Association of stress, anxiety and depression with temporomandibular disorders in young adults – a systematic review

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Abstract

Introduction: The current systematic review aims to explore whether there is an association between temporomandibular disorder (TMD) and psychological factors such as stress, anxiety, and/or depression in young adults.
Material and methods: A systematic search was conducted on 14 March 2023 for publications from inception until February 2023, according to the PRISMA guidelines, using five major databases: the Cochrane Database of Systematic Reviews, PubMed, EMBASE, Web of Science, SCOPUS, and Google Scholar. The PECO framework formulated the focused question "Is there an association between TMD and psychological factors (stress/depression/anxiety) among young adults?" The study was previously registered with trial no. CRD42023407502. Articles were selected according to the inclusion criteria. For each study, risk of bias was applied to assess the quality of the included article using the Newcastle-Ottawa scoring system. The level of evidence was determined using GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) scoring.
Results: Sixteen studies were included for final qualitative synthesis and the certainty of evidence assessment out of the 15 546 studies identified initially from different databases, with the total of 6362 participants. The included studies confirmed the association between different types of TMD and psychological factors in young adults. The risk of bias among the included studies was low, and the GRADE evidence reported was very low among included studies.
Conclusions: Within the scope of this systematic review, it could be concluded that there is an association between temporomandibular disorder and psychological factors. Painful TMD in young females was associated with anxiety and stress.

Key words: temporomandibular disorder, stress, anxiety, depression, young adults.

Introduction

Temporomandibular joint disorder (TMD) is associated with muscular and neuromuscular impairment of the temporomandibular joint, affecting masticatory muscles and the associated structures [1]. This disorder is classified into two subgroups: of muscular and articular origin. When TMD is due to muscular dysfunction, the signs and symptoms are associated with stomatognathic structures. If TMD is due to articular dysfunction, the signs and symptoms are related to the temporomandibular joint [2].

The etiological factors associated with TMD are still unknown; however, it is acknowledged to have a multifactorial origin. This condition can occur due to parafunctional habits (bruxism, clenching, etc.), psychological (anxiety, stress, depression, etc.), physiological structure (occlusion, trauma), and genetic conditions. Studies have suggested that psychological, parafunctional, and physiological factors predispose, initiate, and perpetuate the development of signs and symptoms associated with TMD [3–5].

According to recent research on the prevalence of TMD, approximately 31% of adults/elderly and 11% of children in the general population have some type of TMD [2]. While evaluating the subgroups of TMD (articular and muscular), it was reported that the most prevalent subgroup was disc displacement with reduction, affecting around 26% of adults and 7.2% of children [2]. Studies describe various acute and chronic symptoms such as locking or limitations in jaw opening, closing, and lateral movements. Other symptoms include pain and/or discomfort in the temporomandibular joint (TMJ), ears, mastication, and pain around the eyes and face [6–9].

Previously published studies have mentioned that psychological disorders and impairments significantly affect the development of temporomandibular disorders [3, 4, 6, 7, 10, 11]. According to the prospective orofacial pain evaluation and risk assessment (OPERA) analysis, individuals suffering from TMD encounter higher psychological issues than healthy individuals [4]. Hence, psychological factors act as both perpetuating and initiating agents correlated with the progression of TMD [11]. Psychosomatic factors such as stress, depression, and anxiety may contribute to the development and initiation of painful temporomandibular disorder.

The direct connection between depression and TMD in young adults has been a much-debated topic in oral and maxillofacial research. Research has focused on the interrelation between TMD and depression, with less emphasis on stress and anxiety [12]. However, chronic stress and anxiety lead to depression, leading to painful TMD in young adults [7].

Studies have strongly indicated the correlation between painful TMD and stress [13–15]. Compared to healthy controls, patients with painful TMD report high psychological impairment [16, 17]. Academic stress is reported to be high in university students, leading to parafunctional habits such as bruxism, disturbed sleep, and chronic TMD [9, 18]. Although studies have shown a positive relationship between anxiety and painful TMD [16, 17], the role of stress in the onset of TMD is arguable. It has been postulated that state anxiety and stress have a bi-directional relationship, where a stressful situation influences anxiety.

Previous studies also indicated that anxiety is frequently found as an associated risk factor in the perpetuation of TMD, because it can alter pain perception and provoke release of neurotransmitters linked with parafunctional habits, resulting in hyperactive temporomandibular joint muscles related to chewing, leading to joint overload [7, 8, 19–22]. Anxiety is divided into two subgroups according to the symptoms, state anxiety and trait anxiety. State anxiety is defined as a pathological emotional reaction of varied severity, whereas trait anxiety is an altered emotional state that forms a stable behavior character [13, 23]. A recent systematic review identified an association between anxiety and TMD, stating that anxiety is associated with TMD [13, 24]. Similarly, other systematic reviews have evaluated the association of TMD with depression and anxiety and found that both are associated [2]. Another review evaluated the association of stress and anxiety with TMD and found an association between both factors [15, 25].

