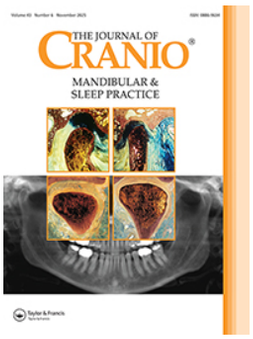

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Associations between temporomandibular disorders and tinnitus – a systematic review

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LITERATURE REVIEW

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Associations between temporomandibular disorders and tinnitus – a systematic review

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ABSTRACT

Objectives: Temporomandibular disorders (TMD) and tinnitus are highly prevalent conditions, that affects about 10–30% of the adult population and seem to co-exist. The primary objective of this systematic review was to investigate any associations between TMD and tinnitus. The secondary objective was to investigate if the associations differ between painful and non-painful TMDs.

Methods: An electronic literature search in five databases was performed, from the inception of the databases until 26th of October 2022. This was to identify clinical trials with prevalence numbers of patients with TMD, with and without tinnitus and vice versa. From 1240 studies, a total number of 32 studies were included in the meta-analysis. A risk of bias analysis was made using the Methodological Evaluation of Observational Research (MORE).

Results: Seventeen studies showed low risk of bias, while fifteen studies showed some risk of bias. Among patients with TMD, 57.5% also displayed tinnitus. In contrast, among patients with tinnitus, 92.9% also suffered from TMD. There was a strong association between patients with TMD that also had tinnitus, and patients with tinnitus that also had TMD (p's < 0.001). The odds ratio for TMD-patients also having tinnitus was 1.556 ($p < .05$), while it for tinnitus-patients also having TMD was 2.859 ($p < .05$). Six studies examined the psychological status, and there was a higher degree of psychosocial distress among patients with TMD and TMD/tinnitus.

Conclusions: There is a strong significant association between TMD and tinnitus, but further research is needed to unravel the nature of this association and its clinical implication.

KEYWORDS
Temporomandibular disorders; tinnitus; systematic review; human; association

Introduction

Temporomandibular disorders (TMD) encompass various conditions affecting the masticatory muscles, temporomandibular joints (TMJ), and related structures [1]. It is the leading non-odontogenic source of orofacial pain [2]. Currently, approximately 5–31% of individuals experience TMD, with an incidence in children reaching 11%. In addition, TMD is more prevalent in women, especially those of childbearing age [3,4].

While the exact cause of TMD remains uncertain, it has been proposed that the psychological profile, state of pain amplification, as well as general health and global symptoms play an important role in the etiology of painful TMDs [5,6]. Thus, TMDs seem to be biopsychosocial in nature, i.e. caused by several risk factors such as psychosocial, autonomic and genetic factors [7–11]. The biopsychosocial model includes the interactions between biological, psychological, and social perspectives on pain [12]. When it comes to the biological part of TMD genetic factors, physical health, pain modulation, hormonal changes, and sex are included in the model. Further, the included psychological factors on TMD can involve individual beliefs, coping abilities, anxiety, fear, depression, sleep disturbances, and mood changes. Finally, the social factors of the model can include relationships, communication and intimacy, culture, socioeconomic status, as well as school or work environments [9–11,13,14].

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Clinically, the major signs and symptoms related to TMD are pain in the temporomandibular joint (TMJ) and masticatory muscles, impaired jaw movements, TMJ sounds and otologic symptoms such as hearing loss, vertigo, dizziness, ear pain, and tinnitus [6]. In addition, studies have demonstrated a high frequency of otologic symptoms in TMD patients with tinnitus representing 52.1% among the otologic symptoms [6].

Tinnitus is defined as hearing noises without an external source causing the noise [15]. The exact mechanisms of tinnitus have not yet been determined, although it seems to be generally accepted that tinnitus often exists as a consequence of destruction of outer auditory structures, resulting in a disruption of the intrinsic neural activity in the central auditory pathway [16]. The pooled prevalence estimates of any tinnitus in young and older adults have been reported to be of 13.7% and 23.6%, respectively, which impairs their quality of life [17,18].

