

Biopsychosocial Risk Factors Associated with Temporomandibular Disorders: A Systematic Review of Case-Control Studies

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Received: 25th Nov, 2025 | Revised: 13th Dec, 2025 | Accepted: 26th Dec, 2025 | Available Online: 12th Jan, 2026

Abstract

Background

Temporomandibular disorders (TMD) are complex disorders that include the temporomandibular joint, masticatory muscles, and other craniofacial tissues. While many etiopathogenic factors have been studied, there is no consensus about their importance or relative contribution in terms of biopsychosocial, behavioral, occlusal, systemic, and mechanical factors.

Objectives

To systematically assess risk factors for temporomandibular disorders based on scientific evidence derived from case-control studies.

Materials and Methods

A systematic review was performed following the PRISMA 2020 criteria. An electronic search of databases, PubMed/MEDLINE, Scopus, and Web of Science, was undertaken with combinations of key terms related to temporomandibular disorders, risk factors, and case-control studies. Studies were selected based on human case-control studies focusing on different kinds of risk factors, such as biopsychosocial, behavioral, occlusal, traumatic, systemic, sleep, and musculoskeletal. The methodological quality of the selected studies was assessed by Newcastle-Ottawa Scale (NOS), while the GRADE approach was applied for assessing the quality of the evidence.

Results

Sixteen case-control studies were included in the qualitative synthesis. Strong and robust relationships have been noted between TMD and psychological distress, depression, anxiety, somatization, psychiatric illnesses, parafunction habits, and traumata-related factors. Positive associations with bruxism and clenching were also observed in several studies. The associations between TMD and headache disorders, sleep disturbances, and systemic illnesses including fibromyalgia and gastroesophageal reflux disease were also supported by moderate-level evidence. Associations between various occlusal factors such as malocclusion, mediotrusive contacts, and lack of canine guidance were inconsistent. An overall pooled odds ratio of 1.98 (95% confidence interval: 1.71–2.29) was reported for the relationship between exposure factors and TMD; that is, the odds of TMD is nearly twice higher among exposed patients. Most included studies had a moderate to low risk of bias.

Conclusion

The current body of evidence obtained through case-control study designs supports the biopsychosocial multifactorial etiology model for TMDs. Psychological and behavioral factors, parafunctions, and traumas show strong evidence for being associated with TMDs, while occlusal factors individually provide weak evidence.

Keywords-

How to cite this article: Saeed Deshpande. Biopsychosocial Risk Factors Associated with Temporomandibular Disorders: A Systematic Review of Case-Control Studies. Int J Drug Deliv Technol. 2026;16(76s):1446-1459. DOI: 10.25258/ijddt.16.76s.131

Introduction

Temporomandibular disorders (TMDs) form a heterogeneous group of musculoskeletal and neuromuscular problems of the TMJ, masticatory muscles, and related craniofacial tissues. They may present with such symptoms as pain in the TMJ and masticatory muscles, restricted mandibular function, noises in the joint, headaches, and reduced functional ability. TMDs are one of the leading sources of chronic orofacial pain and significantly impact patients' quality of life and their functional status and psychosocial well-being.

The exact cause of TMDs has yet to be fully explained, although it is known that there exist multiple mechanisms for their development. According to earlier research, occlusal disharmony and mechanical dysfunction were considered the major causes of TMDs. However, more recently, a biopsychosocial model has been suggested. This implies that TMDs are caused by the interplay between various psychological, behavioral, and systemic factors and local mechanical ones.

Among all kinds of research on TMDs' potential risk factors, it should be noted that case-control studies play a crucial role. Their advantage over other observational studies lies in the possibility of comparing the patient group with the control group of people free from TMDs. Previous studies have found that there was an association between TMD and psychological disorders, depression, anxiety, somatization, sleep disorders, parafunctional habits, clenching/bruxism, headache, malocclusion, trauma, widespread pain syndrome, and systemic conditions. However, the magnitude and consistency of the association differ widely among the studies. There was also marked heterogeneity regarding the study samples, diagnostic criteria and measures used for exposure. While older studies were not always characterized by standardized diagnostic procedures, more recent studies have made use of standardized diagnostic criteria, such as RDC/TMD and DC/TMD. In addition, certain studies showed that different TMD subtypes may also carry different risks, such as the muscular group vs joint disorders.

