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Fernanda Berretta Teixeira

ASSOCIAÇÃO ENTRE DISFUNÇÕES TEMPOROMANDIBULARES E ANSIEDADE EM ADULTOS: UMA REVISÃO SISTEMÁTICA

Florianópolis
2019

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Orientador: Prof. André Luís Porporatti, Dr.

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Fernanda Berretta Teixeira

ASSOCIAÇÃO ENTRE DISFUNÇÕES TEMPOROMANDIBULARES E ANSIEDADE EM ADULTOS: UMA REVISÃO SISTEMÁTICA

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

Prof. Henrique Rosário, Dr.
Unisul

Prof. Lucas Cardinal, Dr.
Universidade de São Paulo

Profª. Beatriz Dulcinéia Mendes de Souza, Drª.
Universidade Federal de Santa Catarina

Certificamos que esta é a **versão original e final** do trabalho de conclusão que foi julgado adequado para obtenção do título de mestra em Clínicas Odontológicas pelo Programa de Pós-Graduação em Odontologia da Universidade Federal de Santa Catarina.

Elena Riet Correa Rivero:69108390053

Assinado de forma digital por Elena Riet Correa Rivero:69108390053
Dados: 2019.09.30 10:38:31 -03'00'

Profª. Elena Riet Correa Rivero, Drª.
Coordenadora do Programa

Andre Luis Porporatti:01039845932

Assinado de forma digital por Andre Luis Porporatti:01039845932
DN: cn=Andre Luis Porporatti:01039845932, ou=UFSC - Universidade Federal de Santa Catarina, o=ICPEdu
Dados: 2019.09.29 20:00:44 -03'00'

Prof. André Luís Porporatti, Dr.
Orientador

Florianópolis, 2019.

Dedico esta dissertação às pessoas mais importantes para mim, minha querida mãe, Ana Maria, principal responsável pela minha vida e a quem devo meu caráter e que me ensinou o amor à profissão e aos pacientes. Ao mesmo tempo, estendo esta dedicatória aos meus irmãos Renata e Bruno, por serem os melhores irmãos que alguém poderia ter.

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Sempre que houver alternativas, tenha cuidado.
Não opte pelo conveniente, pelo confortável.
Opte pelo que faz o seu coração vibrar.
Opte pelo que gostaria de fazer, apesar de todas as consequências.
(Osho)

APRESENTAÇÃO

Esta revisão sistemática foi originalmente escrita como um artigo na língua inglesa, com o objetivo de ser submetido ao periódico *Journal of Oral Rehabilitation* (JOR) em parceria com os pesquisadores da Universidade Federal de Santa Catarina Dr. André Luís Porporatti, Drª. Beatriz Dulcineia Mendes de Souza, Drª. Graziela De Luca Canto, a doutoranda Morgane Marion Kuntze e a mestranda Luiza Pereira Nascimento; com a pesquisadora da Universidade de São Paulo (USP) Drª. Juliana Stuginski-Barbosa; e o pesquisador Dr. Bruce D. Dick da University of Alberta (Canadá).

RESUMO

Objetivo. Avaliar, através de uma revisão sistemática, a literatura disponível sobre estudos que avaliaram a associação entre disfunção temporomandibular e ansiedade em adultos. **Métodos**. Foram considerados estudos elegíveis que utilizaram os Critérios de Diagnóstico para Pesquisa em Disfunção Temporomandibular (RDC/ TMD) ou Critérios Diagnósticos (DC/ TMD) e questionários validados para avaliar a ansiedade. Seis principais bases de dados eletrônicas foram pesquisadas, complementadas com três bases de dados da literatura cinzenta. O risco de viés foi avaliado utilizando a ferramenta *Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies, Case control, and Cohort studies.* **Resultados**. Foram encontradas 1087 referências identificadas colocar na metodologia 18 estudos observacionais foram incluídos para a síntese qualitativa. No geral, uma associação positiva entre DTM e ansiedade foi observada em 13 estudos. Considerando ferramentas específicas para avaliação da ansiedade, foram encontrados resultados conflitantes. Heterogeneidade clínica e metodológica foram observadas entre os estudos. Subgrupos diagnósticos de DTM (como muscular e articular) foram frequentemente mal informados. Entre cinco artigos investigando diagnósticos específicos de DTM, uma associação positiva com sintomas de ansiedade foi observada em dois estudos que avaliaram o deslocamento de disco e em um estudo que investigou a dor miofascial crônica. Em relação ao risco de viés, 13 estudos foram julgados com baixo risco e cinco com risco moderado. **Conclusão**. Considerando as evidências disponíveis, uma associação positiva entre DTM e sintomas de ansiedade foi apoiada pela maioria dos estudos incluídos.

Palavras-chave: Odontologia baseada em evidências. Disfunção temporomandibular. Ansiedade. Revisão sistemática.

ABSTRACT

Purpose. To systematically review and critically appraise available literature regarding studies that evaluated the association between temporomandibular disorder and anxiety in adults. **Methods.** We considered eligible studies that used the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/ TMD) or Diagnostic Criteria (DC/ TMD) and validated tools for assessing anxiety. Six main electronic databases were searched, complemented with three grey literature databases. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklists, Case-Control, and Cohort studies. **Results.** Out of 1087 references identified up to June 2018, 18 observational studies were included for the qualitative synthesis. Overall, a positive association between TMD and anxiety was observed in 13 studies. Considering specific tools for anxiety assessment, conflicting results were found. Substantial clinical and methodological heterogeneity across studies were observed. TMD diagnostic subgroups (such as muscular and articular) were often poorly reported. Among five articles investigating specific TMD diagnoses, a positive association with anxiety symptoms was observed in two studies evaluating disc displacement and in one study investigating chronic myofascial pain. Regarding risk of bias, 13 studies were judged with low risk and five with moderate risk. **Conclusions.** Considering the available evidence, a positive association between TMD and anxiety symptoms was supported by most of the included studies.

Keywords: Evidence-based medicine. Temporomandibular disorder. Anxiety. Systematic review.

LISTA DE FIGURAS

LISTA DE TABELAS

LISTA DE ABREVIATURAS E SIGLAS

ATM - Articulação Temporomandibular
DTM - Disfunção Temporomandibular
DSM-V - Diagnóstico e Manual de Transtornos Mentais
RS - Revisão Sistemática

Do inglês

BAI - Beck Anxiety Inventory
CI - Confidence Interval
EAS - Emotion Assessment Scale
DC/DTM - Diagnostic Criteria for Temporomandibular Disorders
DASS-42 - Depression, Anxiety, and Stress Scale
DSM-V - Diagnostic and Statistical Manual of Mental Disorders
GAD-7- Patient Health Questionnaire
HADS - Hospital Anxiety and Depression Scale
OR - Odds Ratio
PRISMA - Preferred reporting items for systematic review and meta-analysis protocols
PROSPERO - Prospective Register of Systematic Reviews
RDC/DTM - Research Diagnostic Criteria for Temporomandibular Disorders
SCL-90-R - Symptom Checklist-90-R
SR - Systematic Review
STAI - State-Trait Anxiety Inventory
STPI - State-Trait Personality Inventory
TMD - Temporomandibular Disorder
TMJ - Temporomandibular Joint

SUMÁRIO

1 INTRODUÇÃO

A disfunção temporomandibular (DTM) é um termo genérico, abrangendo condições que envolvem a articulação temporomandibular (ATM), os músculos mastigatórios e/ou estruturas associadas. Além disso, a DTM pode resultar em dor articular ou muscular e muitas vezes pode ser acompanhada por cefaleia, sintomas otológicos, limitação do movimento da mandíbula e altos níveis de incapacidade relacionada à dor (CAIRNS, 2010).

Nas condições de dor orofacial de origem não dental, as DTM são consideradas as mais frequentes. Uma revisão sistemática prévia estimou a prevalência de DTM em nível populacional, e variou de 2,6% considerando artralgia, 9,7% para distúrbios musculares, chegando até 11,4% para deslocamento de disco com redução (MANFREDINI et al., 2011). Deve-se mencionar que essas estimativas foram baseadas nos Critérios Diagnósticos para Disfunções Temporomandibulares (RDC/TMD) (DWORKIN e LERESCHE, 1992) ou Critérios Diagnósticos (DC/TMD) e provavelmente serão reavaliados com a adoção de critérios diagnósticos atualizados (MANFREDINI et al., 2011).