Notwithstanding, the clinical potential connections between these conditions remain under-researched, despite existing evidence suggesting their existence as well as co-existence [19,20]. In this direction, studies have identified bi-directional links between tinnitus and TMD, with varying findings related to the severity of TMD and tinnitus [20–22]. A meta-analysis revealed that individuals with TMD faced a 4.45 times higher likelihood of experiencing tinnitus compared to those without TMD, yet only three studies were included in this quantitative assessment [23]. Further, there are some previous systematic reviews, however, there is a need to broaden the search-terms and make them more inclusive since the previous ones only included few studies and did not do risk-assessments [23–25]. Therefore, a review with broader but still specific search-terms, including all diagnostic systems of TMD and tinnitus is necessary to be conducted in order to bring to light what possible cause-relationships exist. When this knowledge increases, it could provide clinicians and researchers points of departure for future research projects but also for choosing individualized treatment approaches. Based on this, the primary objective of this systematic review was to investigate if there are any associations between tinnitus and TMD, and the secondary objective to investigate if these associations differ between painful and non-painful TMDs.

Materials and methods

Protocol and research question

This systematic review was registered beforehand in Prospero (the International Prospective Register of Systematic Reviews), registration number (CRD42022356896). The research question was formed using the PECO framework [26], being an acronym for: *p* = Patients, E = Exposure, C = Control, O = Outcome. The population comprised patients (P) suffering from TMD, while the investigated condition/exposure (E) was tinnitus. The outcome (O) was which associations there are between patients suffering from TMD in general or divided in painful as well as non-painful TMDs (P) and patients suffering from tinnitus. The control (C) was patients without TMD or tinnitus. The present systematic review followed the Preferred Reporting Items for The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-Analyses of Health Care Interventions (the PRISMA-P checklist) [27] (Supplemental file 1).

The inclusion criteria were ***a)*** clinical trials, cross-sectional, case-control studies, and observational studies; ***b)*** adult individuals (over the age of 18) having TMD; ***c)*** adult individuals (over the age of 18) having tinnitus; ***d)*** adult individuals (over the age of 18) having TMD and tinnitus.

The following exclusion criteria were applied: ***a)*** Studies that cannot be found in other languages other than English or Scandinavian languages (Danish, Norwegian and Swedish); ***b)*** publications irrelevant to the research question; ***c)*** editorials, letters, legal cases, interviews, case-series, case reports and reviews.

Search strategy and selection criteria

The search strategy was developed and performed in MEDLINE (Ovid) in collaboration with the librarians LL and ELS at the University Library at (blinded). The search strategies were developed by LL in collaboration with GDC and NC, then peer-reviewed by another librarian (ELS) before LL performed the final searches. Together with the authors NC, EA, and MC each search concept was identified using the Medical Subject Headings (MeSH-terms) and free text terms. Finally, in order to translate the search into the other databases the Polyglot Search Translator was used [28]. The final electronic search was performed in the databases MEDLINE, EMBASE, CINAHL, the Cochrane Central Registry of Controlled Trials (CENTRAL), and Web of Science from the inception of each database to the 26th of October 2022. Also, a de-duplication was performed using the method described by Bramer et al.. (2016) [29]. Lastly, one final step was added to compare digital object identifiers (DOI) as well as a search in the reference-lists of the included studies and in several systematic reviews

found in the search was performed. The complete search strategy (for all databases) is available in Supplemental file 2.

Selection of studies

In order to avoid any risk of biasness in the process of screening the studies, the web-based tool Rayyan was used [30]. This was done independently and in a blinded mode by two of the authors (TS and VM). In cases when there was disagreement regarding eligibility this was resolved by discussion with the author (NC) who served as a judge making the final decision. When all disagreements were resolved the authors (TS and VM) attempted to retrieve the full texts of the included and potentially eligible studies. The studies that were retrieved were then reviewed in full text by the same authors (TS and VM) to determine whether they aligned with the inclusion criteria or not. As before, any disagreement was resolved through a discussion with the author (NC). Finally, additional articles were identified by means of citation search. The full texts of these identified studies were then retrieved and reviewed in the same manner as presented before.

Analysis of risk of bias

Risk of bias and quality assessment of the included articles were performed with the Methodological Evaluation of Observational Research protocol (MORE) [31] that distinguishes between external and internal validity. While external validity refers to the degree that the outcomes of the study can be applied to the general population, internal validity refers to the degree that the outcomes of the study are accurate for the studied subjects. *External validity* is assessed by six parameters, which are: **1)** sampling of subjects; **2)** assessment of sampling bias; **3)** estimate of sampling bias; **4)** exclusion rate from the analysis; **5)** address of sampling bias in the analysis; and **6)** subject flow. *Internal validity* is assessed by five parameters, and these are **1)** source to measure outcomes; **2)** definition of outcomes; **3)** measurements of outcomes; **4)** outcomes in subpopulations; and **5)** reporting of outcomes. Thus, the assessment was done on the level of parameters where minor or major flaws could be identified. Two authors (TS and VM) evaluated the risk of bias for each study blinded and independently. In cases where conflict aroused it was resolved by discussion with the author (MC), who served as a judge. The individual quality assessment of each included study is presented in Table 1. Even though "Healthcare-based sampling frame" is considered a major flaw according to the MORE quality assessment tool, these studies were decided beforehand to be included in this systematic review since it is not possible to completely avoid this in the present area.

