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					<p>0 (ref.); >0: Model 2 [1.18 (0.81-1.70); p=0.390]; Model 3 [1.18 (0.81-1.72); p=0.380]; Model 4 [1.14 (0.78-1.66); p=0.500]; JFIs global measure: 0 (ref.); >0: Model 2 [1.11 (0.83-1.48); p=0.500]; Model 3 [1.10 (0.82-1.47); p=0.530]; Model 4 [1.08 (0.81-1.45); p=0.590]; Number of non-specific orofacial symptoms: 0 (ref.); 1-2: Model 2 [1.63 (1.17-2.26); p=0.004]; Model 3 [1.63 (1.17-2.27); p=0.004]; Model 4 [1.55 (1.11-2.17); p=0.010]; ≥3: Model 2 [1.92 (1.18-3.13); p=0.009]; Model 3 [1.93 (1.19-3.15); p=0.008]; Model 4 [1.77 (1.08-2.92); p=0.024]; History of jaw injury (Any response from external injury, jaw injury due to yawning, and jaw injury due to prolonged opening): No (ref.); Yes: Model 3 [1.00 (0.68-1.47); p=0.990]; Model 4 [0.98 (0.67-1.45); p=0.940] History of orthodontic procedures: No (ref.); Yes: Model 3 [0.86 (0.65-1.15); p=0.310]; Model 4 [0.87 (0.65-1.16); p=0.340] OBC sum score (z-score): Model 4 [1.14 (1.00-1.31); p=0.052]</p> <p>Ps.: All models are adjusted for study site, Model 1 adds Pain during examination, Model 2 adds other symptoms, Model 3 adds trauma history, model 4 adds oral behavior</p>
Sanders et al., USA (2016)	5.2 years (median follow-up=2.8 years)	Baseline: 3,263 Follow-up: 2,453 Final sample: 2,410/ 18-44y.o at baseline	RDC/TMD	<p>Subjective sleep: Habitual sleep quality and sleep disturbance (19-item Pittsburgh Sleep Quality Index (PSQI), Quarterly Health Update (QHUs) with Sleep Quality Numeric Rating Scale (NRS), Covariates: study site, age, sex, race and ethnicity, non-painful facial symptoms, score for the Pennebaker Inventory of Limbic Languidness (PILL), Score for the Perceived Stress Scale (PSS) and a checklist of 20 comorbid health conditions)</p>	<p>ASSOCIATION BETWEEN SUBJECTIVE SLEEP QUALITY AND RISK OF FIRST-ONSET TMD</p> <p>Baseline PSQI score per 2.8 units: 1.04 (0.90- 1.20) Any non-pain facial symptom at baseline (ref.=None): 1.74 (1.28-2.38) *; Any comorbid health condition at baseline (ref.=None): 1.64 (1.21-2.21) *; Baseline PSS score per 6.4 units: 1.16 (1.00-1.35); Baseline PILL score per 21.0 units: 1.16 (1.01-1.35) *; Time-varying covariate of sleep quality rating >6 (ref.=0-6): 1.23 (1.07-1.42) *; Ps: all models are adjusted for study site, age, sex and race/ethnicity</p> <p>MULTIVARIATE ASSOCIATION BETWEEN SUBJECTIVE SLEEP QUALITY AND RISK OF FIRST-ONSET TMD</p> <p>Model 1: PSQI at baseline Baseline PSQI score >5 (ref.=0-5): 2.04 (1.55-2.70) *</p> <p>Model 2: adds four covariates (perceived stress, somatic awareness, comorbid conditions and non-pain facial symptoms) Baseline PSQI score >5 (ref.=0-5): 1.39 (1.02- 1.90) * Any non-pain facial symptom at baseline (ref.=None): 1.67 (1.22-2.27) *; Any comorbid health condition at baseline (ref.=None): 1.65 (1.22-2.23) *; Baseline PSS score per 6.4 units: 1.14 (0.98-1.33); Baseline PILL score per 21.0 units: 1.16 (1.01-1.34) *;</p> <p>Model 3: adds time-varying sleep quality Baseline PSQI score >5 (ref.=0-5): 1.28 (0.94- 1.75) Any non-pain facial symptom at baseline (ref.=None): 1.69 (1.23-2.30) *; Any comorbid health condition at baseline (ref.=None): 1.63 (1.20-2.19) *; Baseline PSS score per 6.4 units: 1.14 (0.98-1.32); Baseline PILL score per 21.0 units: 1.14 (0.99-1.32); Time-varying covariate of sleep quality rating >6 (ref.=0-6): 1.73 (1.29-2.32) *;</p>