A etiologia da DTM é considerada complexa e multifatorial. A literatura atual aponta para uma combinação de fatores psicológicos, fisiológicos, estruturais e genéticos (CHISNOIU et al., 2015). Além disso, sugere-se que os indivíduos com DTM possam apresentar reação anormal ao estresse, baixa habilidade de enfrentamento e baixo limiar de tolerância à dor, o que pode indicar uma relação mais forte com fatores psicológicos em particular (MANFREDINI et al., 2003).

Entre esses fatores, os transtornos de ansiedade são um dos mais frequentes, tornando-se a sétima condição mais onerosa de todas as doenças em todo o mundo (ROSE e DEVINE, 2014). Os indivíduos que apresentam sintomas graves de ansiedade sem estímulos adequados podem ser incluídos na categoria de transtornos de ansiedade, conforme descrito na seção Diagnóstico e Manual de Transtornos Mentais (DSM-V) (AMERICAN PSYCHIATRIC ASSOCIATION, 2013). Os sintomas de ansiedade incluem angústia geral, dispneia, cefaleia, tontura, sudorese e inquietação, que são frequentemente avaliados por meio de instrumentos validados de mensuração (ROSE e DEVINE, 2014). Além disso, os questionários mais comumente usados para avaliar os sintomas de ansiedade incluem a Escala Hospitalar de Ansiedade e Depressão (HADS) e o Inventário de Ansiedade Traço-Estado (STAI) (JULIAN, 2011).

Embora uma associação entre fatores psicológicos e DTM seja consistentemente proposta por estudos anteriores, (MANFREDINI et al., 2003; ROLLMAN e GILLESPIE,

2000) não foi encontrada uma avaliação sistemática dos achados da literatura com relação aos sintomas de ansiedade em particular. Portanto, o objetivo desta revisão sistemática (RS) foi avaliar criticamente as evidências disponíveis e responder à seguinte questão focada: "Existe uma associação entre disfunções temporomandibulares e ansiedade em adultos?"

2 OBJETIVO

2.1 Objetivo Geral

Avaliar criticamente as evidências disponíveis em relação a associação entre disfunções temporomandibulares e ansiedade em adultos.

2.1 Objetivos Específicos

- Interpretar os achados na literatura e descrever as evidências científicas disponíveis;

- Realizar uma síntese qualitativa dos estudos a fim de responder se existe relação entre disfunções temporomandibulares e ansiedade.

3 CAPÍTULO 1

Association between temporomandibular disorders and anxiety in adults: a systematic review

Running headline: Temporomandibular disorders and anxiety

Authors: Fernanda Berretta[1], Luiza Pereira Nascimento[1], Morgane Marion Kuntze[1], Beatriz Dulcineia Mendes de Souza[2], Juliana Stuginski-Barbosa[3], Bruce Dick[4], Graziela De Luca Canto[2], André Luís Porporatti[2]

[1]Postgraduate Program in Dentistry, Federal University of Santa Catarina (UFSC), Florianópolis, Santa Catarina, Brazil.

[2]Department of Dentistry, Federal University of Santa Catarina (UFSC), Florianópolis, Santa Catarina, Brazil.

[3]Bauru School of Dentistry, University of São Paulo (USP), São Paulo, São Paulo, Brazil.

[4]Faculty of Medicine and Dentistry, Department of Dentistry, University of Alberta, Edmonton, Alberta, Canada.

Corresponding author: Fernanda Berretta
Department of Surgery, Federal University of Santa Catarina
University Campus, Mailbox 476 – Trindade
Florianópolis, Santa Catarina, Brazil
Zip code: 88040900
E-mail: ferberretta@gmail.com

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ABSTRACT

Purpose. To systematically review and critically appraise available literature regarding studies that evaluated the association between temporomandibular disorder and anxiety in adults. **Methods.** We considered eligible studies that used the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) or Diagnostic Criteria (DC/TMD) and validated tools for assessing anxiety. Six main electronic databases were searched, complemented with three grey literature databases. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklists. **Results.** Out of 1087 references identified up to June 2018, 18 observational studies were included for the qualitative synthesis. Overall, a positive association between TMD and anxiety was observed in 13 studies. Considering specific tools for anxiety assessment, conflicting results were found. Substantial clinical and methodological heterogeneity across studies were observed. TMD diagnostic subgroups (such as muscular and articular) were often poorly reported. Among five articles investigating specific TMD diagnoses, a positive association with anxiety symptoms was observed in two studies evaluating disc displacement and in one study investigating chronic myofascial pain. Regarding risk of bias, 13 studies were judged with low risk and five with moderate risk. **Conclusions.** Considering the available evidence, a positive association between TMD and anxiety symptoms was supported by most of the included studies.

Keywords: Evidence-based medicine; temporomandibular disorder; anxiety; systematic review.

INTRODUCTION

Temporomandibular disorders (TMD) is an umbrella term, embracing conditions that involve the temporomandibular joint (TMJ), the masticatory muscles, and/or associated structures. Moreover, TMD may result in articular or muscular pain and might often be accompanied by headache, otologic symptoms, limited jaw motion, and high levels of pain-related disability.[1]

Within orofacial pain conditions of nondental origin, TMD are considered the most frequent. A previous systematic review estimated TMD prevalence at population level, and it ranged from 2.6% considering arthralgia, 9.7% for muscle disorders, reaching up to 11.4% for disc displacement with reduction.[2] It should be mentioned that these estimates were based on the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[12] or Diagnostic Criteria (DC/TMD) and are likely to be reappraised with the adoption of updated diagnostic criteria.[2]

The etiology of TMD is considered complex and multifactorial. Current literature points toward a combination of psychological, physiological, structural, and genetic factors.[3] Moreover, it is suggested that TMD individuals might present abnormal reactivity to stress, poor coping skill, and low pain tolerance threshold, which might indicate a stronger relation with psychological factors in particular.[4]

Among these factors, anxiety disorders are one of the most frequent, becoming the seventh most burdensome condition of all diseases worldwide.[5] Individuals experiencing severe anxiety symptoms without adequate stimuli might be encompassed under the umbrella category of anxiety disorders, as described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V).[6] Symptoms of anxiety include general distress, dyspnea, headache, dizziness, sweating, and restlessness, which are often assessed through validated

measurement tools.[5] In addition, questionnaires most commonly used to evaluate symptoms of anxiety.

Although an association between psychological factors and TMD is consistently proposed by previous studies,[4, 8] no systematic assessment of findings from the literature with regards to anxiety symptoms in particular was found. Therefore, the purpose of this systematic review (SR) was summarize and critically appraise available evidence and answer the following focused question: "Is there an association between temporomandibular disorders and anxiety in adults?"

MATERIALS AND METHODS

Protocol and registration

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)[9] was used to elaborate a review protocol, which was registered at Prospective Register of Systematic Reviews (PROSPERO)[10] under the registration number CRD42018106073. Furthermore, this SR followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist (PRISMA).[11]

Eligibility criteria

Observational studies that evaluated the association between TMD and anxiety in adults (18-65 years old) and compared to a control group were included. No restriction regarding sex or time of publication were applied. TMD must have been assessed through RDC/TMD[12] or DC/TMD.[13] Anxiety symptoms must have been evaluated through validated questionnaires such as Hospital Anxiety and Depression Scale (HADS),[14] State-Trait Anxiety Inventory (STAI),[7] Beck Anxiety Inventory (BAI),[15] Symptom Checklist-90 Revised (SCL-90-R),[16] or others.

Exclusion criteria were as follow: 1) Studies in children or adolescents (<18 years old) or elderly (>65 years old); 2) Studies that did not investigate the association between TMD and anxiety or that did not provide separate results for TMD and/or anxiety; 3) Studies using TMD diagnostic tool other than the RDC/TMD or DC/TMD; 4) Studies in which TMD diagnostic criteria were not clearly reported; 5) Studies with no control group; 6) Reviews, letters, conference abstract, personal opinions, case reports; 7) Studies not published in the Latin-Roman alphabet; and 8) Full-text not available.

Information sources

Appropriate search strategy was performed on electronic databases: Latin American and Caribbean Health Sciences (LILACS), LIVIVO, PsycINFO, PubMed, SCOPUS, and Web of Science. A partial grey literature search was executed on Google Scholar, Open Grey, and ProQuest. All electronic database searches were performed on June 08, 2018. Detailed search strategies are provided in Appendix 1. The reference lists of included studies were hand-searched to identify any additional references. The software EndNote X8 (Thomson Reuters) was used for reference management.