Numerous studies have evaluated the impact of psychological stress and depression on university students' academic performance and well-being. Research indicates high mental health issues among university students and professionals [17]. In 2010, Stallman *et al.* reported that 19.2% of Australian university students had mental health disorders and 67.4% had subsyndromal symptoms [26], substantially higher than the general population. Job-related stress and TMD were positively corelated in an Indonesian study. These findings suggest that university students and young professionals are more stressed and depressed than the general population. This systematic review focused on individuals aged 18–40, based on Carlsson and Gonçalves' conclusion that symptoms of TMD were most prevalent in this age spectrum [27, 28].

Despite the massive literature, an agreement on the burden of psychological factors as a reliable indicator of the prevalence of a psychological disorder in patients with TMD is lacking. Moreover, no review has evaluated the interrelation and association of these three psychological factors in the initiation, perpetuation, and development of different types of TMD in young adults. Hence, this systematic review aims to evaluate the association of psychological factors (stress, depression, and anxiety) with different types of TMD in young adults.

Material and methods

The current systematic review followed the Preferred Reporting System for Systematic Review

and Meta-analyses (PRISMA) guidelines [29]. Institutional review board approval was waived as this was a review, and no patient data were accessed. Following this, a protocol was prepared and submitted to PROSPERO (CRD42023407502) before starting this review.

Focus question

The focus question for this systematic review was, "Is there an association between temporomandibular joint disorder and psychological factors (stress/depression/anxiety) among young adults?" Therefore, our selection criteria according to PECO (population, exposure, comparison, and control) was to screen observational studies involving young adults between the age of 18 to 40 years (P) exposed to TMD (E) as compared to patients without TMD (C), who had the presence of psychological factors (stress/anxiety/depression) (O).

Study selection

Studies were included if they (1) reported original data; (2) reported TMD, stress and/or anxiety and/or depression among young adults; (3) were studies published in peer-reviewed journals; (4) used a valid method (including questionnaire) to assess for TMD, stress, depression, and anxiety in the young cohort; (5) studies with standard sample size. Studies reporting the same cohort with a similar sample size were only included if the research question differed. Studies that did not provide measurable outcomes and qualitative data were excluded. Studies reporting psychological factors other than stress, depression, and anxiety, without a valid method for estimation and evaluating TMD with other conditions, were not included. Case reports, case series and letter to editors were also excluded. Electronic searches were combined with evaluating the cited reference and cross-references of the review articles of similar studies to identify additional studies. Two reviewers (H.A. and L.A.) independently searched the data and reviewed the titles, abstracts, and complete articles. Disagreements were resolved by consensus.

Search strategy

Electronically, the Cochrane Database of systematic reviews, PubMed, EMBASE, Web of Science, SCOPUS, and Google Scholar were searched on March 14, 2023, for studies published from inception until February 2023. The investigators conducted the literature search after discussing the protocol of the study. The search strategy employed Medical Subject Headings (MeSH) keywords: ['temporomandibular disorder' (MeSH) or 'TMD'] AND ['Axis II' or 'Axis I' or 'psychosocial' or 'depression' or 'anxiety' or 'stress' (MeSH) or 'chronic pain' (MeSH)]. A summary of the data search is illustrated in Supplementary Table SI.

Study selection process

The articles were selected by two evaluators (L.A. and H.A.). All references were exported and managed by EndNote 20 software only after inclusion and exclusion criteria were identified. Following the exclusion of the duplicate studies (n = 9367), articles were screened according to inclusion criteria based on title and abstract. The resulting bibliographies (n = 27) were fully read and excluded if they did not meet the researchers' PECO criteria. Supplementary Table SII shows excluded studies with reasons.

Data extraction

Two evaluators independently (H.A. and L.A.) extracted the information from the included article using a standardized format: (1) name of author/country/year of publication; (2) study design; (3) sample size, age, male:female ratio; (4) association of TMD with depression/anxiety/stress; (5) diagnostic instrument or rating scale used in the study; (6) statistical analysis; (7) key findings; (8) inference. One evaluator conducted the complete abstraction of the data, and the other two verified the accuracy.

Risk of bias

The Newcastle-Ottawa Scale (NOS) for calculating the risk of bias tool [30] for cross-sectional and case-control studies was employed to measure the methodological quality of the included studies. According to the NOS guidelines, stars were used to indicate the methodological scoring of each article, with a scale from 0 to 10. Two evaluators performed a risk of bias assessment to evaluate the quality of the included article. Three key domains were considered during the assessment of case-control and cross-sectional studies: 1) selection of the sample (appropriate defining of case and control), 2) exposure (exposure verification, nonresponse rate, and evaluation methods), and 3) compatibility. The judgment of each domain was based on a maximum score of 10 and presented a low risk of bias; if two or more domains were less than four, the study would present a high risk.