Extraction of data

After the risk of bias and quality assessment, data extraction followed. A data extraction form was designed, developed by the authors (EA, AG, and GDC), and pilot-tested independently on three randomly selected studies by two of the authors (TS and VM) to ensure consistency in extraction. The extracted data included information on the characteristics of the included studies and study participants, such as the authors, study type, diagnosis/criteria that had been used, number of participants, mean age of participants, male-female ratio, prevalence of tinnitus, prevalence of TMD, presence of tinnitus among patients with TMD, and presence of TMD among patients with tinnitus. Any disagreement in the data extracting process was resolved by the author (EA), who served as a judge.

Statistical analysis

All of the tests were performed in SPSS (v.25 IBM, New York, USA), by the author GTC. Descriptive analyses were used to report frequencies. The Chi-square test was used to compare the prevalence ratios of both the presence of tinnitus among patients with TMD, as well as the presence of TMD among patients with tinnitus. The odds ratio was also determined in the two groups to determine the probability of patients with tinnitus to have TMD and the probability of patients with TMD to have tinnitus. The odds ratio was used as a measure in a random effects model with a 95% confidence interval. The Chi-square test of association was performed to assess the association between TMD and tinnitus. The strength of the associations was also determined using Phi. A significance level of $p < .05$ was applied when performing all of the tests. The results of the individual studies that differed between painful and non-painful TMD were narratively described.

Results

Literature search outcome

The entire literature search from all databases resulted in a total of 1240 articles, but after the removal of duplicates 618 publications remained. The title and abstracts of those articles were then screened which resulted in an exclusion of 533 articles, leaving 85 full

Table 1. Table illustrating the extracted study characteristics of the seventeen included studies.

Author, year	*Study type*	*Number of participants*	*Male: Female ratio*	*Mean age of participants*	*Diagnostical system for TMD*	*Type of TMD*	*Prevalence of TMD (%)*	*Prevalence of tinnitus (%)*	*Presence of tinnitus in patients with TMD (%)*	*Presence of TMD in patients with tinnitus (%)*
Akhter et al., 2013 [45]	CSS	1930	1:1	19	Questionnaire	I: Clicking only II: Pain in TMJ only III: Difficulty in mouth opening only IV: Clicking and pain in TMJ V: Clicking and difficulty in mouth opening VI: Pain in TMJ and difficulty in mouth opening VII: Clicking, pain in TMJ and difficulty in mouth opening	I = 58.7% II = 3.9% III = 3.3% IV = 5.3% V = 8.8% VI = 2.0% VII = 17.8%	Total 7%	6% 47.6% 5.6% 55.2% 4.2% 9.1% 4.1%	Total 39%
Algieri et al., 2017 [50]	CSS	200	1:4	44	Clyde H Wilke	Not specified	100%	60.0%	60.0%	100%
Bush, 1987 [32]	CSS	105	1:6	39	Questionnaire	Not specified	100%	33.0%	33.0%	100%
Bernhardt et al., 2011 [42]	CSS	3300	1:10	NA	Questionnaire	TMJ pain	5.8%	9.9%	NA	13.1%
Buergers et al., 2014 [46]	Prospective CT	951	1:1	54	RDC/TMD	Not specified	6.8%	7.2%	36.6%	44.1%
Cebi, 2020 [47]	CSS	288	1:3	33	DC/TMD	(1) disk displacement with reduction (2) disk displacement without reduction	Total 100%	8.7% 2.8%	75.8% 24.2%	100%
Ciancaglini et al., 1994 [39]	CSS	797	1:2	37	Not specified	TMJ	100%	6.4%	6.4%	100%
Edvall et al., 2019 [36]	CSS	2482	1:1	NA	Questionnaire	Not specified	19.6%	100%	100%	19.6%
Fernandes et al., 2013 [44]	CSS	224	1:5	38	RDC/TMD	(1) Painful TMD (2) Nonpainful TMD	(1) 72.3% (2) 27.7%	Total 57.6%	70.4% 24.2%	88.4% 11.6%
Fernandes et al., 2014 [60]	CSS	261	0:1	37	RDC/TMD	(1) Painful TMD (2) Nonpainful TMD	(1) 82.8% (2) 17.2%	Total 62.5%	70.3% 24.4%	Total 93.3%
Henderson et al., 1992 [38]	CSS	21	1:20	28	Not specified	Myofascial pain *and* internal derangement	100%	85.7%	85.7%	100%
Hilgenberg et al., 2012 [43]	CSS	200	1:2	39	RDC/TMD	Not specified	85.0%PG, 55%CG	100%PG, 0% CG	100%PG, 0%CG	85%PG, 55%CG
Kim et al., 2017 [35]	CSS	11745	1:1	NA	Questionnaire	Not specified	NA	21.8%	NA	9.9%
Kong et al., 2021 [37]	CSS	5786	2:1	NA	Questionnaire	Not specified	21.9%	24.9%	35.0%	31.0%
Kusdra et al., 2018 [51]	CSS	485	1:3	NA	RDC/TMD	Not specified	100%	46.0%	46.0%	100%
Kuttila et al., 2005 [41]	CSS	1720	3:4	45	Questionnaire	TMD pain	8.0%	15.0%	53.0%	20.5%