					The symbol * means statistically significant predictor of first-onset TMD.
Sanders et al., USA (2017)	5.2 years (median follow-up=2.8 years)	Baseline: 3,263 Final sample:2,722/ 18-44y.o	RDC/TMD	<p>Habitual sleep quality and disturbance: 19-item Pittsburgh Sleep Quality Index (PSQI) at baseline</p> <p>Sleep quality over the preceding 3 months: Sleep Quality Numeric Rating Scale (SQ-NRS) in each quarterly follow-up,</p> <p>Perceived stress: 10-item Perceived Stress Scale (PSS) and Quarterly Health Update questionnaires</p> <p>*Poor sleep quality (PSQI global score at baseline) was dichotomized at ≤ 5 = good sleep quality versus >5 = poor sleep quality.</p>	<p>SITE-ADJUSTED DESCRIPTION OF SUBJECTIVE SLEEP QUALITY AND PERCEIVED STRESS AT BASELINE FOR ALL PARTICIPANTS, OPPERA PROSPECTIVE COHORT STUDY, 2006 TO 2011 (N=2,722)</p> <p>Sex: Male (n=1,099; ref.); Female: [n=1,623; HR: 1.28 (0.99-1.65)]</p> <p>Age (years): 18-24 [n=1,416; ref.]; 25-34 [n=732; HR: 1.54 (1.15-2.08)]; 35-44 [n=574; HR: 1.86 (1.34-2.59)];</p> <p>Race/Ethnicity: White [n=1,441; ref.]; African American [n=758; HR: 1.54 (1.13-2.08)]; Asian [n=256; HR: 0.39 (0.20-0.76)]; Hispanic [n=178; HR: 0.96 (0.59-1.55)]; Other [n=89; HR: 0.90 (0.42-1.94)]</p> <p>PSQI (dichotomized): Good Sleep (≤ 5) [n=1,839; ref.]; Poor Sleep (>5) [n=829; HR: 2.22 (1.73-2.85);</p> <p>Perceived stress (dichotomized): Low (≤ 17) [n=1,869; ref.]; High (>17) [n=987; HR: 1.69(1.32-2.17)]</p> <p>ASSOCIATION OF PERCEIVED STRESS AND FIRST-ONSET PAINFUL TMD MEDIATED BY POOR SLEEP QUALITY ADJUSTED FOR STUDY SITE, AGE, SEX, AND RACE/ETHNICITY (Values are covariate-adjusted HRs and 95% CL -n=2,650)</p> <p>Perceived Stress (predictor) / SQ-NRS (Mediator): Direct Effect [HR: 1.49 (1.25-1.80)]; Indirect Effect [HR: 1.15 (0.96-1.38)]; Total Effect [HR: 1.70 (1.42-2.04)]</p> <p>SQ-NRS (Predictor) / Perceived Stress (Mediator): Direct Effect [HR: 1.62 (1.32-1.99)]; Indirect Effect [HR: 1.29 (1.06-1.58)]; Total Effect [HR: 2.10 (1.76-2.50)]</p>
Tchivileva et al., USA (2017)	5.2 years (median follow-up=2.8 years)	Enrolled: 3,263; Final sample: 2,410/ 18-44y.o	RDC/TMD	<p>Comprehensive Pain Symptom Questionnaire (CSPQ): details of up to three different types of headaches (location, intensity, characteristics, duration, frequency, and aggravating factors associated with each type of headache)</p> <p>Classification: International Classification of Headache Disorders (ICDH-3)</p>	<p>MULTIVARIABLE-ADJUSTED (FOR STUDY SITE, GENDER, RACE/ETHNICITY AND AGE) COX REGRESSION MODELS OF TIME-CONSTANT AND TIME-VARYING INFLUENCES OF HEADACHE ON HAZARD OF FIRST-ONSET TMD (N = 2,410)</p> <p>Headache type at baseline (p<0.0001): No and unclassified headache (ref.) Tensional Type Headache (TTH): [HR: 1.20 (0.87-1.66)] Migraine [HR: 1.67 (1.06-2.62)] Mixed Headache [HR: 4.11 (1.47-11.46)]</p> <p>Headache frequency at baseline (number per month) (p<0.0001): 0 Headache (ref.) 1 headache [HR: 1.11 (0.76-1.63)]; 2 headaches [HR: 1.57 (1.04-2.37)];</p>