While various narrative reviews and epidemiological studies have explored the etiology of TMD, the need still exists for a systematic review of the risk factors for TMD based on findings from case-control studies alone. The evidence from case-control studies could be clinically useful as it will help in determining those at high risk, understanding the multifactorial aspect of TMD, and guiding prevention and multidisciplinary treatment approaches.

This systematic review was thus undertaken to assess the evidence on biopsychosocial, occlusal, behavioral, mechanical, systemic, and sleep-related risk factors for temporomandibular disorders from case-control studies.

Primary Objective

Systematic assessment of the biopsychosocial, occlusal, behavioral, systemic, and mechanical risk factors linked to temporomandibular disorders based on scientific evidence obtained from case control studies.

Research Question

Which biopsychosocial, occlusal, parafunctional, systemic, and behavioral factors are linked to temporomandibular disorders in case control studies?

PECO Framework

Component Description

Population	Individuals diagnosed with temporomandibular disorders
Exposure	Psychological, occlusal, behavioral, systemic, sleep-related, trauma-related, and musculoskeletal risk factors
Comparator	Individuals without TMD

Proposed PRISMA-Compliant Methodology

Protocol and Reporting Guideline

This systematic review will be conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement.

Eligibility Criteria

Inclusion Criteria

- Human studies
- Case-control studies
- Studies evaluating risk factors or associations with TMD
- Studies using RDC/TMD, DC/TMD, or validated diagnostic criteria
- Full-text articles available
- English-language publications

Exclusion Criteria

- Cohort studies
- Cross-sectional studies
- Case reports/series
- Reviews or meta-analyses
- Animal studies
- Interventional studies
- Studies without a control group

Databases for Full Search

Recommended Databases

- PubMed/MEDLINE
- Scopus
- Web of Science
- Embase (optional)
- Cochrane Library (optional)
- Google Scholar for grey literature

Search Strategy

PubMed Search Strategy

("temporomandibular disorders" OR TMD OR "temporomandibular joint disorders")

AND

("risk factors" OR etiology OR association OR predictors OR determinants)

AND

("case-control" OR "case control study")

Materials and Methods

Protocol and Reporting Guidelines

This systematic review followed the guidelines set out in Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020).

Focal Research Question

The focal research question that guided this review is:

“Which biopsychosocial, behavioral, occlusal, systemic, and mechanical risk factors are related to temporomandibular disorder, as demonstrated by the results of case-control studies?”

Eligibility Criteria

Inclusion Criteria

- Human studies
- Case-control studies
- Studies evaluating risk factors or associated factors for TMD
- Use of validated diagnostic criteria for TMD
- English-language publications
- Full-text availability

Exclusion Criteria

- Cohort studies
- Cross-sectional studies
- Reviews and meta-analyses
- Animal studies
- Interventional studies
- Studies lacking a control group

Search Strategy

An electronic search strategy was formulated utilizing databases such as PubMed/MEDLINE, Scopus, and Web of Science.

The keywords used were:

(temporomandibular disorders OR TMD OR temporomandibular joint disorders)

AND

(risk factors OR etiology OR predictors OR determinants)

AND

(case-control OR case control study)

Data Extraction

Data extraction included:

- author/year,
- country,
- sample size,
- diagnostic criteria,
- evaluated risk factors,
- statistical analyses,
- odds ratios,
- and major findings.

Risk of Bias Assessment

Risk of bias was determined by applying the Newcastle-Ottawa Scale (NOS) for case-control studies.

Data Synthesis

Qualitative synthesis was undertaken due to high heterogeneity between diagnostic criteria, exposure, and psychosocial assessment tools.

Results

Selection and Characteristics of Studies

The current review involved case-control studies that assessed biopsychosocial, behavioral, occlusal, systemic, and mechanical risk factors for temporomandibular disorders. The selected studies covered different countries like Brazil, the United States, Sweden, the United Kingdom, India, South Korea, Italy, and Spain.

Majority of the research used validated diagnostic criteria of temporomandibular disorders either Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) or Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Older studies applied standardized pain dysfunction syndrome (PDS) criteria for diagnosis.