Study selection

An online software (Rayyan, Qatar Computing Research Institute) was used for the selection phase. In phase-one, two reviewers (F.B. and L.P.N.) blindly screened titles and abstracts of all references, and discrepancies were resolved by a consensus discussion; if necessary, a third reviewer was consulted (M.M.K.), and used as judge. In phase-two, the same two reviewers performed the full-text reading of eligible articles and the third reviewer was also involved in cases of unsolved discrepancies. Moreover, studies were included for analysis if minimum inclusion criteria were met.

Data collection process and data items

Data was blindly collected by two reviewers (F.B. and L.P.N) and information was then cross-checked to warrant integrity of contents. Extracted data encompassed the following: authors, year of publication, country, study design, sample groups, mean age, TMD diagnostic methods, anxiety diagnostic methods, main findings, and main conclusion.

Risk of bias in included studies

The risk of bias was assessed by using the Joanna Briggs Institute Critical Appraisal Checklist specific for cross-sectional, case-control, and cohort studies.[17] Two reviewers (F.B. and L.P.N.) blindly performed the risk of bias assessment. Judgments were as follow: "high risk" when the study reaches up to 49% score "yes", "moderate risk" when the study reached 50% to 69% score "yes", and "low risk" when the study reached more than 70% score "yes". Any disagreements were discussed and decided with a third review (M.M.K.). Figures were generated using a computer software (Review Manager 5.3, The Cochrane Collaboration).

Summary measures

The effect measures for continuous data were mean values (MV) and mean differences (MD), which measured the absolute difference between TMD and anxiety groups. Moreover, outcome measures for dichotomous data, such as odds ratios (OR) and its 95% confidence intervals (95%CI), were considered, as well as quantitative data reported in relative or absolute frequencies.

Synthesis of results

A qualitative analysis of results based on the presence of TMD and anxiety symptoms was performed. Furthermore, if available, quantitative data was synthesized and presented in forest plots generated using software (Review Manager 5.3; The Cochrane Collaboration).

Risk of bias across studies

Clinical heterogeneity was assessed by comparing variability among participant's parameters (such as mean age and gender), methodological heterogeneity by comparing variability in study design (such as different tools for the assessment of anxiety symptoms), and also by comparing risk of bias in individual studies.

RESULTS

A total of 1087 references were identified from main electronic databases after duplicates had been removed. There was no included study from the grey literature since these were already within main databases. In phase-1 (title and abstract reading), 69 studies were considered eligible for inclusion. In phase-2 (full-text reading), 51 were excluded and a full description regarding reasons for exclusion are available in Appendix 2. Thereafter, 18 studies were finally included for analysis. A flow diagram presenting the complete process of study identification and selection is available in Figure 1.

With regards to study design, 15 were cross-sectional studies, 2 case-control studies, and 1 cohort study. A total of 6119 participants were enrolled across included studies, however, information regarding participants gender was not available in 4. [18-21] Nonetheless, considering studies which this information was available (n=3412), most of the participants were women (n=2164; 62.42%). Included studies were published between 1996 and 2018, and were conducted in Australia,[22] Brazil,[19, 23] Canada,[24, 25] China,[26] Germany,[27-29] India,[30, 31] Nigeria,[32] Romania,[18] Thailand,[33] and United States of America.[20, 21, 34, 35]

Regarding diagnostic methods, most of include used the RDC/TMD criteria, with the exception of Jivnani *et al.* (2017), which applied the most recent DC/TMD criteria. With regards to anxiety symptoms evaluation, the HADS tool was used in 5 studies,[27, 30-33] SCL-90R in 5,[20, 21, 24, 25, 34] STAI in 5,[19, 20, 26, 29, 32] and DASS-42 in 2 studies.[22, 23] Other tools such

as BAI,[18] STP1 and EAS,[35] and GAD7[28] were applied once in single studies. Descriptive characteristics of included studies are available in Table 1.

Risk of bias within studies

Risk of bias of included studies was assessed according to study design. Considering cross-sectional studies, 10 were judged as with low risk[19, 21, 22, 24, 25, 28, 30, 31, 33, 35] and 5 with moderate risk of bias.[18, 27, 29, 32, 34] Concerns regarding bias in these 5 studies were related to poor description of confounding factors (such as use psychotropic medications or presence of chronic painful conditions) and strategies to deal with these confounders. Both case-control studies[20, 25] and the single cohort study were judged as with low risk of bias. More detailed information is available in Figure 2 and Figure 3.

Results of individual studies

HADS

From the 5 studies that used the HADS tool,[27, 30-33] two reported significantly higher anxiety scores in TMD group compared to controls.[30, 33] It should be noted that Jivnani *et al.* (2017)[30] found a positive association of TMD with anxiety compared to non-TMD individuals; no differences were observed comparing TMD subgroups with regards to anxiety scores. Moreover, no significant differences regarding anxiety scores were observed in other two studies.[27, 32] A single study reported results separately for different levels of anxiety,[31] suggesting that significant differences between TMD and control groups were observed regarding borderline abnormal anxiety (scores 8-10) and abnormal anxiety scores (scores 11-21).

SCL-90R

Five studies used the SCL-90R tool,[20, 21, 24, 25, 34] of which significant higher scores of anxiety were observed in TMD individuals in 3 studies.[20, 24, 25] From these, the study of Velly *et al.* (2002)[24] supported a positive association of anxiety with disc displacement, whilst

Velly *et al.* (2003)[25] suggested a positive association with myofascial pain. No significant differences were observed in the study of De Leeuw *et al.* (2005).[34] It should be mentioned that List *et al.* (2012)[21] investigated an association of headache and/or TMD with anxiety symptoms; mean SCL-90R anxiety scores were 0.21±0.28 for TMD individuals (without headache) and 0.10±0.18 for controls. Statistical analyses comparing these two groups in particular were not available.

STAI

From 5 studies in which the STAI tool was used,[19, 20, 26, 29, 32] significantly higher anxiety scores in both STAI-State and STAI-Trait were observed in one study,[29] whilst other two reported significantly higher anxiety scores in STAI-Trait in particular.[20, 26] It must be highlighted that the study of Yu *et al.* (2015)[26] included only male individuals (pilots) in the study. Moreover, no significant differences regarding both STAI-State and STAI-Trait were observed in two studies.[19, 32]

DASS-42

Two studies evaluated anxiety symptoms using the DASS-42 tool, [22, 23] of which significantly higher anxiety scores in TMD group were observed in the study of Brandini *et al.* (2011).[22] The study of Vedolin *et al.* (2009)[23] evaluated female dentistry students in multiple time periods (week prior, week of academic examination, week after, and after summer vacation) during one year; it was found that no significant differences in anxiety were observed between TMD and controls at any time.

Other anxiety assessment tools

The remaining three studies have assessed anxiety symptoms through different tools. Chisnoiu *et al.* (2015)[18] used the BAI tool, reporting that TMD individuals presented a significantly higher median of anxiety compared to controls. Curran *et al.* (1996) used the STPI and EAS tools; significantly higher anxiety scores in the baseline evaluation were found

in both scales compared to controls.[35] Mora *et al.* (2012) used the GAD-7 tool, reporting that TMD individuals presented higher levels of anxiety compared to controls.

Synthesis of results

Clinical and methodological heterogeneity across studies were found to be substantial. In addition, few studies presented sufficiently homogeneous data within subgroups to properly perform a statistical pooling of data. Although no meta-analysis was performed, stand-alone forest plots were used to better visualize quantitative data, without pooling results.[36] This information is presented in Figure 4a (HADS), Figure 4b (SCL-90R), and Figure 4c (STAI).

Moreover, additional information was requested by email contact with articles' corresponding authors. Crude data was provided regarding the study of Fernandes Azevedo *et al.* (2017)[19] (Souza, M.B.C; personal communication, February 14th, 2019). Other authors did not respond to email request or have informed that crude data was not available. These papers were included in forest plots although quantitative data was not estimable.

Overall, a positive association of TMD with anxiety symptoms in adults was found in 13 out of 18 included studies. Considering specific tools for anxiety assessment, conflicting results were found. A positive association between TMD and anxiety symptoms was found in 3 out of 5 studies considering either the HADS, SCL-90R, or STAI tools. Both studies that used the DASS-42 tool and all studies using other tools reported a positive association between TMD and anxiety. In addition, it should be mentioned that two studies investigated TMD diagnosis separately and anxiety was positively associated with both disc displacement[24] and chronic myofascial pain.[25]

Risk of bias across studies

Substantial clinical and methodological heterogeneity across studies were observed. TMD diagnostic subgroups (such as muscular and articular) were often poorly reported and

related information was available in only five studies.[23-25, 27, 30] In addition, although most studies used convenience samples, populations in two studies were restricted to male pilots[26] and female dentistry students.[23]It must be highlighted that sample sizes were also considerably discrepant, ranging from approximately 30 individuals up to 1800. In addition, since differences were observed regarding sample composition (such as age and gender), anxiety assessment tools, and in study design (cross-sectional and longitudinal studies), direct comparisons across studies were often considered not appropriate.