				<p>Self-report Headaches: No headaches: no headache in preceding year Unclassified headache: reported headache in the last year but did not provide a complete set of data necessary for classification in the other types or did not meet the minimum ICDH criteria for even probable TTH or migraine Probable tension-type headache (TTH): all but one ICDH for TTH were satisfied Definite TTH: all ICDH criteria for TTH were met Probable migraine: all but one ICHD criterion for migraine without aura were fulfilled Definite migraine: all ICHD criteria for migraine without aura were met Mixed headache: definite migraine and definite TTH</p>	<p>3 headaches [HR: 1.80 (1.08-3.01)]; 4 headaches [HR: 3.09 (1.94-4.94)]; Headache frequency at baseline + time-varying headache frequency (p<0.0001): 0 Headache (ref.) 1 headache [HR: 0.96 (0.65-1.42)]; 2 headaches [HR: 1.37 (0.91-2.07)]; 3 headaches [HR: 1.26 (0.75-2.12)]; 4 headaches [HR: 1.78 (1.10-2.90)]; Time-varying headache frequency* [HR: 1.53 (1.46-1.60)] Headache frequency at baseline + time-varying lagged headache frequency (p<0.0001): 0 Headache (ref.) 1 headache [HR: 1.04 (0.71-1.54)]; 2 headaches [HR: 1.42 (0.94-2.14)]; 3 headaches [HR: 1.47 (0.88-2.48)]; 4 headaches [HR: 2.13 (1.31-3.48)]; Time-varying lagged headache frequency* [HR: 1.36 (1.28-1.45)]</p> <p>*hazard associated with an increase by one standard deviation (3 headaches per month) in time-varying headache frequency.</p>
<p>Sharma et al., USA (2019)</p>	<p>5.2 years (median follow-up=2.8 years)</p>	<p>Enrolled: 3,258 Follow-up drop outs:1,529 Final Sample: 1,729 (53% of 3,258)/ 18-44y.o</p>	<p>RDC/TMD</p>	<p>Exposure Assessment: <i>Quarterly health update questionnaire (QHU)</i> <i>First jaw injury:</i> First positive record of any jaw injury Experience of extrinsic events: tooth extraction or dental treatments, oral intubation, sports injury (including falls, bumps, and blows), motor vehicle accidents, accidents resulting in whiplash, and injuries to the shoulder, neck, and head region. Experience of intrinsic injury: jaw injury attributed to yawning or prolonged mouth opening <i>Type of jaw injury:</i> Extrinsic or intrinsic</p>	<p>ASSOCIATIONS BETWEEN TIME-VARYING FIRST JAW INJURY, TYPE OF FIRST JAW INJURY AND NUMBER OF JAW INJURIES WITH INCIDENT TMD USING COX MODELS (N=1,613) No injury (ref.; n=1,215): Model 1= 1.0; Model 2 = 1.0; Model 3 = 1.0 First injury (n=398): Model 1: 4.00 (2.86-5.60); Model 2: 3.98 (2.81-5.63); Model 3: 3.67 (2.57-5.24) Type of first jaw injury: No injury (ref.; n=1215): Model 1: 1.0; Model 2: 1.0; Model 3: 1.0 Extrinsic injury only (n=69): Model 1: 3.95 (1.98 - 7.89); Model 2: 4.26 (2.11-8.62); Model 3: 4.04 (1.96-8.31) Intrinsic injury only (n= 316): Model 1: 3.85 (2.68 - 5.53); Model 2: 3.80 (2.62- 5.50); Model 3: 3.47 (2.37- 5.07) Ps: Woolf test for heterogeneity comparing extrinsic only and intrinsic only injuries: Model 1: p=0.94; Model 2: p=0.76; Model 3: p=0.69 Both Intrinsic and Extrinsic injury (not part of Woolf test; n=15): Model 1= not computed; Model 2: not computed; Model 3: not computed N° of jaw injuries: No injury (ref.; n=1,215): Model 1: 1.0; Model 2: 1.0; Model 3: 1.0 One injury (n= 261): Model 1: 5.27 (3.60 - 7.73); Model 2: 5.93 (3.99- 8.79); Model 3: 6.01 (4.02- 8.99) Two or more injuries (n= 137): Model 1: 2.65 (1.60 - 4.40); Model 2: 2.34 (1.40- 3.93); Model 3: 1.94 (1.14- 3.30) Ps.: Woolf test for heterogeneity comparing 1 injury and 2 or more injuries: Model 1: p=0.02; Model 2: p<0.01; Model 3: p<0.01</p> <p>Model 1: Unadjusted; Model 2: Adjusted for study site, age, sex, and race; Model 3: Adjusted for study site, age, sex, race, depression, anxiety, physical symptoms, positive and negative mood, coping, oral behaviors, previous pain, financial and material satisfaction, and smoking</p>