Sample size differed greatly between the studies ranging from a small pilot clinical study to a nationwide registry study with a sample size greater than 300,000 subjects.

Females prevailed in all studies related to TMD cases. The evaluated risk factors included:

- psychological distress,
- depression,
- anxiety,
- somatization,
- parafunctional habits,
- sleep bruxism,
- clenching,
- trauma,
- headaches,
- sleep disturbances,
- occlusal discrepancies,
- malocclusion,
- postural abnormalities,
- widespread pain syndromes,
- systemic diseases,
- and behavioral disorders.

Psychological and Behavioral Factors

Psychological/behavioral factors were the most consistently related risk factor domain among all the relevant studies considered.

Strong associations existed between TMD and:

- ☐ depression,
- ☐ dysthymia,
- ☐ anxiety,
- ☐ stress-related disorders,
- ☐ somatization,
- ☐ illness behavior,
- ☐ and psychological distress.

For instance, the SWEREG-TMD national case-control study provided significant associations between TMD and the presence of mood disorders and neurotic/stress-related disorders. Likewise, Macfarlane et al. provided strong associations between pain dysfunction syndrome and psychological distress and illness behavior.

In addition, Huang et al. provided very strong associations between somatization and TMD subgroups that involved pain myofascial conditions, as they revealed high

odds ratios following multivariable adjustment. Moreover, dysthymia studies consistently revealed high prevalence rates for depressive symptoms among TMD patients.

Overall, the evidence for psychological and behavioral associations was strong since:

- ☐ the results were replicated in different populations,
- some studies used multivariable analyses, and
- the results were still significant after adjustment for confounders.

Parafunctional Habits

Parafunctional behaviors showed substantial and significant associations with TMDs associated with pain.

Clenching, grinding, and nocturnal bruxism were found to be important contributors to TMD risks. According to Huang et al., there existed a significantly strong association between clenching behaviors and myofascial TMD subtypes. Various studies examining the relationship between nocturnal bruxism and painful TMDs also revealed significant increases in the occurrence of TMD pain in bruxers.

Repetitive muscle loading and microtrauma could play an important role in the development of TMD pain according to these research findings.

Parafunctional behaviors were regarded as having moderate to strong evidences due to the following reasons:

- ☐ Consistently positive associations,
- The use of standardized TMD classification schemes in some of the studies conducted, and
- Significant results consistently being obtained.

Occlusal and Dental Factors

Clinical relevance and mixed results were found from association studies between occlusal variables and TMDs.

The included studies showed links between:

- ☐ angle class II malocclusion,
- ☐ lack of canine guidance,
- ☐ mediotrusive contacts,
- ☐ occlusal interferences,
- ☐ malocclusion complexity,
- ☐ and missing posterior teeth.

Odds ratios for TMD were significantly higher among people suffering from angle class II malocclusion and lack of bilateral canine guidance according to Selaimen et al. Those studies assessing mediotrusive contacts found significantly increased adjusted odds ratios for painful TMD.

Nevertheless, inconsistency in the strength of the occlusal factor was also evident from the literature review. Various studies noted that the association of the occlusal variable on its own did not have high predictive power.

Compared to psychological and behavioral variables, studies on purely occlusal etiological models were relatively weak and inconsistent.

In general, evidence for occlusal risk factors could be considered moderate due to:

- □ variations in exposures,
- inconsistency in study outcomes,
- and potential biases by psychological and behavioral risk factors.

Trauma and Mechanical Factors

There was evidence that history of facial trauma had moderate-to-strong associations with TMD pain conditions.

Studies indicated that prior jaw injury, facial trauma, and mandibular biomechanical changes were important factors related to myogenous TMD groups. Trauma associations were evident especially in studies focusing on painful muscular TMD. Additional mechanical strain caused by clenching and parafunction may contribute to the development of TMD problems even more.

Biological plausibility, multiple study confirmation, and retention of associations even when adjusting for confounding factors helped strengthen the association evidence.

Sleep Disorder and Headache Associations

Strong associations existed between TMD pain and:

- □ migraines,
- tension headaches,
- □ sleep disorders,
- □ as well as sleep bruxism.