DISCUSSION

This SR aimed to summarize and critically appraise current evidence regarding TMD and anxiety symptoms in adults. Although included studies were greatly heterogeneous, mostly due to different tools in regards to anxiety assessment, a positive association of TMD and anxiety symptoms was supported by most included articles. Since TMD is considered a multifactorial condition, physicians and dental practitioners should be aware of these findings when handling their patients in order to achieve more effective treatment planning and to provide better recommendations.

The possible role of psychological factors, such as anxiety, in TMD might be related to the induction of muscle hyperactivity and fatigue; it is proposed that this may result in contracture of masticatory muscles and internal disturbances in regards to the temporomandibular joint.[3] Moreover, it has been proposed that psychiatric conditions, such as depression and some anxiety disorders, might be associated with hypothalamic-pituitary-adrenal (HPA) deregulations[37]; HPA activation results in the release of adrenocorticotropic hormone (ACTH) and corticoids into the blood stream, inducing defense-related emotions that could generate anxiety, fear, and panic.[38] It should be mentioned that HPA hyperactivity is often reported in the literature regarding TMD individuals, thus it could be hypothesized

that a possible association with anxiety symptoms might involve stimulus-specific compensatory responses, such as pain in the facial region.[37] Nonetheless, further research is recommended to further explore common mechanisms involved in these conditions.

Several reasons for performing quantitative assessment of psychological and behavioral factors among TMD patients have been proposed. Since personality, emotional, and behavioral factors might play a role in the etiology of TMD, it is important to use standardized psychometric instruments to obtain objective information that might be useful to predict outcomes of interest and to help to develop better treatment strategies.[39]

The majority of anxiety assessment tools found within included studies were based on questionnaires, most of which are applied through self-report,[7, 15, 16] with the exception of the HADS tool that can also be applied through interview.[14] Overall, these instruments collect information regarding several domains (such as mood, cognition, behavior, and somatic symptoms), which can provide valid and reliable assessments of anxiety. [5] It should be mentioned, however, that these tools might present inaccuracies due to overlap of symptoms related to stress, depression, and anxiety, thus certain tools focusing on a narrow scope of symptoms, such as the BAI and HADS tool, might provide limited assessment of anxiety.[7]

It should be mentioned that increased somatization, stress, anxiety, and depression are observed in individuals with TMD when compared to healthy individuals.[8] With regards to somatization in particular, numerous somatic symptoms have been suggested to be strongly related to emotional and cognitive symptoms of psychological distress.[40] In fact, a recent epidemiological SR found that psychological disorders, such as severe-to-moderate somatization and depression, were highly prevalent in TMD patients.[41] Since anxiety symptoms were often more frequently observed among TMD participants compared to controls in most of included studies, it might be proposed that findings from this SR are in accordance with previous reports of possible links between psychological factors and TMD.

Another interesting aspect to consider in the association between TMD and anxiety symptoms might be the role of the hypervigilant behavior. Hypervigilance is characterized as a behavior involving exaggerated search of environmental stimuli or for threatening information.[42] Several studies have suggested that signs of hypervigilance could be observed under conditions of state anxiety[43] and that it might also be associated with the likelihood of developing TMD symptoms.[44] It should be mentioned, however, there are few studies investigating the role of hypervigilance with regards to these conditions, thus further research on this topic is recommended.

Although included studies did not focus on gender differences regarding the association between TMD and anxiety symptoms, it should be highlighted that approximately 60% of participants enrolled were women. In this regard, studies suggested that signs and symptoms of TMD might be more prevalent amongst female individuals.[45, 46] Moreover, it is also proposed that prevalence of some anxiety disorders, such as the generalized anxiety disorder, might be twice as high among female compared to male individuals.[47] It should also be highlighted that two studies included in this SR presented populations with limited external validity, since Yu et al. (2015)[26] investigated only civilian male pilots, whilst Vedolin et al. (2009)[23] only included female students attending the first two years of Dental School. Therefore, findings from this SR should be interpreted with caution as some limitations regarding external validity might be present.

Overall consistent results were found with regards to a positive association of TMD with anxiety symptoms. Nonetheless, studies were considered heterogeneous with regards to tools for anxiety assessment. Although standardized psychometric instruments were applied, results were often not directly comparable and sometimes conflicting. This might partially be explained by the fact that instruments provide different scores, which makes intuitive interpretation and communication more difficult.[5] Moreover, it should be highlighted that

most included studies were cross-section in design, which does not provide useful information for inferences regarding causality.[48] Therefore, further studies are recommended to investigate whether the presence of anxiety symptoms could predict the onset of TMD or the opposite direction.

CONCLUSION

On the basis of current evidence, TMD was overall positively associated with anxiety symptoms among adults, however, tools for anxiety assessment were considered fairly heterogeneous across studies and evidence was considered limited to further explore inferences with regards to causality. Thus, further longitudinal studies using homogeneous tools for anxiety assessment are recommended.

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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 and generated using the software Review Manager 5.3, The Cochrane Collaboration).

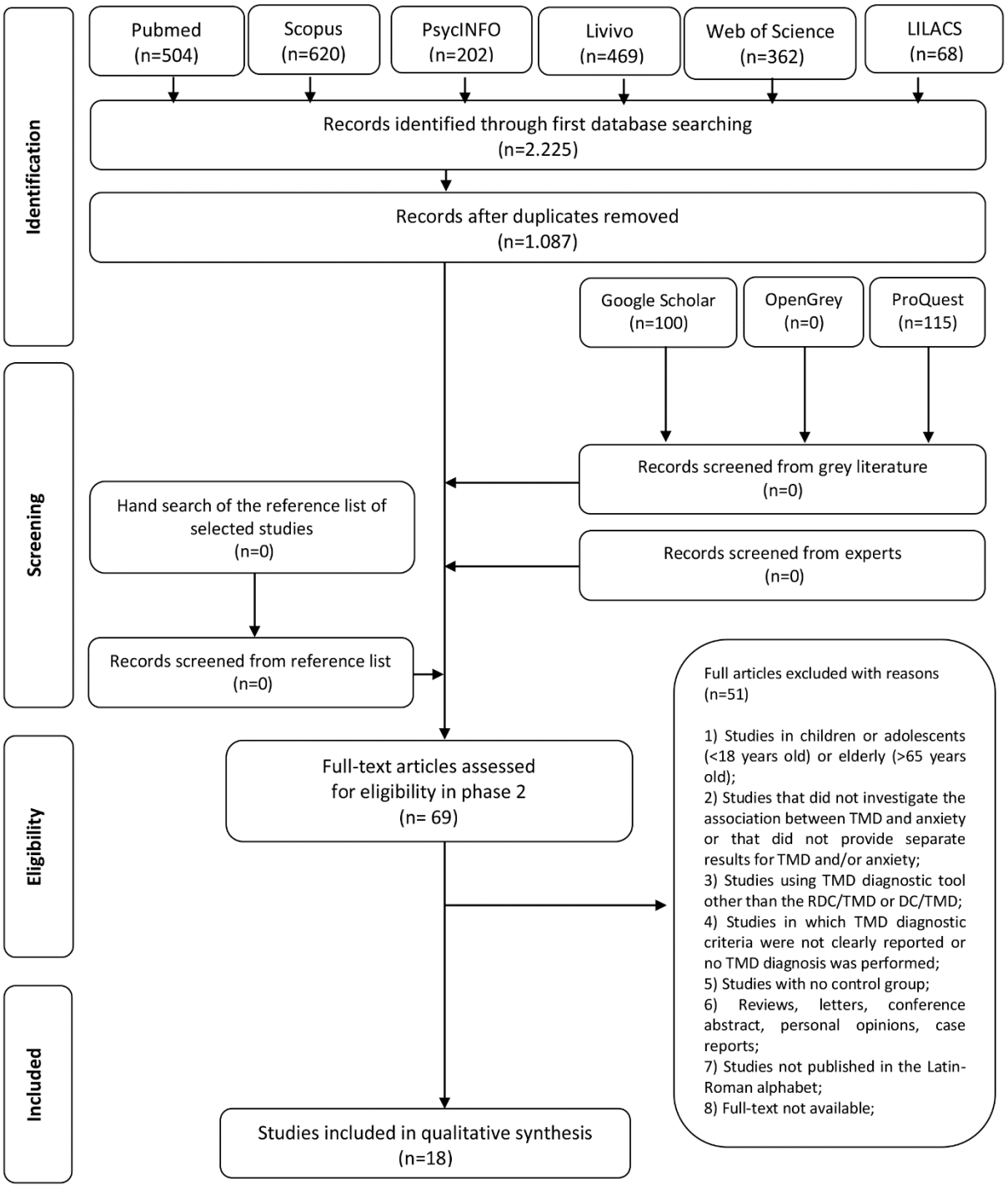


Figure 2 - Risk of bias summary, assessed by the Joanna Briggs Institute Critical Appraisal Checklist for analytical cross-sectional studies; author's judgments for each included study (generated using the software Review Manager 5.3, The Cochrane Collaboration).