(*Continued*)

Table 1. (Continued).

Author, year	*Study type*	*Number of participants*	*Male: Female ratio*	*Mean age of participants*	*Diagnostical system for TMD*	*Type of TMD*	*Prevalence of TMD (%)*	*Prevalence of tinnitus (%)*	*Presence of tinnitus in patients with TMD (%)*	*Presence of TMD in patients with tinnitus (%)*
Lam et al., 2001 [40]	Retrospective CT	776	3:2	39	RDC/TMD	(1) Myalgia (2) TMJ pain (3) Combination of both	Total 43.0%	Total 24.7%	NA	Total 64.1%
Lee et al., 2016 [33]	Retrospective CS	37925	19:1	NA	Not specified	Not specified	100%PG, 0%CG	4.8%PG, 1.7%CG	4.8%PG, 0%CG	100%PG, 0%CG
Maciel et al., 2018 [52]	CSS	251	1:3	NA	Questionnaire	Not specified	70.5%	15.9%	18%	80%
Manfredini et al., 2015 [20]	CSS	238	10:3	49	Not specified	(1) Myalgia (2) Nonpainful internal derangement (3) Nonpainful TMJ arthrosis	Total 100%	Total 30.4%	32.8% 29.3% 33.7%	Total 100%
Michiels et al., 2019 [54]	CSS	6115	1:10	NA	Questionnaire	Not specified	7.0%	100%	100%	7%
Oliveira et al., 2023 [48]	Retrospective CT	57	9:1	NA	Not specified	TMD pain	100%	72%	72%	100%
Parker & Chole, 1995 [56]	CSS	1032	1:2	NA	Questionnaire	(1) TMJ click *and* TMJ pain (2) TMJ click *or* TMJ pain	Total 32.8%	Total 19.6%	54.8% 23.7%	Total 58.9%
Pavaci et al., 2019 [53]	CSS	230	1:1	53	Not specified	Not specified	48.5%PG, 33.0%CG	100%PG, 0% CG	NA	48.0%PG, 0%CG
Peleg et al., 2022 [4]	CSS	51	9:8	52	DC/TMD	TMD	27.5%	100%	100%	27.5%
Riga et al., 2010 [59]	Prospective CT	40	1:9	43	Questionnaire	Arthralgia	100%	70%	70%	100%
Ren & Isberg, 1995 [57]	CSS	135	1:2	NA	Questionnaire	disk displacement with reduction and disk displacement without reduction	Total 100%	Total 39.3%	Total 39.3%	Total 100%
Rubinstein et al., 1990 [55]	CSS	102	3:2	56	Helkimo's index	TMJ click *and* TMJ pain	82.4%	100%	100%	82.4%
Saldanha et al., 2012 [43]	CSS	200	1:3	37	RDC/TMD	Ia: myofascial pain Ib: myofascial pain with limited opening IIa: disc displacement with reduction IIb: disc displacement without reduction with limited opening IIc: disc displacement without reduction without limited opening IIIa: arthralgia IIIb: osteoarthritis IIIc: osteoarthrosis	Ia = 27.0% Ib = 27.5% IIa = 36.5% IIb = 0.5% IIc = 5.0% IIIa = 38.5% IIIb = 1.5% IIIc = 1.0%	Total 50%	32.0% 39.0% 44.3% 0% 6.2% 53.5% 3.0% 1%	Total 85%
Song et al., 2018 [34]	CSS	17575	9:1	43	Questionnaire	Not specified	11.7%	22.0%	NA	17%
Tuz et al., 2003 [58]	Prospective CT	250	1:4	30	Unspecified	(1) Myofascial pain (2) Internal derangement (3) Painful TMD *and* internal derangement (4) No TMD	(1) 11.0%PG, 0%CG (2) 77%PG, 0%CG (3) 12%PG, 0%CG (4) 0%PG, 100%CG	Total 41.6%	59.1%PG, 0%CG 44.2%PG, 0%CG 41.6%PG, 0%CG 0%PG, 26%CG	100%PG, 0%CG
Yap et al., 2022 [21]	CSS	200	1:3	19	DC/TMD	Not specified	59.5%	35.0%	46.0%	NA