Quantitative analysis (meta-analysis)

Due to discrepancies in the methodological quality of included studies, such as participants' age, TMD diagnosis, and presentation of anxiety, stress, and depression indices in different ways,

conducting a meta-analysis was challenging. Furthermore, studies with individuals of a similar age and the same TMD diagnosis and anxiety analysis methods had varied methodological quality. Consequently, the meta-analysis of results would exhibit inconsistency and significant heterogeneity. Hence, in this systematic review, the authors incorporated a concise overview of the findings derived from the GRADE system.

GRADE tool for evidence

The grading of recommendations assessments, development, and evaluation (GRADE) was employed to inspect the level of evidence. This grading system provides evidence of the quality of articles and measures the strength of healthcare recommendations [31]. The level of evidence is measured as low or very low if there is a severe flaw in the risk of bias, inconsistency, impression, indirectness, and bias in the publication of articles. The GRADE system does not evaluate the effect and dosage of the treatment entity [31]. Hence, in this study, GRADE was used to measure psychological factors associated with TMD in young individuals and is divided into six parts according to the psychological factors.

Results

Study selection and characteristics

A total of 15 546 studies were found through different databases. Out of these, 9367 were removed due to duplication with the help of the reference manager. The title and abstract of the remaining 6179 articles were examined. This resulted in the exclusion of 6152 articles and the selection of 27 articles for full-text reading. The authors excluded studies that did not meet the PECO criteria. The reasons were as follows: age group above 40, other psychological factors (sleep disturbance), and access to full articles. Therefore, this systematic review includes 16 studies for qualitative synthesis (Figure 1).

Results of individual studies

Out of 16 selected studies, there were eight cross-sectional studies [19, 32–37], two longitudinal studies [38, 39], and five case-control studies [17, 40–43]. The research question was answered after analyzing the data extraction of the included studies. The data extraction table indicates an association between TMD in young adults and psychological factors (Table I). Most studies [14, 23, 37, 44] evaluated TMD as associated with anxiety, primarily in college-going females [15, 23, 37, 45]. The included studies were carried out in 10 different countries: India (n = 2), Brazil (n = 3), Indonesia (n = 2), Singapore (n = 2), Iran (n = 1), Australia (n = 1), Saudi Arabia (n = 2), Poland (n = 2), and China (n = 1). Hence, the included studies came from epidemiological studies that included populations from four different continents.

The cohorts of included studies were mainly (n = 5) dental students followed by university institutions (n = 4) and medical students (n = 2); one study each was conducted on the general population, hospital settings, high school graduates, and college students taking entrance exams. Certain studies may have obtained their sample selection from more than one location.

The diagnostic criteria used in the included studies for temporomandibular disorder were