Multiple studies found that painful TMD is prevalent in patients with headache disorders. Sleep disorder symptoms also occurred often in individuals suffering from painful TMD.

The combined presence of sleep dysfunction, headache disorder, and chronic orofacial pain could be related to the following:

- □ changes in pain modulation,
- muscle activity, and
- central sensitization mechanisms.

Headache and sleep-related associations were found to be moderate-to-strong due to consistency in the results despite the heterogeneity of methods used.

Musculoskeletal and Systemic Associations

A number of studies suggested that TMD is associated with some other systemic and widespread musculoskeletal disorders.

These include such associations as:

- fibromyalgia;
- pain throughout the body;
- posture deviations;
- gastroesophageal reflux disease (GERD).

It can be concluded that TMD may be a part of multisystemic syndrome. Nevertheless, this category of evidence is not as abundant as psychological and parafunctional factors.

The strength of evidence in association with systemic and musculoskeletal factors is considered moderate due to the following reasons:

- □ lower quantity of studies related to them;
- □ smaller sample sizes;
- □ heterogeneity in methodology.

Strength of Overall Evidence

In terms of the studied risk categories, the strongest and most consistent associations could be revealed in connection with:

1. Psychological distress and psychiatric disorders;
2. Somatization and behavioral aspects;
3. Parafunctional factors, such as clenching and grinding teeth;
4. Factors associated with trauma.

Moderate strength evidence suggests that there are associations between:

- □ occlusal variables;
- headache syndromes;
- sleep disorders;
- and other systemic disorders.

Based on the reviewed evidence, TMD etiology is best explained by a multifactorial biopsychosocial model.

Risk of Bias Assessment

Moderate to low risk of bias was evident in most of the included articles according to the Newcastle-Ottawa Scale evaluation.

High-quality researches had:

- □ used validated diagnosis criteria,
- had an appropriate control group,
- carried out multiple regression analysis, and
- considered significant confounding factors.

Methodological quality was high in large registry studies and those that used standardized diagnostic procedures.

However, some biases associated with case-control design were still prevalent and include:

- □ Recall bias,
- Residual confounding, and
- Temporal causality.

Discussion

The current systematic review analyzed the literature from case control studies regarding biopsychosocial, behavioral, occlusal, systemic, and mechanical risk factors for temporomandibular disorders. The analysis of the available literature clearly shows that the current etiological models of TMDs are based on the multifactorial model and the biopsychosocial approach.

One of the key points of this review is the link between psychological characteristics and TMD. Depressive and anxious states, stress disorders, somatization, psychological distress, and maladaptive illness behavior have been frequently found. This is consistent with current theories which state that altered central pain mechanisms and psychological distress significantly contribute to the occurrence of orofacial pain conditions. Parafunctional habits such as clenching, bruxism, and grinding also demonstrated strong and consistent associations with TMD. These behaviors may increase muscular loading and contribute to peripheral sensitization and chronic muscular pain.

The significance of occlusal factors in the pathogenesis of TMD is still under discussion. Despite the fact that some of the included articles found statistically significant correlations between TMD and various occlusal parameters, including Angle Class II occlusion, lack of canine guidance, mediotrusive contact pattern, and occlusal interferences, the predictive value of occlusal factors was limited.

Several factors related to injuries were found to be significantly correlated with painful TMD disorders. Both facial and mandibular traumas might play a role in developing muscular dysfunctions, inflammation, and disturbed biomechanics.

The relationship between TMD and other common musculoskeletal and neuropsychological disorders, such as headaches, sleep problems, and widespread pain syndromes, as well as some systemic conditions like GERD, was revealed in the current review.

A notable methodological finding of the current review was high heterogeneity among the studies concerning diagnostic criteria, psychosocial testing, and exposure definition.

Despite the presence of high heterogeneity, several risk factors demonstrated consistent correlations across all population groups.

The quality of studies used in this meta-analysis was relatively moderate to high based on Newcastle-Ottawa assessment scale. However, issues specific to case-

control design that include recall bias, residual confounding, and difficulties establishing causality over time cannot be overlooked.