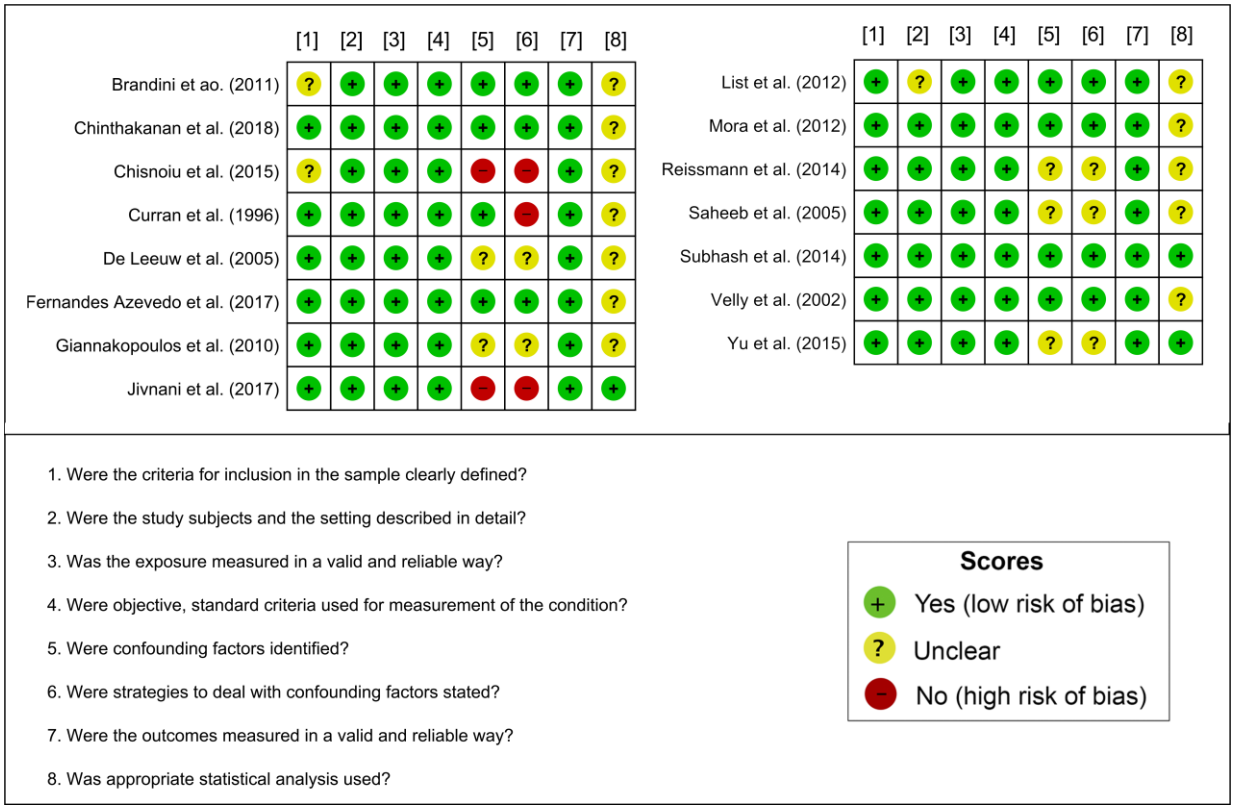


Figure 3 - Risk of bias summary, assessed by the Joanna Briggs Institute Critical Appraisal Checklist for case-control studies (a) and cohort studies (b); author's judgments for each included study (generated using the software Review Manager 5.3, The Cochrane Collaboration).

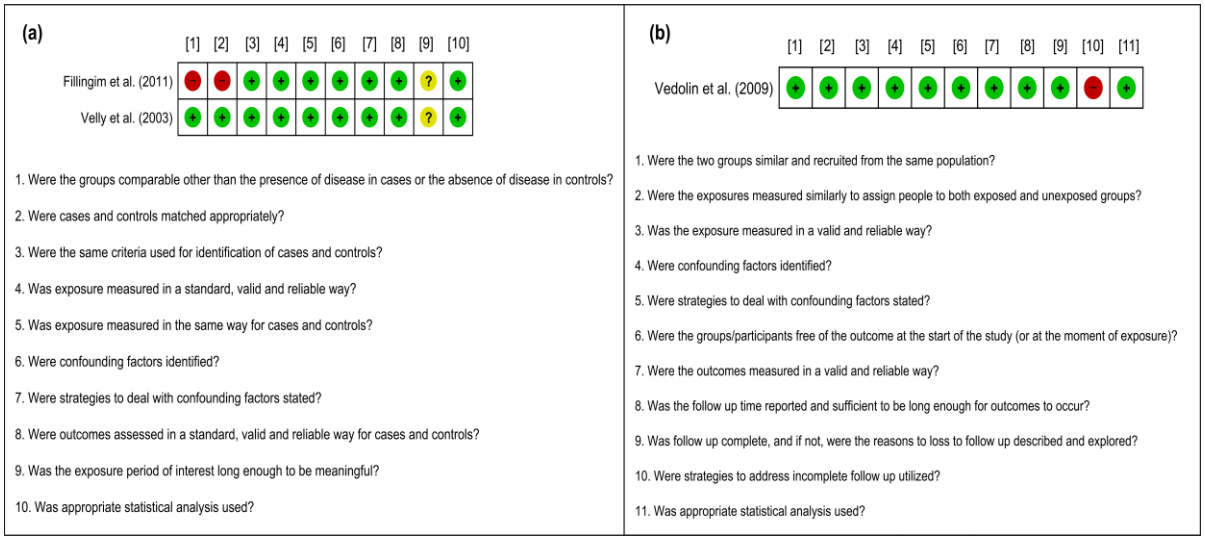
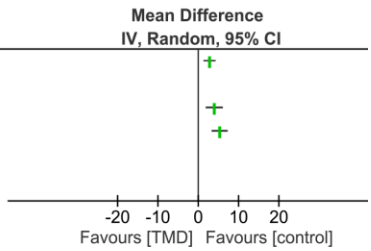


Figure 4 - Forest plot of TMD and anxiety scores for HADS (a), SCL-90R (b), and STAI (c) (generated using the software Review Manager 5.3, The Cochrane Collaboration).

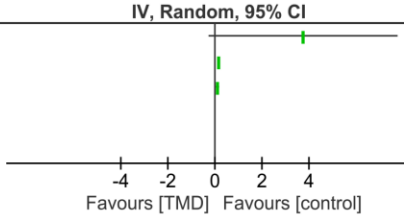
(a)

Study or Subgroup	TMD Mean	TMD SD	TMD Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
Chinthakanan et al. (2018)	7.1	2.9	21	4.3	2.1	23	2.80 [1.29, 4.31]
Giannakopoulos et al. (2010)	0	0	0	0	0	0	Not estimable
Jivnani et al. (2017) - articular TMD	9.26	4.05	19	5.29	3.21	34	3.97 [1.85, 6.09]
Jivnani et al. (2017) - pain related TMD	10.6	3.33	15	5.29	3.21	34	5.31 [3.31, 7.31]
Saheeb et al. (2005)	0	0	0	0	0	0	Not estimable
Subhash et al. (2014)	0	0	0	0	0	0	Not estimable



(b)

Study or Subgroup	TMD Mean	TMD SD	TMD Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
De Leeuw et al. (2005)	53.4	11.05	55	49.65	10.45	55	3.75 [-0.27, 7.77]
Fillingim et al. (2011)	0.35	0.03	185	0.19	0.01	1818	0.16 [0.16, 0.16]
List et al. (2012)	0.21	0.28	86	0.1	0.18	149	0.11 [0.04, 0.18]
Velly et al. (2002)	0	0	0	0	0	0	Not estimable
Velly et al. (2003)	0	0	0	0	0	0	Not estimable



(c)

Study or Subgroup	TMD Mean	TMD SD	TMD Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
Fernandes Azevedo et al. (2017)	42.3	5.2	37	43.4	4.8	67	-1.10 [-3.13, 0.93]
Fillingim et al. (2011)	32.69	0.73	185	30.9	0.24	1633	1.79 [1.68, 1.90]
Reissmann et al. (2014)	42.4	11.5	320	36.4	8.7	888	6.00 [4.62, 7.38]
Saheeb et al. (2005)	40.3	9.5	24	39.4	11.4	24	0.90 [-5.04, 6.84]
Yu et al. (2015)	0	0	0	0	0	0	Not estimable

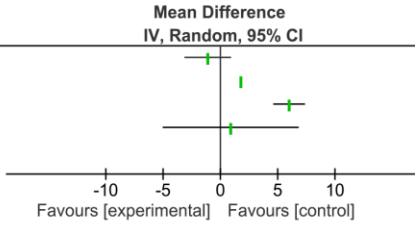


Table 1 - Summary of descriptive characteristics of included articles (n=18).