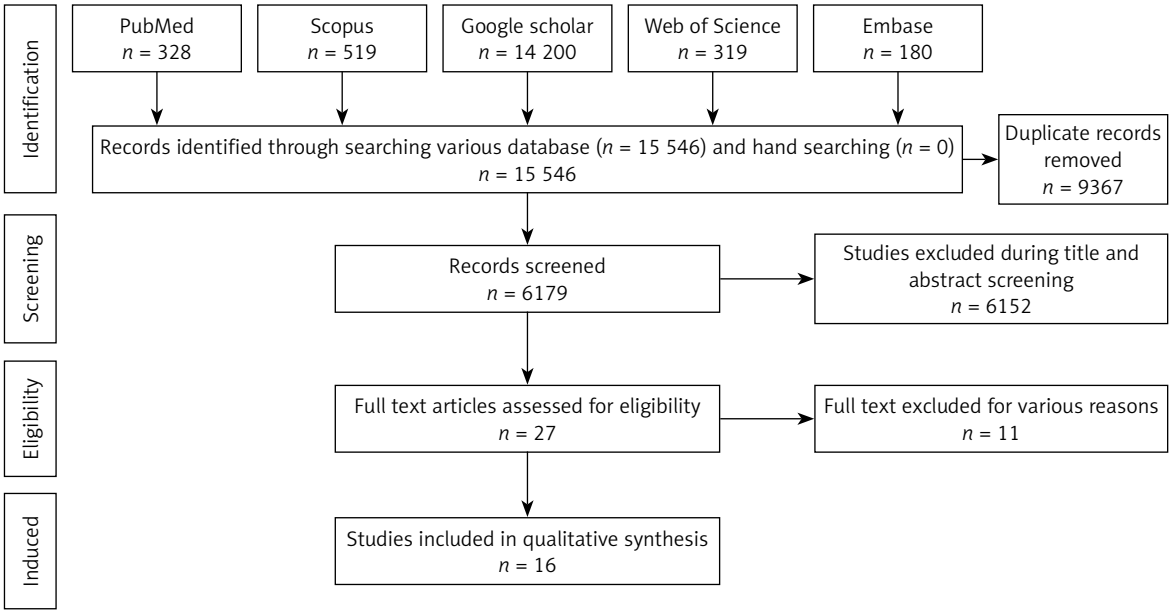

Figure 1. PRISMA flowchart

Table I. Basic characteristics of included articles

S. No.	Authors, year, country	Study design	Cohort (size, age, % M/F)	TMD and stress, depression, anxiety	Measures used (scales and questionnaire)	Statistical analysis	Findings	Inference
	Arya *et al.*, 2023, India [40]	Case-control study	855, ≥ 17 years, M (49.20%), F (50.80%)	All	DC/TMD and DASS 21	Mean, Kruskal-Wallis test and Whitney *U* test	Strongest correlations depression (rs = –0.52 to –0.65) with painful TMD symptoms	Psychological stress and anxiety increase the prospects of pain-related and intra-articular/combined TMD symptoms
2.	Yap *et al.*, 2022a, Singapore and Indonesia [42]	Cross-sectional study	901, 17–24 years, M (35%), F (65%)	All	FAI and DASS-21	Kruskal-Wallis and Spearman's rank	Strongest correlations between FAI and anxiety (rs = 0.50), and depression the weakest (rs = 0.37)	Anxiety may contribute to TMDs more than depression. Being female and anxious could increase the prospect of TMDs
3.	Yap *et al.*, 2022b, China [44]	Case-control study	961, mean age 33.2 years, M (200), F (761)	All	FAI and DASS 21	χ^2 test, Mann-Whitney, and Spearman correlation test	Significant differences were present in depression, anxiety, and stress scores	Stress and anxiety are associated with TMD. However, no significant association was found among the groups
4.	Yap *et al.*, 2022c, Singapore [35]	Cross-sectional study	734, 18–22 years, M (71), F (288)	All	RDC/TMD, Axis I and II, and DASS 21	Mann-Whitney test, Kruskal-Wallis and multivariate logistic regression	Depression and TMD have the strongest relation (odds ratio = –0.52 to 0.65). Multiple analyses found a strong association of anxiety in women associated with TMD (odds ratio = 2.07)	Anxiety and depression are associated with painful TMD, mostly in females
5.	Homeida *et al.*, 2022, Saudi Arabia [32]	Cross-sectional study	93, mean age 22.3 years, M (45), F (48)	Depression and anxiety	DC/TMD and PHQ Scale	Mean and frequency	A positive response to PHQ-4 (73%) had been diagnosed with painful TMDs. Moderate to severe anxiety associated with TMDs (p = 0.006)	Anxiety was associated with painful TMD, mostly in females
6.	Namvar *et al.*, 2021, Iran [41]	Case-control study	120, 18–24 years, M (55), F (65)	All	RDC/TMD, Axis I, and DASS-21	Mean, standard deviation, and numbers in univariate and multivariate regression model	Stress, anxiety, and depression had a significant effect on TMD (p < 0.2)	TMD is associated with all three factors, and females are more affected than males
7.	Cao *et al.*, 2021, Singapore [43]	Case-control study	400, 17–25 years, M (171), F (209)	All	FAI and DASS 21	Non-parametric and logistic regression tests	Moderate-to-severe depression, anxiety, and stress were present in 31.0%, 36.8%, and 16.5% of the subjects	Psychological factors are associated with TMD, mainly in females

Table I. Cont.