Abbreviations: TMD = temporomandibular disorders; CSS = cross sectional study; CS = cohort study; CT = clinical trial; NA = not available; PG = Patient group; CG = Control group; TMD = temporomandibular disorders; TMJ = temporomandibular joint.

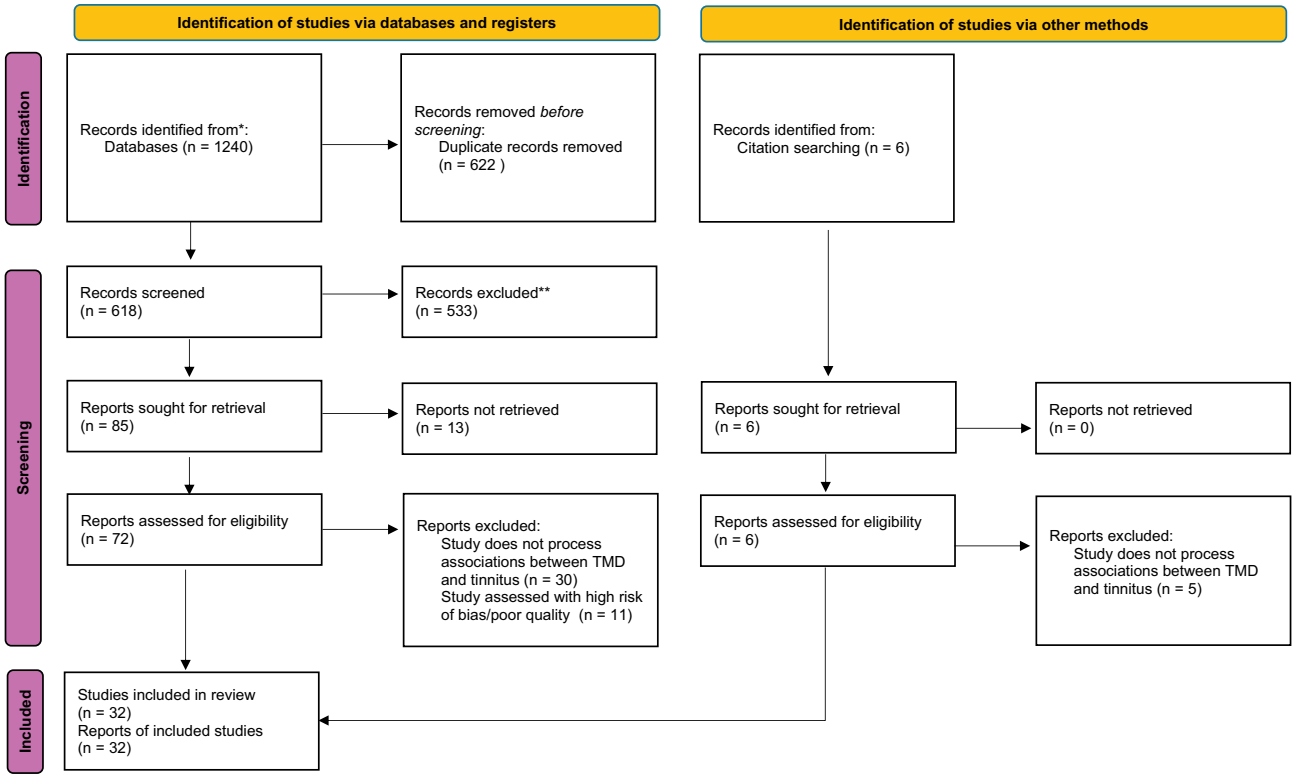

Figure 1. The figure illustrates the PRISMA flow-chart of the database search strategy. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. *From*: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

texts that were sought for retrieval, of which 72 were successfully retrieved. Additionally, 6 articles were found by citation searching. Out of these 78 full-texts, 35 of them did not meet the inclusion criteria and were excluded in this stage. After the risk of bias/quality assessment an additional 11 full-texts were excluded, which resulted in a total of 32 full-texts included in this systematic review [4,20,21,32–60]. The PRISMA flow-diagram including the process of evaluating full-texts for inclusion is shown in Figure 1.