STUDY CHARACTERISTICS	**POPULATION CHARACTERISTICS**			**EXPOSITION CHARACTERISTICS**		**MAIN FINDINGS**			
Author (Year); Country **Study design**	**Sample (n/F)**	**Groups (n)**	**Mean age±SD or age range (in years)**	**TMD diagnostic methods and classification**	**Anxiety diagnostic methods**	**Results (Mean±SD, or other pertinent findings)**			**Main conclusion**
Brandini et al. (2011); Australia Analytical cross-sectional	n=29 (29F)	**TMD** N=15 **Control** N=14	**TMD** 31.3±10.7 **Control** 28.9±5.0	RDC/TMD	DASS-42	**TMD and anxiety** 10.86±10.9	**Control and anxiety** 1.42±1.91	**p-value** p=0.005	The TMD patients exhibited significantly higher anxiety scores than the control group.
Chinthakanan et al. (2018); Thailand Analytical cross-sectional	n=44 (32F)	**TMD** N=21 **Control** N=23	**TMD** 22.00±0.62 **Control** 26.05±1.34	RDC/TMD	HADS	**TMD and anxiety** 7.1±2.9	**Control and anxiety** 4.3±2.1	**p-value** p<0.01	TMD individuals showed significantly higher anxiety scores compared to controls.
Chisnoiu et al. (2015); Romania Analytical cross-sectional	n=79 (NR)	**TMD** N=37 (22F) **Control** N=42	**TMD** M.a.: 36 (IQ 28; 52) **Control** M.a.: 32 (IQ 22.5; 43.5)	RDC/TMD	BAI	**TMD and anxiety** Median 20 (IQ 11; 30)	**Control and anxiety** Median 10 (IQ 6; 18)	**p-value** p<0.001	The presence and level of anxiety is linked to the signs and symptoms of anxiety and temporomandibular joint disorder
Curran et al. (1996); United States of America Analytical cross-sectional	n=46 (46F)	**TMD** N=23 (23F) **Control** N=23 (23F)	**TMD** 26.9±NR **Control** 27.4±NR	RDC/TMD	STPI EAS	**STPI Baseline** TMD Mean: 23.83 **EAS Baseline** TMD Mean: 24.7	**STPI Baseline** Control Mean: 19.35 **EAS Baseline** Control Mean: 12.87	**STPI Baseline** p<0.03 **EAS Baseline** p<0.02	TMD individuals exhibited significantly higher anxiety scores in baseline evaluation in both STPI and EAS scales compared to the control group.

De Leeuw et al. (2005); United States of America Analytical cross-sectional	n=110 (106F)	**TMD** N= 55 (53F) **Control** N=55 (53F)	**TMD** 32.3±12.5 **Control** 32.6±12.7	RDC/TMD	SCL90-R	**TMD and anxiety** 53.40±11.05	**Control and anxiety** 49.65±10.45	**p-value** p=0.071	No significant differences were observed regarding anxiety scores in TMD comparing to the control group.
Fernandes Azevedo et al. (2017); Brazil Analytical cross-sectional	n=105 (NR)	**TMD** N= 38 **Control** N=67	NR	RDC/TMD Axis I	STAI	**TMD and anxiety** <u>State-anxiety</u> Mild (n=22) Moderate (n=15) <u>Trait-anxiety</u> Mild (n=24) Moderate (n=14) <u>State-anxiety</u> 42.3 ± 5.2 <u>Trait-anxiety</u> 43.3 ± 4.5	**Control and anxiety** <u>State-anxiety</u> Mild (n=47) Moderate (n=20) <u>Trait-anxiety</u> Mild (n=36) Moderate (n=31) <u>State-anxiety</u> 43.4 ± 4.8 <u>Trait-anxiety</u> 44.3 ± 6.2	**p-value*** <u>State-anxiety</u> p=0.224 <u>Trait-anxiety</u> p=0.348 *Chi-Square test	No significant differences were observed regarding state- and trait-anxiety in TMD comparing to the control group.
Fillingim et al. (2011); United States of America Case-control	n=1818 (NR)	**TMD** N=185 (NR) **Control** N=1633 (NR)	18-44 years	RDC/TMD	SCL-90R STAI	**SCL-90R (mean±standard error)** Control (0.19±0.01) TMD (0.35±0.03) p<0.0001 **STAI State (mean±standard error)** Control (30.90±0.24) TMD (32.69±0.73) p=0.0162 **STAI Trait (mean±standard error)** Control (35.50±0.24) TMD (38.59±0.81) p<0.0001			Significant higher scores of both SCL-90R and STAI scales were observed in TMD individuals compared to control groups. A greater degree of anxiety, as measured by SCL-90R and STAI scales, was associated with statistically significant greater TMD odds, with OR ranging

						Standardized OR (95%CI)*	**Standardized OR (95%CI)***	**Imputed effect estimates**	from 1.2 to 1.5.
						SCL-90R OR=1.4 (95%CI, 1.2-1.6)	**SCL-90R** OR=1.5 (95%CI, 1.3-1.7)	**SCL-90R** OR=1.4 (95%CI, 1.3-1.7)	
						STAI State OR=1.2 (95%CI, 1.1-1.4)	**STAI State** OR=1.3 (95%CI, 1.1-1.5)	**STAI State** OR=1.3 (95%CI, 1.1-1.5)	
						STAI Trait OR=1.4 (95%CI, 1.2-1.7)	**STAI Trait** OR=1.5 (95%CI, 1.3-1.7)	**STAI Trait** OR=1.5 (95%CI, 1.3-1.7)	
						*Adjusted for study site	*Fully adjusted effect		
Giannakopoulos et al. (2010); Germany Analytical cross-sectional	n=222 (161F)	**TMD** Myofacial pain only (n=88/67F) Joint pain only (n=43/32F) **Control** Non-TMD chronic facial pain (n=45/35F) No chronic pain (n=46/27F)	**TMD** Myofacial pain only Male (40.3±14.4) Female (41.2±14.5) Joint pain only Male (35.3±10.8) Female (39.6±14.5) **Control** Non-TMD chronic facial pain Male (42.7±12.4) Female	RDC/TMD	HADS	**TMD and anxiety** Myofacial pain only Male (5.43±3.9) Female (6.56±4.34) Joint pain only Male (5.09±4.64) Female (5.34±3.57)	**Control and anxiety** Non-TMD chronic facial pain Male (6.60±3.86) Female (4.86±3.58) No chronic pain Male (5.05±3.66) Female (6.04±4.88)	**p-value*** **Males** p=0.772 **Females** p=0.217 ***ANOVA**	No significant differences were observed regarding HADS anxiety scores in both males and females considering the TMD and control subgroups.