S. No.	Authors, year, country	Study design	Cohort (size, age, % M/F)	TMD and stress, depression, anxiety	Measures used (scales and questionnaire)	Statistical analysis	Findings	Inference
8.	Maślak-Bereś *et al.*, 2019 Poland [17]	Case-control study	260, mean age 18 years	Depression and stress	TMD/RDC and PSS-10, and BDI	ANOVA, Kruskal-Wallis test, and Shapiro-Wilk test	BDI = 7.07 and PSS-10 = 19.7 A group with mild TMD, 4.96 (0–13) and 15.96 (5–24) in group with chronic pain TMD and 8.3 (0–19) and 20.3 (5–30) in a group with arthralgia and joint pain in TMD	Stress and depression are associated with TMD. However, no significant association was found among the groups
9.	Sójka *et al.*, 2019, Poland [19]	Cross-sectional study	271, 18–32 years, M (91), F (180)	All	The questionnaire and 4DSQ questionnaire	Mean and frequency	Students with TMD reported a high stress level compared to healthy students. There was a statistically significant result noted for responses in both the groups	Symptoms of TMD, such as the amount of stress and non-bite parafunction, were more intense in females than males
10.	Alahmary, 2019, Saudi Arabia [23]	Cross-sectional study	105, 20–35 years, M (9), F (96)	Depression and anxiety	FAI and HAD scale	Multivariate logistic and univariate logistic regression model	HAD scale = 83.4% had anxiety or depression, 36.2% were borderline for anxiety or depression, 76.2% had mild anxiety or depression	Females have a higher level of TMD associated with anxiety and depression
11.	Akhter *et al.*, 2019, Australia [37]	Cross-sectional study	145, 17–25 years, M (58), F (87)	All	RDC/TMD, and TSK/TMD, and DASS	χ^2 test	A significant relation was found between the DASS score and TMD	Anxiety and depression are associated with painful TMD, mostly in females
12.	Fernandes Azevedo *et al.*, 2018, Brazil [33]	Cross-sectional study	105, 17–24 years,	Anxiety	(RDC/TMD) – Axis I and STAI	Frequency and χ^2 test	According to the state anxiety level, 65.7% of students had mild anxiety, whereas results of trait anxiety showed that 57.1% had mild anxiety. No significance was measured	No association of anxiety with TMD
13.	Calixtre *et al.*, 2014, Brazil [38]	Longitudinal study	107, mean age 20.66 years, M (31), F (76)	Depression and anxiety	MFIQ Questionnaire and HADS Scale	Shapiro-Wilk test, Student's *t*-test and Spearman test	The MFIQ score was higher for high anxiety and depression (T-test, $p = 0.08$, ES = 0.582)	Anxiety and depression were not significantly associated with clinical symptoms of TMD in low to high-depression and anxiety patients
14.	Majumder *et al.*, 2015, India [36]	Cross-sectional study	1000, 17–28 years, M (450), F (550)	All	Helkimo anamnestic dysfunction index and HAD	χ^2 test	TMD was significantly associated with anxiety and depression (66.2%)	TMD is associated with stress and anxiety

Table I. Cont.

S. No.	Authors, year, country	Study design	Cohort (size, age, % M/F)	TMD and stress, depression, anxiety	Measures used (scales and questionnaire)	Statistical analysis	Findings	Inference
15.	Reis Diniz *et al.*, 2012, Brazil [39]	Longitudinal study	155, 18–25 years, M (107), F (48)	Stress and anxiety	A questionnaire, ISSL, and BAI	Pearson's and Spearmen's corelation	Throughout the year, 58.2% of students were stressed, and 40.2% suffered anxiety leading to TMD	Stress and anxiety are associated with TMD. However, no significant association was found among the groups
16.	Monteiro *et al.*, 2011, Brazil [34]	Cross-sectional study	150, 17–30 years, M (117), F (33)	Anxiety	(RDC/TMD) – Axis I and II, and STAI	χ^2 test	35.4% (*n* = 53) of the subjects had low anxiety, 48.6% (*n* = 73) had moderate anxiety, 16% (*n* = 24) had high or severe anxiety	A positive and significant relationship was found between trait-anxiety levels and chronic TMD

FAI – Fonseca Anamnestic Index, DASS-21 – Depression Anxiety Stress Scales-21, ISSL – Lipp's Inventory of Stress Symptoms for Adults, BAI – Beck Anxiety Inventory, TSK/TMD – Tampa-scale for Kinesiophobia, BDI – Beck's Depression Inventory, DC/TMD – Diagnostic criteria for TMD, HADS – Hospital Anxiety and Depression Scale, STAI – State-Trait Anxiety Inventory, PSQ4 – Perceived Stress Scale, RDC/TMD – Research Diagnostic Criteria.

RDC/TMD, Axis I and/or Axis II followed by diagnostic criteria (DC/TMD), Fonseca's Anamnestic Index and clinical examination, Helkimo anamnestic dysfunction index, Tampa Scale for Kinesiophobia (TSK/TMD) and questionnaire. For stress assessment, instruments that were used included Lipp's Inventory of Stress Symptoms for Adults (ISSL), and the Perceived Stress Scale (PSQ4). Anxiety assessment instruments utilized were the State-Trait Anxiety Inventory (STAI) and the Beck Anxiety Inventory (BAI). For assessing depression, Beck's Depression Inventory was employed. For anxiety and depression assessment, instruments were the Hospital Anxiety and Depression Scale, the Patient Health Questionnaire-4 (PHQ-4) scale, and the Four-Dimensional Symptom Questionnaire (4DSQ), and for all the psychological factor assessment, Depression Anxiety Stress Scales (DASS) and 4DSQ were employed in all the studies.