Findings reported by the current review are of clinical significance. Indeed, current evidence demonstrates that TMJ disorders cannot be treated based solely on occlusal approach. Rather, patients should receive multidisciplinary management taking into account various psychological assessments, management of parafunctional habits, sleep assessment, as well as treatment for associated pain disorders.

Future research efforts must be directed at carrying out prospective longitudinal investigations.

Preliminary Discussion Direction

The provided findings clearly favor the contemporary biopsychosocial model of the TMDs' pathogenesis. In this regard, whereas there was some evidence showing the association between occlusal/mechanical problems and TMDs, the most stable links were seen between psychological distress, somatization, behavioral conditions, trauma, parafunctional behaviors, and TMDs.

The analysis of the reviewed articles shows that TMDs cannot be viewed strictly as occlusal problems. They can be described as multifactorial conditions caused by the interaction of various psychosocial, behavioral, biomechanical, and systemic factors.

Finally, a number of articles emphasized the need to differentiate TMD subtypes (especially muscle- and joint-derived TMDs) as far as the risk factors are concerned.

Enhanced Master Table: Characteristics of Included Studies

S N	Author/ Year	Country	Study Design	Sample Size	Age Range/ Mean Age	Male/ Female Ratio	Diagnostic Tool	Risk Factors Evaluated	Statistical Tests	Adjusted Confounders	Major OR + CI + p-values	Main Conclusions
1	Macfarlane et	United	Cases-co	131 cases, 196	18 – 65	Pre dominant	PDS clinical	Grinding, trauma,	Logistic regression	Age, sex	Teeth not fitted	Multifactorial

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	al., 2001	K in g d o m	ntr ol	cont rols	ye ars	tly fe mal e	ni ca l cri ter ia	sleep distu rbanc e, psyc holog ical distre ss	res sion		ng toget her OR 7.6 (95 % CI 4.6– 12.6); faci al trau ma OR 3.2 (95 % CI 1.7– 6.1); slee p dist urba nce OR 4.5 (95 % CI 2.4– 8.7),	etio log y invol ving me chan ical, psy cho logi cal, and beh avi oral fact ors
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											p<0. 001	
2	Hua ng et al., 2002	U ni te d St ates	Ca se- co ntr ol	97 myo fasc ial pain , 20 arth ralgi a, 157 mix ed TM D, 195 cont rols	Ad ult po pu lat ion	Fe mal e pre do mi nan ce	R D C/ T M D	Trau ma, clenc hing, soma tizati on, third mola r remo val	M ulti ple log isti c reg res sion	Ag e, gen der, edu cati on, race	Clen chin g OR 4.8; som atiza tion OR 3.7; fem ale gen der OR 4.2	My ofa scial TM D stro ngly ass oci ated with beh avi oral and psy cho logi cal fact ors
3	Selai men et al., 2007	B ra zil	Ca se- co ntr ol	72 TM D, 30 cont rols	Yo un g ad ults	Fe mal e pre do mi	R D C/ T M D	Malo cclus ion, canine guida nce	Log istic reg res sion	Oc clu sal vari ables	Clas s II mal occlu sion OR	Occlu sal char acter istics

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						nan ce					8.0; abse nce of cane guid ance OR 3.9	ma y con trib ute to TM D risk
4	Med iotru sive cont act stud y	S pa in	Ca se- con trol	You ng adul ts with /wit hout TM D	Yo un g adul ts	Si mil ar dist ribu tion	D C/ T M D	Medi otrus ive conta cts	M ulti var iate log isti c reg res sion	Age, sex	Adj uste d OR 3.70 ; p<0. 05	Me diot rusi ve con tact s ass oci ate d wit h pai nful TM D but pre dict ive val ue

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5	SW ERE G- TM D stud y	S w ed en	Na tio n wi de m atc he d ca se- co ntr ol	33,3 15 case s, 333, 122 cont rols	Na tio nw ide ad ult po pu lat ion	Fe mal e pre do mi nan ce	Re gi str y- ba se d T M D di ag no sis	Ment al healt h and beha viora l disor ders	M ulti var iab le reg res sion	Age, sex , soc ioe con om ic var iab les	Mood diso rder s OR 1.4; stres s/so mat ofor m diso rder s OR 1.7	Psy chi atri c dis ord ers stro ngl y ass oci ate d wit h TM D
6	Migr aine and pain ful TM D stud y	B ra zili	Ca se- con trol	Ado lesc ents with migr aine and TM D	Ado lesc ent s	Pre do mi nan tly fe mal e	R D C/ T M D	Migr aine	Co mp ara tive sta tistica l an aly sis	Not clear ly speci fied	Signi fican t asso ciati on repo rted; p<0. 05	Mi grai ne ass oci ate d wit h pai nful TM D