			(44.0±15.9) No chronic pain Male (46.3±15.3) Female (38.4±16.7)						
Jivnani et al. (2017); India Analytical cross-sectional	n= 68 (34F)	**Group 1 (Non-TMD)** N=34 **Group 2 (pain related TMD and headaches)** N=15 **Group 3 (intra-articular joint disorders/disc displacement)** N=19	**Group 1** 21.12±1.97 **Group 2** 21.79±2.18 **Group 3** 21.79±2.18	DC/TMD	HADS	**TMD and anxiety** **Group 2** 10.60±3.33 **Group 3** 9.26±4.05	**Control and anxiety** **Group 1** 5.29±3.213	**p-value** **Group 1 vs group 2** P<0.001 **Group 1 vs group 3** P<0.001 **Group 2 vs Group 3** P>0.05	A positive association of TMD with anxiety was found compared to non-TMD individuals; however, there was no association between anxiety and type of TMD diagnosis.
List et al. (2012); United States of America Analytical cross-sectional	N=705 (NR)	**Infrequent episodic headaches and TMD (IEHA TMD+)** N=72 **Frequent episodic headaches and TMD (FEHA TMD+)** N=172 **Chronic headaches and TMD (CHD TMD+)**	**HA- TMD+** 37.8±15.1 **IEHA TMD+** 34.7±12.9 **FEHA TMD+** 35.1±11.8 **CHD TMD+** 41.5±13.7 **HA- TMD-** 37.6±13.4	RDC/TMD	SCL-90R	**TMD and anxiety** **HA- TMD+** 0.21±0.28 **IEHA TMD+** 0.32±0.48 **FEHA TMD+** 0.32±0.45 **CHD TMD+** 0.70±0.78	**Control and anxiety** **HA- TMD-** 0.10±0.18	**P-value for trend across TMD+ groups** p<0.001	Emotional functioning showed a significant score increase, *i.e.*, more impaired emotional functioning in anxiety (P < .001) with increased frequency of headache

		N=65 **No headache and TMD (HA-TMD+)** N=86 **Control No headache and no TMD (HA- TMD-)** N=149							
Mora et al. (2012); Germany Analytical cross-sectional	N=106 (89F)	**Chronic TMD** N=36 (28F) **Pain free bruxism** N=34 (29F) **Control** N=36 (32F)	**Chronic TMD** 27.4±6.8 **Pain free bruxism** 25.7±4.5 **Control** 24.3±5.8	RDC/TMD axis I	GAD-7	**TMD and anxiety** **Chronic TMD** 14.05±2.65 **Pain free bruxism** 12.00±2.95	**Control and anxiety** **Control** 10.72±3.00	**MANOVA** P<0.0001 ***Post-hoc* Scheffé group comparison** **TMD and anxiety only** P<0.0001	Individuals with TMD reported higher levels of anxiety compared to healthy controls
Reissmann et al. (2014); Germany Analytical cross-sectional	N=1208 (1157F)	**TMD** N=320 (269F) **Control** N=888 (503F)	**TMD** 39.4±15.4 **Control** 40.4±11.8	RDC/TMD	STAI	**STAI State** TMD and anxiety 42.4±11.5 **STAI Trait** TMD and anxiety 41.7 (40.5-42.8)	**STAI State** Control and anxiety 36.4±8.7 **STAI Trait** Control and anxiety 38.4 (37.8-39.0)	**STAI State** P<0.001 **STAI Trait** P<0.001	TMD patients were more psychosocially impaired compared to controls, as indicated by the RDC/TMD Axis II measures. Moreover, STAI scores indicated that trait anxiety was more pronounced in TMD patients than in controls.
Saheeb et al. (2005); Nigeria Analytical cross-sectional	N=48 (24F)	**TMD** N=24 (12F) **Control** N=24 (12F)	**TMD** 43.9±15.9 19 to 70 **Control** 44.1±NR	RDC/TMD	STAI and HADS	**STAI-X1 scores** TMD and anxiety 40.3±9.5 **STAI-X2 scores** TMD and anxiety	**STAI-X1 scores** Control and anxiety 39.4±11.4 **STAI-X2 scores**	**STAI-X1 scores** P>0.05 **STAI-X2 scores**	No significant association was observed in STAI and HADS measurements regarding TMD individuals compared to

			18 to 70			37.0±9.9 **HADS anxiety** TMD and anxiety ≥11: 33.3% <11: 66.7%	Control and anxiety 39.7±9.2 **HADS anxiety** Control and anxiety ≥11: 25% <11: 75%	p>0.05 **HADS anxiety** p>0.05	healthy controls.
Subhash et al. (2014); India Analytical cross-sectional	N=505 (180F)	**TMD (Group 1)** N= 255(77F) **Control (Group 2)** N= 250(103F)	**TMD** 29.07 18 to 49 **Control** 30.12 18 to 49	RDC/TMD	HADS	**TMD and anxiety scores** Males 0-7: 81 8-10: 78 11-21: 19 Females 0-7: 31 8-10: 37 11-21: 9 Overall 0-7: 112 8-10: 115 11-21: 28	**Control and anxiety scores** Males 0-7: 116 8-10: 30 11-21: 1 Females 0-7: 84 8-10: 18 11-21: 1 Overall 0-7: 200 8-10: 48 11-21: 2	**p-value** Males 0-7* 8-10* 11-21* Females 0-7* 8-10* 11-21* Overall 0-7* 8-10* 11-21* *p<0.05	The majority of the subjects (both male and female) in group 2 had normal anxiety levels when compared to group 1. Subjects with borderline abnormal anxiety (scores of 8–10) and abnormal anxiety (scores of 11–21) levels were more in group 1 in comparison with group 2. These results showed statistically significant difference with regards to anxiety levels between group 1 and group 2.
Vedolin et al. (2009); Brazil Cohort study	n=68 female	**Masticatory myofascial pain** N=15 **Control** N=14	**Masticatory myofascial pain** 31.3±10.7 **Control** 28.9±5.0	RDC/TMD	DASS-42	**Masticatory myofascial pain and anxiety** T1 (week prior) 1.6±0.8[a] T2 (week of academic examination) 1.6±0.8[a]	**Control and anxiety** T1 (week prior) 1.7±0.8[ab] T2 (week of academic examination) 1.8±1.0[a]		There was no difference between groups in anxiety at any time (p>0.05). When comparing the levels of anxiety and stress between times in each group, T2 had higher

						T3 (week after) 1.0±0.7[b] T4 (after summer vacation) 1.2±1.2[ab] Times with the same letter do not have significant difference, in the specified group	T3 (week after) 1.2±1.0[ab] T4(after summer vacation) 1.2±0.9[b] Times with the same letter do not have significant difference, in the specified group	values, although not statistically significant for both groups.
Velly et al. (2002); Canada Analytical cross-sectional	N=159 (107F)	**Disc displacement*** N=59 (43F) **Control** N=100 (64F) *Without myofascial pain	36.0±NR 18 to 58	RDC/TMD	SCL-90R	**Disc displacement and anxiety** Crude OR Category ≤0.6 OR=1.0 (reference) Category ≤0.6 OR=2.02 (95%CI, 1.05-4.63)	**Disc displacement and anxiety** Initial model* Category ≤0.6 OR=1.0 (reference) Category ≤0.6 OR=2.53 (95%CI, 1.09-5.89)	**Disc displacement and anxiety** Final model** OR=1.0 (reference) Category ≤0.6 OR=2.40 (95%CI, 1.01-5.73)	Higher levels of anxiety were associated with disc displacement.
Velly et al. (2003); Canada Case-control	N=183 (131F)	**Chronic myofascial pain** N=83 (67F) **Control** N=100 (64F)	31.4±5.9 23 to 52	RDC/TMD	SCL-90R	**Chronic myofascial pain and anxiety** Category ≤0.6 N=53 Category >0.6 N=30 **Control and anxiety** Category ≤0.6 N=86 Category >0.6 N=14	**Adjusted OR Model II*** Category ≤0.6 OR=1.0 (reference) Category ≤0.6 OR=4.39 (95%CI, 1.07-18.10) *All putative risk factors and confounders,	**Adjusted OR Model III**** OR=1.0 (reference) Category ≤0.6 OR=3.48 (95%CI, 1.69-7.15) **Risk factors and confounders noted in the study, plus anxiety.	Higher levels of anxiety were associated with chronic myofascial pain.

						plus anxiety **Crude OR** Category ≤0.6 OR=1.0 (reference) Category ≤0.6 OR=3.48 (95%CI, 1.69-7.15)		
Yu et al. (2015); China Analytical cross-sectional	N=616 male pilots	**TMD** N=205 **Control** N=411	31.4±5.9 23 to 52	RDC/TMD	STAI-Trait	**TMD and non-TMD*** **STAI-T score** Z=-1.97 **Multiple logistic regression** **STAI-T score** OR=2.48 (95%CI, 1.25-4.90)	**p-value Kruskal-Wallis test** p=0.049 **Multiple logistic regression** p=0.009	A significant association was observed in STAI-T scores regarding TMD individuals compared to controls.