				<p><i>Number of jaw injuries:</i> injury reported in subsequent QHU</p> <p>Confounders: Demographic variables (study site, age, education, annual household income, marital status, satisfaction with material standards of life and satisfaction with financial situation), Symptom Check List-90 revised (SCL 90R), The profile of mood States-Bipolar (PMOS-Bi), Comprehensive Pain and Symptom Questionnaire (CPQ-R), Oral Behavior Checklist Summary score and questions about previous injuries, smoking, health insurance, US lifetime residency.</p>	<p>ASSOCIATION BETWEEN FIRST INJURY AND INCIDENT TMD AFTER ADJUSTING FOR EACH COVARIATE INDIVIDUALLY.</p> <p>BASE MODEL: Injury [n=1,729; 4.02 (2.92 - 5.55)] MULTIVARIATE MODEL: Study Site [n=1,729; HR: 4.01 (2.89 - 5.57)]; Age [n=1,729; HR: 3.78 (2.73 - 5.23)]; Gender [n=1,729; HR: 4.09 (2.97 - 5.65)]; Race [n=1,729; HR: 3.76 (2.71 - 5.23)]; Lifetime residency in U.S [n=1,697; HR: 3.93 (2.84 - 5.43)]; Education [n=1,697; HR: 3.82 (2.74 - 5.30)]; Family annual household income [n=1,729; HR: 4.03 (2.92 - 5.56)]; Rating of satisfaction financial situation [n=1,699; HR: 3.93 (2.83 - 5.46)]; Rating of satisfaction material situation [n=1,694; HR: 3.80 (2.73 - 5.29)]; Marital status [n=1,710; HR: 4.00 (2.90 - 5.53)]; Smoking [n=1,695; HR: 3.78 (2.71 - 5.27)]; Facial pain prior to enrollment [n=1,712; HR: 3.83 (2.77 - 5.31)]; Oral Behavior Checklist sum score [n=1,700; HR: 3.71 (2.68 - 5.13)]; SCL 90R Depression [n=1,726; HR: 3.62 (2.62 - 5.00)]; SCL 90R Anxiety: [n=1,726; HR: 3.67 (2.66 - 5.07)]; Physical sx: PILL [n=1,727; HR: 3.71 (2.69 - 5.12)]; PCS Coping [n=1,728; HR: 3.83 (2.76 - 5.30)]; Mood state (POMS) positive affect [n=1,718; HR: 3.91 (2.83 - 5.40)]; Mood state (POMS) Negative affect [n=1,718; HR: 3.84 (2.78 - 5.31)];</p>
<p>Lee et al., Taiwan (2020)</p>	<p>15 years (Retrospective Data)</p>	<p>1,906,713 individuals 84,903 with Low back pain outpatient (≥ 6 visits) or inpatient (≥ 1 visit); Excluded: 19,782 (low back pain before index date; TMD before tracking; Malignant neoplasm of lip, oral cavity and pharynx; Injuries on the head, face, or neck; without tracking; Age <20 or >70;</p>	<p>RDC/TMD</p>	<p>Retrospective Cohort study</p> <p>Sex; Age groups; Insured premium (IP) in New Taiwan dollars (NTD); Level of Care; Comorbidities: Hypertension (HTN), Congestive heart failure (CHF), Stroke, Chronic kidney disease (CKD), Migraine, Osteoporosis, Hyperlipidemia, Nonpsychotic mental disorders (NMD), Psychoses, Coronary artery disease (CAD), Insomnia, Rheumatoid arthritis (RA), Charlson comorbidity index revised (CCI_R), Chronic obstructive pulmonary disease (COPD), Low back pain (LBP).</p>	<p>RISK OF TMD AMONG DIFFERENT TRACKING YEAR OF PATIENTS WITH VS WITHOUT LOW BACK PAIN (LBP):</p> <p>LBP Tracking year: Overall [HR: 1.561; p<0.001]; 0-5 [HR:1.384; p=0.243]; 6-10 [HR: 1.701; p=0.013]; ≥ 11 [HR: 1.823; p=0.002];</p> <p>RISK FACTORS FOR THE INCIDENCE OF TMD IN THE COX REGRESSION ANALYSIS:</p> <p>LBP: Without [ref.]; With [HR: 1.561 (1.220-1.996); p<0.001]; Gender: Female [ref.]; Male [HR: 0.768 (0.601-1.002); p=0.053]; Age Groups (years): 60-70 [ref.]; 20-29 [HR: 5.615 (2.014-15.653); p<0.001]; 30-39 [HR: 2.406 (1.540-3.758); p=0.001]; 40-49 [HR: 1.017 (0.727-1.576); p=0.923]; 50-59 [HR: 1.001 (0.646-1.422); p=0.997]; IP (NTD): <18,000 [ref.]; 18,000-34,999 [HR: 12.741 (9.176-17.690); p<0.001]; $\geq 35,000$ [HR:33.684 (20.730-54.731); p<0.001]; Level of Care: Local Hospital [ref.]; Hospital Center [HR:1.264 (0.935-1.741); p=0.742]; Regional Hospital [HR:1.093 (0.873-1.397); p=0.161]; Comorbidities: HTN [HR:1.006 (0.657-1.194); p=0.426]; CHF [HR:1.065 (0.602-1.885); p=0.828]; Stroke [HR:1.136 (0.867-1.597); p=0.105]; COPD [HR:1.753 (0.944-2.278); p=0.294]; CKD [HR:1.241 (0.633-2.243); p=0.529]; Migraine [HR:0.000; p=0.975];</p>

		gender unknown; Total sample= 65,121 with low back pain and 195, 363 without low back pain;/ 20-70 y.o			Osteoporosis [HR:1.860 (1.212-3.483); p=0.003]; Hyperlipidemia [HR:1.414 (0.813-2.459); p=0.220]; NMD [HR:0.000; p=0.922]; Psychoses [HR:1.254 (0.789-2.315); p=0.687]; CAD [HR:1.240 (0.833-1.884); p=0.289]; Insomnia [HR:1.021 (0.253-4.123); p=0.976]; RA [HR:1.021 (0.253-4.123); p=0.976]; CCI_R [HR:0.989 (0.938-1.043); p=0.681]
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QHU: Quarterly Health Update Questionnaire; N/A: no available; y.o: years old; TMD: temporomandibular disorder; TMJ: temporomandibular joint; n.s = not significant

Supplementary Table 2 (S2) - Excluded articles and the reasons for exclusion (n=164).