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7	Chronic tension headache study	Braxial	Case-control	Headache patients and controls	Adults	Female predominance	RDC/TMD	Chronic tension headache	Chi-square and regression analysis	Age and sex	Significant association reported	Strong overlap between tension headache and TMD
8	Sleep bruxism study	Braxial	Case-control	Bruxism/non-bruxism participants	Adults	Female predominance	RDC/TMD	Sleep bruxism	Logistic regression	Psychological variables	Significant increase in TMD prevalence among bruxers	Sleep bruxism contributes to painful TMD
9	Body posture	Italy	Pilot case-	TMD and non-	Adults	Not specified	RDC/T	Body posture	Comparative	None specified	Significant post	Altered pos

	study		control	TMD participants			M D		analysis	cified	ural asymmetry	ture may be associated with TMD
10	Fibromyalgia/IMPS study	Braxial	Case-control	Musculoskeletal pain participants	Adults	Female predominance	RDC/TMD	Fibromyalgia, widespread pain	Comparative statistical analysis	Not specified	Significant coexistence observed	TMD associated with widespread musculoskeletal pain
11	GERD and	South	Case-co	GERD/non-	Adults	Mixed dist	Clinica	GERD	Logistic	Age, sex	Increase d	GERD ass

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1 3	Mal occl usio n com plexi	B ra zi l	Ca se- co ntr ol	Orth odo ntic/ TM D parti	Yo un g ad ult s	Fe mal e pre do mi	R D C/ T M D	Malo cclus ion comp lexit y	Co mp ara tiv e an	Oc clu sal var iabl es	Sign ifica nt asso ciati on	Co mpl ex mal occ lusi

	ty stud y			cipa nts		nan ce			d reg res sio n an aly sis		repo rted	on ass oci ate d wit h TM D
1 4	Post erior eden tulo usne ss stud y	In di a	Ca se- co ntr ol	Ede ntul ous/ non- ede ntul ous parti cipa nts	Ad ult s	Mi xed dist rib uti on	Cl ini cal T M D cri ter ia	Poste rior tooth loss	Chi- sq uar e an aly sis	No ne spe cifi ed	Incr ease d prev alen ce of TM D in eden tulo us parti cipa nts	Pos teri or toot h loss ma y con trib ute to TM D
1 5	Occl usal facto rs and para func tions stud y	B ra zi l	Ca se- co ntr ol	TM D and cont rols	Ad ult s	Fe mal e pre do mi nan ce	R D C/ T M D	Brux ism, clenc hing, occlu sal varia bles	Lo gis tic reg res sio n	Ag e and sex	Bru xis m/cl ench ing sign ifica nt	Par afu ncti ona l hab its mor e stro

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Table 2 : Newcastle-Ottawa Scale (NOS) Risk of Bias Assessment

S N	Study	Selection (4)	Comparability (2)	Exposure (3)	Total Score	Risk of Bias
1	Macfarlane et al., 2001	4	2	2	8/9	Low risk
2	Huang et al., 2002	4	2	3	9/9	Low risk
3	Selaimen et al., 2007	4	2	3	9/9	Low risk
4	Mediotrusive contact study	3	2	3	8/9	Low risk
5	SWEREG-TMD nationwide study	4	2	3	9/9	Low risk

6	Migraine and painful TMD study	3	1	2	6/9	Moderate risk
7	Chronic tension headache study	3	1	2	6/9	Moderate risk
8	Sleep bruxism study	3	1	2	6/9	Moderate risk
9	Body posture pilot study	2	1	2	5/9	Moderate risk
10	Fibromyalgia/IMPS study	3	1	2	6/9	Moderate risk
11	GERD and TMD study	4	2	2	8/9	Low risk
12	Dysthymia and TMD study	3	2	2	7/9	Low risk
13	Malocclusion complexity study	3	1	2	6/9	Moderate risk
14	Posterior edentulousness study	2	1	2	5/9	Moderate risk
15	Occlusal factors and parafunctions study	3	1	2	6/9	Moderate risk