Legend: BAI: Beck Anxiety Inventory; CI: Confidence Interval; DASS-42: Depression, Anxiety, and Stress Scale; DC: Diagnostic Criteria; EAS: Emotion Assessment Scale; F: Female; GAD-7: Patient Health Questionnaire; HADS: Hospital Anxiety and Depression Scale; NR: Not reported; NS: Not significant; OR: Odds Ratio; PAS-SR: Panic-agoraphobic spectrum self-report; RDC: Research Diagnostic Criteria; SCL-90-R: Symptom Checklist-90-Revised; SD: Standard Deviation; STAI: State-Trait Anxiety Inventory; TMD: Temporomandibular Disorder; STPI: State-Trait Personality Inventory.

APÊNDICE A

Appendix 1 - Database search strategy.

Database	**Search** Jun 8th 2018	**Items found**
PubMed	("anxiety"[MeSH Terms] OR "Anxiety Disorders"[MeSH Terms] OR "anxiety"[All Fields] OR "anxieties"[All Fields] OR "hypervigilance"[All Fields] OR "anxiousness"[All Fields] OR "nervousness"[All Fields] OR "agoraphobia"[All Fields] OR "panic disorder"[All Fields] OR "social phobia"[All Fields] OR "Social Phobias"[All Fields] OR "post traumatic stress disorder"[All Fields] OR "Worry" OR "posttraumatic stress disorder"[All Fields]) AND ("temporomandibular joint disorders"[MeSH Terms] OR "temporomandibular joint"[MeSH Terms] OR "temporomandibular joint"[All Fields] OR "temporo mandibular joint"[All Fields] OR "temporomandibular disorder"[All Fields] OR "temporo mandibular disorder"[All Fields] OR "temporomandibular disorders"[All Fields] OR "temporo mandibular disorders"[All Fields] OR "Temporomandibular dysfunction"[All Fields] OR "Temporo mandibular dysfunction"[All Fields] OR "Temporomandibular dysfunctions"[All Fields] OR "Temporomandibular dysfunctions"[All Fields] OR "TMD"[All Fields] OR "TMJD"[All Fields] OR "TMJ"[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 "costen's syndrome"[All Fields] OR "myofacial pain dysfunction syndrome"[All Fields])	504

Scopus	TITLE-ABS-KEY("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR "Worry" OR "posttraumatic stress disorder") AND TITLE-ABS-KEY("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	620
Web of Science	("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR "Worry" OR "posttraumatic stress disorder") AND ("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	362
PsycINFO	("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR "Worry" OR "posttraumatic stress disorder") AND	202

	("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	
LIVIVO	("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR “Worry” OR "posttraumatic stress disorder") AND ("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	469
LILACS	(tw:("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR “Worry” OR "posttraumatic stress disorder" OR ansiedade* OR "desordens de ansiedade" OR hipervigilância OR nervosismo OR agorafobia OR "transtorno de estresse pós-traumatico" OR "transtorno do pânico" OR “Preocupação OR "transtorno de pânico" OR "desórdenes de ansiedad" nerviosismo OR hipervigilancia OR ahorafobia OR	68

	"trastorno de ansiedad social" OR "trastorno de estrés postraumático" OR “Preocupación” OR "transtorno del pánico")) AND (tw:("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome" OR "Articulação Temporomandibular" OR "Transtornos da Articulação Temporomandibular" OR "Transtornos Craniomandibulares" OR dtm OR temporomandibular* OR "temporo-mandibulares" OR "temporo-mandibular" OR "craniomandibulares" OR "cranio-mandibulares" OR "cranio-mandibular" OR "Articulación Temporomandibular" OR "Trastornos de la Articulación Temporomandibular" OR "Trastornos Craneomandibulares" OR craneomandibular* OR "craneo-mandibular" OR "craneo-mandibulares")) AND (instance:"regional") AND (db:("LILACS"))	
Grey Literature		
Google Scholar	(anxiety OR agoraphobia OR "panic disorder" OR "social phobia") AND ("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporomandibular disorders" OR TMD OR TMJD OR TMJ)	100
OpenGrey	("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR "Worry" OR "posttraumatic stress disorder") AND ("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular	0

	disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	
ProQuest	noft("anxiety" OR "anxieties" OR "hypervigilance" OR "anxiousness" OR "nervousness" OR "agoraphobia" OR "panic disorder" OR "social phobia" OR "Social Phobias" OR "post traumatic stress disorder" OR "Worry" OR "posttraumatic stress disorder") AND noft("temporomandibular joint" OR "temporo mandibular joint" OR "temporomandibular disorder" OR "temporo mandibular disorder" OR "temporomandibular disorders" OR "temporo mandibular disorders" OR "Temporomandibular dysfunction" OR "Temporo mandibular dysfunction" OR "Temporomandibular dysfunctions" OR "Temporomandibular dysfunctions" OR "TMD" OR "TMJD" OR "TMJ" OR "craniomandibular disorders" OR "craniomandibular disorder" OR "Craniomandibular dysfunction" OR "Craniomandibular dysfunctions" OR "costen's syndrome" OR "myofacial pain dysfunction syndrome")	115

APÊNDICE B

Appendix 2 - Articles excluded and the reasons for exclusion (n=51).

Reference	Author (year)	Reasons for Exclusion*
1.	Ajanovic et al. (2009)	3
2.	Azevedo et al. (2015)	3
3.	Broersma-van der Meulen et al. (1994)	8
4.	Burris et al. (2010)	5
5.	Casanova-Rosado et al. (2006)	1
6.	Caspersen et al. (2013)	2
7.	Chen et al. (2005)	7
8.	De Oliveira Solis et al. (2017)	4
9.	Ferrando et al. (2004)	1
10.	Fillingim et al. (2013)	5
11.	Glaros, A. G. (2000)	8
12.	Huang et al. (2001)	7
13.	Jiang et al. (2000)	7
14.	Jones et al. (1997)	1
15.	Kiliçoglu et al. (2009)	3
16.	Kindler et al. (2012)	3
17.	Kuhlow, C. A. (1998)	3
18.	Lajnert et al. (2010)	4
19.	Lei et al. (2016)	7
20.	Lei et al. (2015)	1

21.	Lin et al. (2017)	3
22.	Lin et al. (2016)	3
23.	Liu et al. (1997)	7
24.	McDermid, A. J. (2001)	3
25.	Monteiro et al. (2011)	1
26.	Morris et al. (1997)	3
27.	Munoz-Garcia et al. (2017)	3
28.	Mutlu et al. (2005)	8
29.	Nam et al. (1998)	7
30.	Nifosí et al. (2007)	5
31.	Ohrbach et al. (1998)	5
32.	Pallegama et al. (2005)	3
33.	Panteleev et al. (2014)	7
34.	Pasinato et al. (2011)	2
35.	Pesqueira et al. (2010)	1
36.	Reiter et al. (2017)	5
37.	Reiter et al. (2015)	5
38.	Riggs et al. (1996)	8
39.	Rocha et al. (2017)	3
40.	Segù et al. (1999)	8
41.	Sirirungrojying et al. (1998)	8
42.	Solis et al. (2017)	4
43.	Suvinen et al. (2013)	5
44.	Tavares et al. (2016)	5

45.	Tournavitis et al. (2017)	5
46.	Uhac et al. (2006)	8
47.	Saravejo Ajanovi et al. (2014)	4
48.	Wilson et al. (1994)	3
49.	Xia et al. (2016)	7
50.	Xu et al. (2005)	7
51.	Yang et al. (2014)	7

*Legend:

1) Studies in children or adolescents (<18 years old) or elderly (>65 years old); 2) Studies that did not investigate the association between TMD and anxiety or that did not provide separate results for TMD and/or anxiety; 3) Studies using TMD diagnostic tool other than the RDC/TMD or DC/TMD; 4) Studies in which TMD diagnostic criteria were not clearly reported or no TMD diagnosis was performed; 5) Studies with no control group; 6) Reviews, letters, conference abstract, personal opinions, case reports; 7) Studies not published in the Latin-Roman alphabet; 8) Full-text not available;

APPENDIX 2 – REFERENCES

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4 CONCLUSÃO

Com base nas evidências atuais, na maioria dos estudos, a DTM foi positivamente associada a ansiedade entre adultos. No entanto, ferramentas para avaliação da ansiedade foram consideradas bastante heterogêneas entre os estudos e as evidências foram consideradas limitadas para explorar inferências com relação à causalidade. Assim, estudos longitudinais adicionais usando ferramentas homogêneas para avaliação da ansiedade são recomendados.

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