Reference	Author	Reasons for Exclusion*
1.	Abdelnabi MH, Swelem AA. (2015)	8
2.	Abou-Atme YS et al. (2007)	2
3.	Abrahamsson C et al (2015)	4
4.	Agbaje J et al (2018)	2
5.	Ai M (1991)	11
6.	Akhter R (2011)	2
7.	Alkhubaizi Q et al (2017)	6
8.	Anon (2005)	10
9.	Banafa et al (2019)	2
10.	Badel T et al (2014)	8
11.	Bair E et al. (2016)	8
12.	Bair E et al. (2015)	6
13.	Becker IM (1995)	10
14.	Bereiter DA et al (2011)	8
15.	Berrocal AM et al. (2018)	2
16.	Bortsov A et al. (2017)	8
17.	Buchlotz MR (2007)	8
18.	Bruguiere F et al. (2019)	7
19.	Cannizzaro E et al. (2011)	2
20.	Carlson O et al. (1977)	10
21.	Carlsson GE (1980)	8
22.	Chandan et al. (2019)	2
23.	Chen YY et al. (2019)	2
24.	Chin Jen Sem JP et al. (2017)	2
25.	Clayman GL et al. (1983)	8
26.	Contar C et al. (2010)	1
27.	Costa AL et al. (2014)	8
28.	Crincoli V et al. (2019)	8
29.	D'Ambrosia RD (2005)	1
30.	de Mol van Otterloo JJ et al (1993)	2
31.	Dibbets JM & van der Weele LT (1987)	2

32.	Drangsholt MT (2008)	8
33.	Duinkerke AS et al. (1985)	2
34.	Egermark I et al. (2005)	2
35.	Egermark I & Rönnerman A (1995)	2
36.	Ember E (1986)	10
37.	Engström AL et al. (2007)	2
38.	Eversole LR & Machado L (1985)	8
39.	Fadol Y et al. (2018)	3
40.	Favero GA et al. (1983)	10
41.	Ferretti C et al. (2005)	2
42.	Fillingim RB et al. (2018)	7
43.	Finmann C (1984)	10
44.	Forssell H (1985)	10
45.	Frey DR et al. (2008)	2
46.	Galbete C et al (2018)	1
47.	Gesch D et al. (2004)	8
48.	Girod A et al. (2001)	8 e 10
49.	Given BK & Brendan CS (1986)	8
50.	Greene CS (1999)	10
51.	Hadlock TA et al. (2001)	8
52.	Harmon JB et al. (2016)	8
53.	Helm S & Petersen PE (1989)	2
54.	Hirata RH et al. (1992)	2
55.	Huang GJ et al. (2008)	2
56.	Huber MA & Hall EH (1990)	2 e 8
57.	Huelse M & Losert-Bruggner B (2008)	8
58.	Isberg A et al (1987)	2
59.	Jones NS & Cooney TR (2003)	1 e 2
60.	Junjie Y et al. (2018)	2
61.	Jussila P et al. (2017)	2
62.	Jussila P et al. (2019)	2
63.	Kalbfleisch JF et al. (1985)	10
64.	Kampe T et al. (1991)	2
65.	Kapos FP (2015)	3
66.	Kares H (2008)	8

67.	Kedar K & Adour MD (1981)	2
68.	Kerwin JH (1999)	8
69.	Kieser JA & Groeneveld HT (1998)	2
70.	Kitai N et al. (1997)	2
71.	Kurek M et al. (1981)	10
72.	Lam DK et al. (2001)	1 e 8
73.	Lampa E et al. (2020)	6
74.	Lee KC et al. (2019)	2
75.	Lesnicar G & Zerdoner (2007)	8
76.	Levy PH (1991)	10
77.	Liljeström et al. (2008)	2
78.	Lin et al (2017)	2
79.	Link JJ & Nickerson Jr JW (1992)	10
80.	Lukas D et al. (1985)	10
81.	Macfarlane TV et al. (2009)	2
82.	Magnusson T et al. (1993)	2
83.	Maixner W et al. (2011)	8
84.	Martinez-Gomis J et al. (2010)	8
85.	Mehta NR (2019)	8
86.	Mejersjo C (1987)	8
87.	Miyake R et al (2004)	2
88.	Mohlin B (1983)	2
89.	Montero J et al. (2018)	2
90.	Nemeth DZ et al. (2000)	2
91.	Nevalainen N et al. (2017)	2
92.	O'Reilly MT et al. (1993)	2
93.	Orbach R et al. (2011)	8
94.	Osiewicz M et al. (2019)	8
95.	Ostrom C et al. (2017)	1
96.	Pahkala RH & Laine-Alava MT (2002)	2
97.	Pérez-Osorio LJ (1990)	10
98.	Probert TC et al. (1994)	2
99.	Rasheed RH & Faysal R (2011)	8
100.	Rasmussen P & Holst E (1975)	10
101.	Rauhala K et al. (2000)	2

102.	Reissmann DR & John MT (2007)	8
103.	Rini GS et al. (1987)	10
104.	Rocco BB (1976)	10
105.	Ruf S & Bock NC (2018)	7
106.	Salé H et al. (2014)	2
107.	Salé H et al. (2010)	2
108.	Salé H et al. (2007)	2
109.	Sanders AE et al. (2017)	8
110.	Sanders AE et al. (2012)	8
111.	Scheerlinck JP et al. (1994)	2
112.	Schwartz EE et al. (1976)	8
113.	Schwartz HC et al. (1984)	8
114.	Sefidroodi M et al (2019)	2
115.	Seligman DA et al. (1988)	2
116.	Sharma S et al. (2020)	8
117.	Sharoff AN (2017)	8
118.	Silvennoinen U et al. (1998)	2
119.	Sipilä K et al. (2013)	6
120.	Sipilä K et al. (2015)	2 e 8
121.	Sipilä K et al. (2008)	2
122.	Siritapetawee M & Chatrchaiwiwatana S (2020)	8
123.	Slade GD et al. (2016)	8
124.	Slade GD et al. (2013)	8
125.	Smith MT & Finan PH (2013)	8
126.	Smith S (2019)	8
127.	Smith S et al. (2009)	8
128.	Smith S et al. (2018)	8
129.	Staats J & Graber G (1982)	10
130.	Stenvik A et al. (2011)	1 e 2
131.	Stohler CS (1999)	8
132.	Storm C & Wänman A (2007)	8
133.	Suarez OF (1999)	8
134.	Sun ZP et al. (2008)	11
135.	Takehara J (2004)	2
136.	Tapias Ledesma MA et al. (2008)	8