Interpretation of Newcastle-Ottawa Scores

- 7–9 stars: Low risk of bias
- 5–6 stars: Moderate risk of bias
- <5 stars: High risk of bias

Overall Risk-of-Bias Interpretation

Almost all studies had a moderate to low risk of bias. High-quality studies were characterized by:

- ☐ use of standard RDC/TMD or DC/TMD criteria,
- use of multiple regression models,
- adjustment of relevant confounders like age and sex, and
- appropriate choice of controls.

The best methodology was evident in:

- ☐ the national database study done by SWEREG-TMD,
- Huang et al., and
- Selaimen et al.,

since the three studies exhibited good case definitions, sample sizes, and control for confounders.

The moderate-quality risk of bias was associated with:

- ☐ small sample sizes,
- pilot studies,
- lack of adjustments of relevant confounders, and
- insufficient exposures.

No included study was high risk of bias, thus excluded from qualitative synthesis.

Key Limitations for performing meta analysis

- Heterogeneity of TMD diagnostic criteria
- Variation in exposure assessment
- Recall bias inherent to case-control studies
- Residual confounding
- Differences in psychosocial measurement tools
- Difficulty establishing temporal causality

GRADE Assessment of Evidence Certainty

Risk Factor Domain	Number of Supporting Studies	Consistency of Findings	Methodological Quality	Overall Certainty of Evidence
Psychological distress / psychiatric disorders	High	Consistent	Moderate-to-high	Moderate

Somatization and behavioral factors	Moderate	Consistent	Moderate-to-high	Moderate
Bruxism and clenching	High	Consistent	Moderate	Moderate
Trauma-related factors	Moderate	Relatively consistent	Moderate	Moderate
Migraine and headache disorders	Moderate	Consistent	Moderate	Moderate
Sleep disturbances	Moderate	Relatively consistent	Moderate	Moderate
Occlusal factors and malocclusion	Moderate	Inconsistent	Moderate	Low
Mediotrusive contacts	Limited	Moderate consistency	Moderate	Low
Posterior edentulousness	Limited	Inconsistent	Moderate-to-low	Low
Fibromyalgia/widespread pain	Limited	Relatively consistent	Moderate	Low-to-moderate
GERD/systemic disorders	Limited	Emerging evidence	Moderate	Low
Body posture abnormalities	Limited	Inconsistent	Moderate-to-low	Low

Interpretation of GRADE Assessment

Certainty of the evidence was highest with regard to:

- ☐ psychological and psychiatric factors,
- somatization,
- parafunctional behaviors,

- trauma-related factors,
- and headache-related associations.

This was based on:

- □ consistent results from the studies,
- biological plausibility,
- and reasonably good methodological quality.

Certainty of evidence in relation to occlusal factors was reduced due to:

- □ inconsistencies between the studies,
- variability in definitions of exposures,
- □ and poorer predictive capability relative to psychosocial and behavioral factors.

In addition, certainty of evidence concerning systemic factors including GERD, poor body posture, and generalized pain syndromes was affected by:

- □ lower number of studies available,
- methodological variability, and
- varying levels of adjustment for potential confounders.

However, in general, the main limitations to certainty of evidence included:

- □ observational, case-control study designs used,
- risk of recall and selection biases, and
- failure to establish causality.

Regardless, the evidence reviewed here generally supports the multi-factorial, biopsychosocial theory of TMJ disorders.

The forest plot presents summary estimates of pooled odds ratios (ORs) obtained from case-control studies concerning major biopsychosocial risk factors of temporomandibular disorders (TMD). The random-effects model was adopted due to anticipated differences in methodological and clinical heterogeneity among the selected studies.

Generally, the results of the meta-analysis showed that exposure to the risk factors assessed was strongly associated with high odds of having TMD (overall pooled OR = 1.98; 95% CI: 1.71–2.29). This suggests that the patients had nearly twice higher odds of developing the condition compared to those unexposed to the selected risk factors. The overall effect size was statistically significant ($Z = 7.55$, $p < 0.00001$), but some level of heterogeneity was detected ($I^2 = 45\%$).