The criteria to diagnose TMD disorders were not homogeneous among the included studies and were often biased by preconceived ideas of pain-related muscular and neurological symptoms. The diagnosis was based either on pain-related (headaches and migraine) TMD or bruxism and the clicking sound of TMJ amongst the included studies. A well-established protocol and true controls were recorded in five studies [12, 33, 36–38], and participants were split into subgroups in three studies [17, 23, 34]. Regarding the association between TMD and anxiety alone or in conjunction with depression, studies showed that 83.4% of study participants were either depressed or suffered from anxiety, while 76.2% suffered from mild depression and 36% were moderately depressed and anxious. Concerning stress and depression with TMD, 15.96% of participants suffered from stress-related chronic TMD, and 9.6% suffered from mild TMD pain. Including all three factors and their association with TMD, studies found that university students suffered from at least one form of psychological disorder related to TMD. There were two longitudinal studies [38, 39], but their findings were tempered by the fact that TMD and psychological factors were not the focus of the study, and in one study, the focus was oral health-related quality of life and stress symptoms related to TMD. In 4 studies [19, 32, 34, 37], adopting mean and frequency or unclear statistical analysis limited the statistical findings and robustness of results.

As for the outcomes, a positive association was established by 12 studies; four studies, however, found no significant association between both conditions. In almost all the included studies, the male-to-female ratio was 1 : 3, and it was reported that females in the age group of 18–25 are mostly affected by at least one type of TMD related to

Table II. Risk of bias for cross-sectional studies

Studies		Yap *et al.* 2022a	Homeida *et al.* 2022	Yap *et al.* 2022c	Alhamary 2019	Aktar *et al.* 2019	Sojka *et al.* 2019	Fernandes *et al.* 2018	Majumdar *et al.* 2015	Montario *et al.* 2011
Selection	Representativeness of sample	*	*	*	*	*	*	–	*	*
	Sample size	*	*	*	*	*	–	–	**	*
	Non-respondent	–	*	–	–	–	*	–	–	*
	Uncertainty of exposure	*	**	*	*	*	**	**	*	**
Comparability		*	*	**	*	*	*	**	*	**
Outcome	Assessment of outcome	*	*	*	*	*	*	*	*	*
	Statistical tests	*	*	*	*	*	*	*	*	*
Quality		Fair	Good	Good	Fair	Fair	Good	Fair	Good	Good

psychological conditions. In general, comparing findings between the studies was not possible due to the adoption of highly variable criteria for the inclusion and exclusion of participants and study design.

Qualitative synthesis of the studies

Tables II–IV present the findings of the qualitative assessment by the NOS tool for cross-sectional, case-control and cohort studies. As a result, seven studies are judged to be of high quality, five of moderate quality, and two as low quality with a high risk of bias.

In the studies with a high risk of bias, the main issues were lack of case presentation, no information about verification of exposure, and lack of information of the nonresponse rate. Moderate defects with case representation, sample size, and response rate were demonstrated as medium risk. In the article, a low risk of bias was perceived for the exposure and response rate verification, since the outcome was measured by questionnaire. Therefore, quantitative analysis suggests that questionnaire-based studies are regarded as a probable source of bias.

Even though most of the included studies have similar settings and cohorts, a meta-analysis could not be performed because of differences in methodology, such as the instrument used to analyze TMD, stress, anxiety, and depression levels, and the outcomes were also measured in different ways: mean, median, standard deviation, parametric, non-parametric tests, and frequency. Moreover, studies with the same method to diagnose TMD and psychological factors had varying methodological quality. As a result, meta-analysis would result in high heterogeneity and inconsistency. Therefore, the authors planned to include an abstract of findings using GRADE analysis.

GRADE tool for evidence

The level of evidence was demonstrated under the following outcomes: Stress, depression, and anxiety are not related to TMD; stress, depression, and anxiety are positively related to TMD; stress and anxiety are not related to TMD; stress and anxiety are positively related, anxiety and depression are not related to TMD, and anxiety and depression are positively related. In general, the level of evidence was reported to be low or very low in the majority of studies. Several studies have demonstrated limitations in methodology which might have affected the study outcomes.[1,31] Methodological heterogeneity, such as study design, sample size estimation, and index validation, explains the inconsistency of the results and outcomes of the studies (Table V).

Table III. Risk of bias for case-control studies

–		Arya *et al.* 2023	Cao *et al.* 2022	Namvar *et al.* 2021	Yap *et al.* 2021b	Beres *et al.* 2019
Selection	Case definition adequate	–	*	*	–	*
	Representativeness of cases	*	*	*	*	*
	Selection of controls	–	*	*	–	*
	Definition of controls	–	–	*	*	*
Comparability		*	**	*	*	*
Exposure	Ascertainment of exposure	*	–	*	*	*
	The same method of ascertainment for case and control	–	–	*	–	*
	Nonresponse rate	*	*	–	–	–
Quality	–	Poor	Fair	Good	Poor	Good

Table IV. Risk of bias for cohort studies

Studies		Calixtre *et al.* 2014	Reis Diniz *et al.* 2012
Selection	Representativeness of exposed cohort	*	*
	Selection of non-exposed cohort	N/A	*
	Ascertainment of exposure	*	N/A
	Outcome of interest at the present of study	**	**
Compatibility		N/A	*
Outcome	Assessment of outcome	**	*
	Follow-up duration	*	*
	Adequacy of follow-up	*	*
Quality		Good	Good