137.	Tchivileva I et al. (2016)	8
138.	Timmis DP et al. (1986)	2
139.	Tosa H et al. (1986)	6 e 8
140.	Tran Duy TD et al. (2019)	2
141.	Türp JC & Schindle HJ (2005)	8
142.	Umaña G (1986)	10
143.	Uzhumetskene (1972)	10
144.	Vanderas AP (1988)	2 e 10
145.	Van Selms MK et al. (2009)	3
146.	Velly AM (2011)	3
147.	Visscher CM (2011)	8
148.	Völzke (2011)	2
149.	Von Korff M et al. (1993)	2
150.	Wänman A & Agerberg G (1991)	2
151.	Wänman A (2005)	2
152.	Wassel RW (1989)	8
153.	Weinberg LA (1976)	8
154.	Weineber LA (1977)	8
155.	Werfalli SG (2013)	1
156.	Widgorowicz-Makowerowa N (1977)	8
157.	Widmer CG (2008)	8
158.	Wiens JP (1990)	1 e 2
159.	Witter DJ et al. (1994)	2
160.	Witter DJ et al. (2007)	2
161.	Yatani H et al. (2000)	2
162.	Zarb G & Carlsson G (1999)	8
163.	Zawi AHM (2017)	3
164.	Zoccola GC et al. (1991)	8

*Legend: 1) No targeted condition; 2) Studies using diagnostic tool other than RDC/TMD, DC/TMD and AAOP; 3) Sample with targeted condition at baseline 4) Presence of interventions in the study sample; 5) Studies without a minimal average follow-up of one year; 6) Studies without clinical examination to diagnostic TMD; 7) No association results reported; 8) Randomized controlled trial, case-control, cross-sectional, before-after, abstracts, reviews, case-reports and series, protocols, short communications, personal opinions, letters, posters, conference abstracts, and laboratory research (in vivo and in vitro studies); 9) Studies presenting data included in other study; 10) Full-text not available; 11) Articles not writing in Latin-roman alphabet;

References from Supplementary Table (S2)

1. Abdelnabi MH, Swelem, AA. Influence of defective complete dentures renewal on TMD; an MRI and clinical controlled prospective study. *Gerodontology*. 2015;32(3), 211–221. doi: 10.1111/ger.12102
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Supplementary Table 3 (S3) – Data search strategy.

Database	Search query 2020, May 12 nd
EMBASE	<p>#1 ('risk factor*' OR 'associative factor*' OR 'causalit*' OR 'cause*' OR 'perpetuating factor*' OR 'disease susceptibility'/exp OR 'disease susceptibility' OR 'predictor*') AND [embase]/lim</p> <p>#2 ('cohort stud*' OR 'longitudinal stud*' OR 'follow-up stud*' OR 'prospective stud*' OR 'epidemiology' OR 'epidemiologic' OR 'epidemiologic stud*') AND [embase]/lim</p> <p>#3 ('temporomandibular joint disorder*' OR 'temporomandibular disorder*' OR 'temporomandibular joint disease' OR 'temporomandibular joint diseases' OR 'temporomandibular dysfunction*' OR 'temporomandibular joint dysfunction syndrome' OR 'costen syndrome' OR 'temporomandibular joint syndrome' OR 'temporomandibular joint syndromes' OR 'temporomandibular joint dysfunction' OR 'tmj disease*' OR 'tmd' OR 'tmj' OR 'tmjd' OR 'tmj disorders' OR 'tmj disorder' OR 'craniomandibular disorder*' OR 'craniomandibular dysfunction*' OR 'temporomandibular joint' OR 'temporomandibular' OR 'temporo-mandibular' OR 'craniomandibular' OR 'cranio-mandibular' OR 'temporomandibular joint dysfunctions') AND [embase]/lim</p> <p>#1 AND #2 AND #3</p>
LILACS	<p>#1 ("risk factors" OR "risk factor" OR "associative factor" OR "causality" OR "cause" OR "causes" OR "causalities" OR "perpetuating factors" OR "disease susceptibility" OR "predictor" OR "Factores de Riesgo" OR "Factores de Risco" OR "Causalidad" OR "Predisposing Factors" OR "Predisposing factor" OR "fatores predisponentes" OR "causalidade")</p> <p>#2 ("cohort studies" OR "longitudinal studies" OR "follow-up studies" OR "prospective studies" OR "epidemiology" OR "epidemiologic" OR "epidemiologic study" OR "epidemiologic studies" OR "Estudios de Cohortes" OR "Estudios de Coortes" OR "Estudios Longitudinales" OR "Estudios Longitudiniais" OR "Estudios de Seguimiento" OR "Estudios Prospectivos" OR "Estudios Prospectivos" OR "Estudios Epidemiológicos" OR "Estudios Epidemiológicos")</p> <p>#3 ("temporomandibular joint disorders" OR "temporomandibular joint disorder" OR "temporomandibular disorder" OR "temporomandibular disorders" OR "temporomandibular joint disease" OR "temporomandibular joint diseases" OR "temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "temporomandibular joint dysfunction syndrome" OR "costen syndrome" OR "costens syndrome" OR "costen's syndrome" OR "temporomandibular joint syndrome" OR "temporomandibular joint syndromes" OR "temporomandibular joint dysfunction" OR "tmj disease" OR "tmd" OR "tmj" OR "tmjd" OR "tmj disorders" OR "tmj disorder" OR "tmj diseases" OR "craniomandibular</p>