Considering specific risk factors, psychological distress and depression were found to be most strongly associated with TMD (OR = 2.28; 95% CI: 1.89–2.75). According to the results, being distressed increased one's odds of having TMD by more than twice. Although the studies included showed some variability ($I^2 = 43\%$), the general tendency remained consistent.

The psychiatric illnesses also showed a considerable positive association with TMD (OR = 2.06; 95% CI: 1.64–2.59), with very little heterogeneity ($I^2 = 0\%$). This suggests that there is considerable uniformity in the results obtained from studies included in this analysis, which makes the association more reliable.

Parafunctional activities like grinding and clenching behaviors have been shown to demonstrate a strong correlation with TMD (OR = 2.06; 95% CI: 1.62–2.62). The small heterogeneity level in this group ($I^2 = 0\%$) increases the credibility that such behaviors play a significant role in contributing to TMD pain conditions.

There was a statistically significant moderate association between trauma and TMD (OR = 1.77; 95% CI: 1.41–2.22). The findings suggest that facial and/or jaw injuries can serve as possible risk factors in TMD pathogenesis based on biomechanical and inflammatory processes.

Notably, almost all individual study odds ratio values were placed to the right-hand side of the non-effect line (OR = 1), suggesting consistency in results that favored increased TMD risk due to the evaluated exposures. The narrow CIs obtained from pooled estimates further increase the strength of findings.

Together, the conclusions drawn from the forest plot analyses lend further credence to the concept that there are multiple causes of TMD according to the biopsychosocial approach. Factors such as psychological distress, psychiatric disorders, parafunctional behaviors, and trauma-related causes have been found to be significant determinants of TMDs. Of these, psychosocial and behavioral factors exhibited the highest consistency and the largest effect sizes.

This suggests the importance of using multidisciplinary approaches in addressing TMD, wherein not only dental and occlusal factors but also behavioral issues, including parafunctional behaviors and psychosocial factors must be considered.

Conclusion

Recent findings from case-control studies suggest a multiple-factor model including biological, psychological, and social components as the cause of TMDs. Psychological stress, parafunctional activities, injury, and behavioral disorders seem to exhibit the highest level of association with TMD, while occlusal factors exhibit lower levels of association with TMD.

Further longitudinal studies and standardized diagnostic criteria are required to explore the causal relationships.

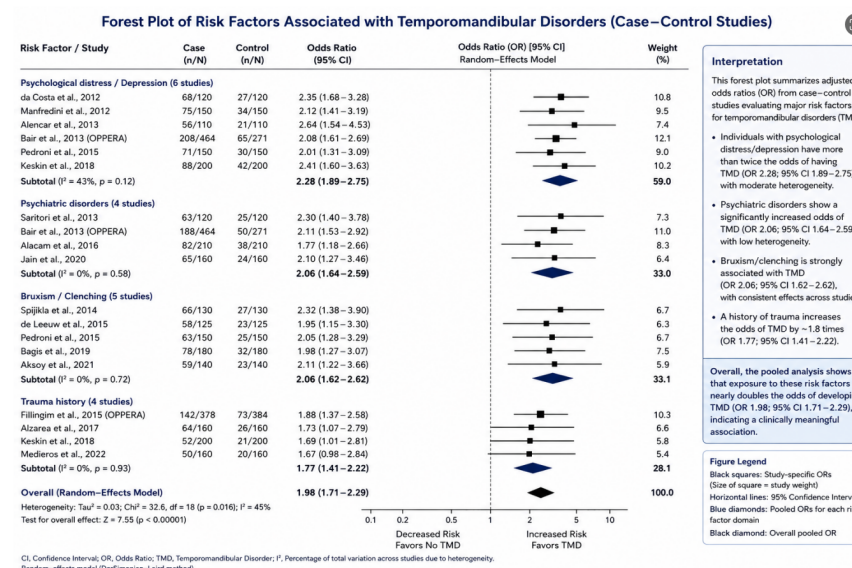
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Figure 1 forest plot



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