Table V. Certainty of evidence (https://gdt.gradepro.org/app/#projects)

Included Studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Impact	Certainty
N = 16	Observational studies[a]	Very serious[b]	Very serious[b]	Very serious[c]	Not serious	Highly suspected in included studies[d]	Twelve studies have shown positive association of anxiety and stress with TMD, while two studies showed no association, and two studies are not sure about the association.	⨁◯◯◯ Very low

[a]observational studies are at higher risk of bias due to criteria of exposed and unexposed population, [b]heterogeneity of instruments to measure TMD and stress, depression, and anxiety, [c]the majority of evidence is from the university students, not from the young population in general, [d]most of the observational studies are prone to publication bias as they do not have registration procedures like randomized control and clinical trials.

Discussion

To our knowledge, this is the first systematic review that has evaluated the association between psychological factors and TMD in young adults. In quantitative synthesis, the result of this review confirmed the association between TMD and anxiety, stress, and depression, even though the level of certainty of the included studies was low. The positive relationship between TMD and psychological factors has been primarily explored in the literature [14, 16, 21, 39, 44–46]. However, despite the specific association between psychological factors and TMD in young adults, it has been the subject of few studies.

Included studies utilized various instruments to measure the temporomandibular disorder and psychological factors. These variations in study design and methodology have led to heterogeneity. Studies have reported that variation in diagnostic criteria of TMD impacts its prevalence [16, 45, 46].

In this systematic review, the heterogeneity in results could be due to using various instruments to measure disease and exposure. Reminiscence of the patient is the starting point for diagnosis of any TMD pain, which is the first part of a functional questionnaire in a diagnostic setting, alone or in conjunction with the RDC/TMD framework. Most of the studies in this review have diagnosed TMD with the RCD/TMD Axis I and Axis II framework, which is a valid tool [16, 39, 47, 48]. This tool consists of two axes: Axis I emphasizes physical diagnosis, while Axis II measures pain-related problems and psychological aspects. Ever since this instrument was introduced, researchers have emphasized the psychological aspect of pain as an important indicator for treatment planning in individuals with pain. However, nine studies have diagnosed TMD using RDC/TMD. Other studies have used assessment methods such as the Fonseca Anamnestic Index, clinical examination, the Tampa Scale for Kinesiophobia and the Pain Catastrophizing scale, and a questionnaire [37].

Almost half of the studies that utilized TMD/RCD indicated that young adults with TMD showed higher stress and anxiety [35, 37, 38, 40, 43, 44], while a few showed no significant difference in the development of TMD and psychological factors [17, 33, 39]. Canales *et al*. evaluated the relation between the diagnosis of TMD and Axis I and II. They reported no specific correlation between Axis I and II's findings in identifying pain and origin [49]. However, the pain intensity and origin correlated with the Axis II findings. Moreover, severe symptoms of pain were associated with higher scores of psychological factors, namely, depression and stress.

Two studies [32, 40] examined different types of TMD with clinical diagnostic criteria (DC/TMD), a recent and updated RCD/TMD instrument. This instrument is a shortened version of the original RCD/TMD and utilizes it for physical (Axis I) and psychological (Axis II) assessments. In Axis II of this instrument, a comprehensive diagnosis of factors more specific to orofacial pain has been added, which is different in RCD/TMD. This relatively new tool for measurement, translation, and validation of this instrument developed gradually [32, 40]. The study using this instrument demonstrated the strongest correlation between painful TMD and depression (r_s = 0.52 to 0.65), respectively. However, the results of the study by Homeida *et al*. [32] demonstrated an association of anxiety and bruxism with painful TMD.

Several instruments are available to measure stress, depression, and anxiety in TMD patients, such as the Depression, Anxiety and Stress Scale, the Four-Dimensional Symptom Questionnaire, for anxiety, the Hospital Anxiety and Depression Scale, the State-Trait Anxiety Scale, and Beck's Anxiety Inventory, and for stress, the Perceived Stress Scale and Lipp's Inventory for Stress Symptoms in Adults. For this systematic review, which focuses on psychological factors and TMD in young adults, only original research that employed validated scales was considered. DASS-21 is the most valid and reliable instrument for calculating depression, anxiety, and stress. The modified and shortened version of DASS utilized 42 questions related to depression, anxiety, and stress. DASS-21 was the only measurement tool in seven included studies [35, 39–43]. A systematic review that measured the quality of this instrument concluded that DASS-21 has a bifactor structure (comprising separate subgroups and overall factors) and should be used to calculate the total scoring of negative effects (stress, depression, and anxiety) [24]. Zanon *et al*. corroborate similar findings; they studied the reliability and variability of DASS-21 in university students across eight countries and found a strong correlation (odds ratio = 0.91 to 0.95) between total DASS-21 and subtypes of TMD in affected patients [50]. Only one study [19] used the Four-Dimensional Symptom Questionnaire (4DSQ) and the Sense of Coherence Questionnaire. The 4DSQ is a self-reported questionnaire comprising 50 items measuring stress, depression, anxiety, and somatization [51]. This questionnaire answers on a 5-point Likert scale and is used mainly in clinical practice. This study found a correlation between stress, anxiety, and painful TMD among medical students and a low sense of coherence [19].