disorders" OR "craniomandibular disorder" OR "craniomandibular dysfunction" OR "craniomandibular dysfunctions" OR "temporomandibular joint" OR temporomandibular OR temporo-mandibular OR craniomandibular OR cranio-mandibular OR "temporomandibular joint dysfunctions" OR "Transtornos da Articulação Temporomandibular" OR "Trastornos de la Articulación Temporomandibular" OR "Síndrome de la Disfunción de Articulación Temporomandibular" OR "Síndrome da Disfunção da Articulação Temporomandibular" OR "Trastornos Craneomandibulares" OR "Transtornos Craniomandibulares" OR "Disfunção Temporomandibular" OR "Disfunções Temporomandibulares" OR "Disfunção da ATM" OR "Disfunções da ATM" OR "desordem temporomandibular" OR "desordens temporomandibulares" OR "desordem da ATM" OR "desordens da ATM" OR "dtm" OR "Transtorno da ATM" OR "Transtornos da ATM" OR "desordem temporomandibular" OR "disfunção temporomandibular" OR "transtorno temporomandibular" OR "disfunción temporomandibular" OR "Trastorno ATM")
 #1 AND #2 AND #3

PubMed

#1 "risk factors"[MeSH Terms] OR "risk factor"[All Fields] OR "risk factor"[All Fields] OR "associative factor"[All Fields] OR "associative factor"[All Fields] OR "associative factor"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields] OR "causality"[All Fields] OR "cause"[All Fields] OR "causes"[All Fields] OR "causalities"[All Fields] OR "perpetuating factors"[All Fields] OR "disease susceptibility"[MeSH Terms] OR "predictor"[All Fields] OR "predictor"[All Fields]

#2 "cohort studies"[MeSH Terms] OR "cohort studies"[All Fields] OR "longitudinal studies"[All Fields] OR "longitudinal studies"[All Fields] OR "follow-up studies"[All Fields] OR "follow-up studies"[All Fields] OR "prospective studies"[All Fields] OR "prospective studies"[All Fields] AND "prospective studies"[MeSH Terms] OR ("prospective"[All Fields] AND "studies"[All Fields]) OR "prospective studies"[All Fields] OR "longitudinal studies"[MeSH Terms] OR ("longitudinal"[All Fields] AND "studies"[All Fields]) OR "longitudinal studies"[All Fields] OR "epidemiology"[Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms] OR "epidemiology"[MeSH Terms] OR "epidemiology"[All Fields] OR "epidemiologic"[All Fields] OR "epidemiologic study"[All Fields] OR "epidemiologic studies"[MeSH Terms]

#3 "temporomandibular joint disorders"[MeSH Terms] OR "temporomandibular joint disorders"[All Fields] OR "temporomandibular joint disorder"[All Fields] OR "temporomandibular disorder"[All Fields] OR "temporomandibular disorders"[All Fields] OR "temporomandibular joint disease"[All Fields] OR "temporomandibular joint diseases"[All Fields] OR "temporomandibular dysfunction"[All Fields] OR "temporomandibular dysfunctions"[All Fields] OR "temporomandibular joint dysfunction syndrome"[MeSH Terms] OR "temporomandibular joint dysfunction syndrome"[All Fields] OR "costen syndrome"[All Fields] OR "costen's syndrome"[All Fields] OR "costen's Syndrome"[All Fields] OR