Regarding the diagnosis of stress alone or in conjunction with depression, two included studies used different validated instruments. The Perceived Stress Scale (PSS), a validated questionnaire consisting of 10 items for calculating stress, was used in one study along with Beck's Depression Inventory [17]. This study demonstrated that the PSS score was higher in the group of patients with painful TMD compared to healthy individuals. Another study used Lipp's Inventory for Stress Symptoms and Beck's Anxiety Inventory, designed to evaluate emotional stress and anxiety among students over 15 years [39]. This study showed a positive relationship between psychological factors and the main anxiety among students preparing for a college entrance exam.

Regarding the diagnosis of anxiety alone or in conjunction with depression, six included studies employed different validated instruments. Three studies [34, 35, 38] calculated levels of anxiety and depression by the Hospital Anxiety and Depression Scale, a validated and reliable scale to measure anxiety and depression clinically. Two studies [34, 35] used the State-Trait Anxiety In-

ventory; this tool consists of two self-administered questionnaires: one with the perceived feeling of tension and anxiety, which increases the activity of the autonomous nervous system, and the other with trait anxiety, which is a stable emotional status of the individual. One study [32] used Patient Health Questionnaire-4 (PHQ-4), an ultra-brief self-report questionnaire consisting of four items focusing mainly on two core questions, each concerning anxiety and depression. Overall, of the 16 included studies, some include more than one measuring device [17, 37, 39], with a different methodological approach that makes it difficult to compare the results. It was observed that almost all the studies showed a positive correlation between psychological factors and TMD. Moreover, some aspects of the included studies coincide with the findings in previous literature [12, 20, 47, 51]. For instance, the prevalence of TMD, stress, and anxiety was higher in females of the age group 20–40 years. In these patients, the main symptom noted was a clicking sound, joint pain, and limitation in mandibular motion.

Previously published systematic reviews have also established a positive association between psychological factors and TMD. Recently, Santos et al. established an association between different types of TMD and anxiety. These results suggested that patients with painful TMD, mainly of articular origin, are more anxious than healthy individuals [52]. Similar findings were obtained by Reis *et al*. in their systematic review, indicating that patients with myofascial pain are more anxious and depressed, especially with disc displacement rather than other subtypes of TMD [18]. However, the authors stated that this evaluation could result from a TMD diagnosis with RCD/TMD, in which myofascial pain is more exaggerated than other subtypes [18, 52]. In their review, de la Torre *et al*. indicated that psychological impairment and disorders are highly prevalent in patients with painful TMD, mainly severe to moderate stress and depression [24]. However, the authors did not place much emphasis on severe physical impairment.

This systematic review is the first to diagnose the relationship between TMD and psychological factors (stress, depression, and anxiety) in young adults. The certainty of evaluation measured by GRADE is low for this review. This could be due to the variation in methodological settings, such as study design, sample representation, description of controls, etc. Despite the low and very low level of certainty, it is essential to note that almost all the included studies showed an association between TMD and psychological factors.

The applicability of results to young adults is limited due to the exclusion of medical conditions and associated comorbidity. Secondly, the heterogeneity was high due to the methodological aspects: the fact that young adults were mainly from medical and dental universities (due to fewer longitudinal studies), different methods of evaluation of psychological factors, statistical measures, and presence or categorization of the control group. Therefore, the evidence is presented in a narrative format, including the certainty of the evidence, rather than using pairwise meta-analysis to compare the exposure and comparison groups. Future epidemiologic studies should include effective participant identification methods, suitable control groups, adequate confounder management in statistical evaluation, and valid and reliable diagnostic instruments for psychological factors and TMD. This could provide more reliable and broad results that might influence clinical decisions and public health policies.

Keeping in mind the limitations of this systematic analysis, the conclusion can be drawn that there is an association of psychological factors, especially stress and anxiety, with the development of temporomandibular disorder. Young females were more affected than their male counterparts. However, the quality of evidence in the included studies was low. Therefore, to establish a high level of evidence associated with the development of TMD and psychological factors, it is necessary to plan further research focusing mainly on one type of temporomandibular disorder (articular and muscular) and evaluating psychological factors as a risk indicator for perpetuation or progression of TMD, which makes it difficult for patients to respond to the treatment of the temporomandibular disorder.

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Conflict of interest

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