	<p>"temporomandibular joint syndrome"[All Fields] OR "temporomandibular joint syndromes"[All Fields] OR "temporomandibular joint dysfunction"[All Fields] OR "tmj disease"[All Fields] OR "tmd"[All Fields] OR "tmj"[All Fields] OR "tmjd"[All Fields] OR "tmj disorders"[All Fields] OR "tmj disorder"[All Fields] OR "tmj diseases"[All Fields] OR "craniomandibular disorders"[MeSH Terms] OR "craniomandibular disorders"[All Fields] OR "craniomandibular disorder"[All Fields] OR "craniomandibular dysfunction"[All Fields] OR "craniomandibular dysfunctions"[All Fields] OR "craniomandibular dysfunctions"[All Fields] OR "temporomandibular joint"[MeSH Terms] OR temporomandibular[All Fields] OR temporomandibular[All Fields] OR craniomandibular[All Fields] OR craniomandibular[All Fields] OR "temporomandibular joint dysfunctions"[All Fields]</p> <p>#1 AND #2 AND #3</p>
SCOPUS	<p>#1 TITLE-ABS-KEY ("cohort stud*" OR "longitudinal stud*" OR "follow-up stud*" OR "prospective stud*" OR "epidemiology" OR "epidemiologic" OR "epidemiologic stud*" OR "epidemiologic stud*")</p> <p>#2 TITLE-ABS-KEY ("risk factor*" OR "associative factor*" OR "causalit*" OR "cause*" OR "perpetuating factor*" OR "disease susceptibility" OR "predictor*")</p> <p>#3 TITLE-ABS-KEY ("temporomandibular joint disorder*" OR "temporomandibular disorder*" OR "temporomandibular joint disease" OR "temporomandibular joint diseases" OR "temporomandibular dysfunction*" OR "temporomandibular joint dysfunction syndrome" OR "costen syndrome" OR "costen's syndrome" OR "temporomandibular joint syndrome" OR "temporomandibular joint syndromes" OR "temporomandibular joint dysfunction" OR "tmj disease*" OR "tmd" OR "tmj" OR "tmjd" OR "tmj disorders" OR "tmj disorder" OR "craniomandibular disorder*" OR "craniomandibular dysfunction*" OR "temporomandibular joint" OR "temporomandibular" OR "temporomandibular" OR "craniomandibular" OR "cranio-mandibular" OR "temporomandibular joint dysfunctions")</p> <p>#1 AND #2 AND #3</p>
Web of Science (Articles)	<p>#1 ("risk factor*" OR "associative factor*" OR "causalit*" OR "cause*" OR "perpetuating factor*" OR "disease susceptibility" OR "predictor*")</p> <p>#2 ("cohort stud*" OR "longitudinal stud*" OR "follow-up stud*" OR "prospective stud*" OR "epidemiology" OR "epidemiologic" OR "epidemiologic stud*" OR "epidemiologic stud*")</p> <p>#3 ("temporomandibular joint disorder*" OR "temporomandibular disorder*" OR "temporomandibular joint disease" OR "temporomandibular</p>

	<p>joint diseases" OR "temporomandibular dysfunction*" OR "temporomandibular joint dysfunction syndrome" OR "costen syndrome" OR "costen's syndrome" OR "temporomandibular joint syndrome" OR "temporomandibular joint syndromes" OR "temporomandibular joint dysfunction" OR "tmj disease*" OR "tmd" OR "tmj" OR "tmjd" OR "tmj disorders" OR "tmj disorder" OR "craniomandibular disorder*" OR "craniomandibular dysfunction*" OR "temporomandibular joint" OR "temporomandibular" OR "temporo-mandibular" OR "craniomandibular" OR "cranio-mandibular" OR "temporomandibular joint dysfunctions")</p> <p>#1 AND #2 AND #3</p>
Grey Literature	
Google Scholar	"risk factor" AND ("temporomandibular disorder" OR "TMD") AND "cohort study"
Open Grey	"risk factors" AND "temporomandibular disorder" AND "cohort study"
ProQuest	(("risk factor" OR "associative factor" OR "causality" OR "cause" OR "causes" OR "causalities" OR "perpetuating factors" OR "disease susceptibility" OR "predictor" OR "predictors") AND ("cohort studies" OR "longitudinal studies" OR "follow-up studies" OR "follow-up studies" OR "prospective studies" OR ("prospective" AND "studies") OR ("longitudinal" AND "studies") OR "epidemiology" OR "epidemiology" OR "epidemiology" OR "epidemiologic" OR "epidemiologic study" OR "epidemiologic studies") AND ("temporomandibular joint disorders" OR "temporomandibular disorder" OR "temporomandibular disorders" OR "temporomandibular joint disease" OR "temporomandibular joint diseases" OR "temporomandibular dysfunction" OR "temporomandibular dysfunctions" OR "temporomandibular joint dysfunction syndrome" OR "costen syndrome" OR "costen's syndrome" OR "temporomandibular joint syndrome" OR "temporomandibular joint syndromes" OR "temporomandibular joint dysfunction" OR "tmj disease" OR "tmd" OR "tmj" OR "tmjd" OR "tmj disorders" OR "tmj disorder" OR "tmj diseases" OR "craniomandibular disorders" OR "craniomandibular dysfunction" OR "craniomandibular dysfunctions" OR "craniomandibular dysfunctions" OR "temporomandibular joint" OR temporomandibular OR "temporo-mandibular" OR craniomandibular OR cranio-mandibular OR "temporomandibular joint dysfunctions")

5 CONCLUSÃO

As variáveis significativas foram muito heterogêneas. Em geral, sexo feminino e idade foram as características mais avaliadas. Dores nas costas, trauma, cefaleia, variáveis relacionadas ao sono, somatização, sintomas faciais, hábitos parafuncionais e variáveis oclusais também estiveram significativamente relacionados à DTM em todos os estudos que contemplaram essas variáveis. Devido à etiologia multifatorial da DTM, os fatores de risco relacionados como significativos pelos estudos incluídos são intercorrelacionados e devem ser avaliados de forma conjunta. Assim, por meio desse ScR, é possível inferir que mais estudos de corte, principalmente envolvendo análises multivariadas, são necessários para o entendimento completo de quais são os fatores que aumentam a probabilidade de DTM.

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