Risk of bias and study characteristics

Sixteen of the thirty-two included articles displayed a "Healthcare-based sampling frame" which is considered a major flaw according to the MORE quality assessment. However, as described in the materials and methods section these studies were included in this systematic review. A total of 17 studies showed a low risk of bias (displayed in green) [32–48] while 15 studies showed some risk of bias (displayed in orange) [4,20,21,49–60], as shown in Table 1. The characteristics of the 32 included studies were compiled into a table containing the type of TMD (painful or non-painful) or non-TMD, mean age of participants, male-female ratio, prevalence of tinnitus, prevalence of TMD, presence of tinnitus among patients with TMD, and presence of TMD among patients with tinnitus, are reported in Table 2.

Relations and associations between tinnitus and TMD

Thirteen of the included studies had tinnitus as the "main group" and assessed the number of participants with TMDs among the tinnitus population. Regarding the TMD studies, 19 of them assessed the number of participants with tinnitus among the TMD populations.

When it comes to the patient group suffering from tinnitus the vast majority of the patients have a diagnosis of TMD (Table 3). However, when it comes to the patient-group suffering from TMD approximately half

Table 2. Table summarizing quality assessment and risk of bias.

Author, year	*External validity*	*Internal validity*	*Comments*	*Risk of bias*
Akhter et al., 2013 [45]	*Minor flaw*: Sampling of the subjects by the investigators	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	–	Low risk of bias
Algieri et al., 2017 [50]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population based sampling method No assessment of sampling bias *Poor reporting*: Exclusion rate from the analysis not reported Estimate bias not reported Exclusion rate from analysis not reported	*Poor reporting*: Validation of outcomes measurements not reported	–	Some risk of bias
Bush, 1987 [32]	*Major flaw*: Healthcare-based sampling frame *Poor reporting*: Not reported estimate bias. The exclusion rate from the analysis not reported	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Bernhardt et al., 2011 [42]	–	–	–	Low risk of bias
Buergers et al., 2014 [46]	*Poor reporting*: Assessment of sampling bias *Major flaw*: Healthcare-based sampling frame	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Cebi, 2020 [47]	*Minor flaw*: Sampling of the subjects by the investigators *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Ciancaglini et al., 1994 [39]	*Minor flaw*: Nongeneral population based sampling method *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Edvall et al., 2019 [36]	*Minor flaw*: Sampling of the subjects by the investigators	–	–	Low risk of bias
Fernandes et al., 2013 [44]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Fernandes et al., 2014	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Poor reporting*: Estimate bias not reported Exclusion rate from the analysis not reported *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Henderson et al., 1992 [38]	*Minor flaw*: Random sampling restricted to geographic area. *Major flaw*: Healthcare-based sampling frame *Minor flaw*: sampling bias not adressed in analysis	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias

(*Continued*)

Table 2. (Continued).

Author, year	*External validity*	*Internal validity*	*Comments*	*Risk of bias*
Hilgenberg et al., 2012 [43]	*Minor flaw*: Random sampling restricted to geographic area. *Major flaw*: Healthcare-based sampling frame *Poor reporting*: Assessment of sampling bias not reported Response rate in total sample not reported Response rate in subgroups not reported Exclusion rate from the analysis not reported Sampling bias not reported in the analysis	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Kim et al., 2017 [35]	*Minor flaw*: Sampling of the subjects by the investigators	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	–	Low risk of bias
Kong et al., 2021 [37]	*Poor reporting*: Exclusion rate from the analysis not reported	–	–	Low risk of bias
Kusdra et al., 2018 [51]	*Poor reporting*: Sampling of the subjects by the investigators not reported Exclusion rate from the analysis not reported Address Bias not reported *Minor flaw*: Nongeneral population based sampling method *Major flaw*: Medical records based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases *Poor reporting*: Reliability of the estimates not reported	–	Some risk of bias
Kuttila et al., 2005 [41]	*Minor flaw*: Random sampling restricted to geographic area *Poor reporting*: exclusion rate from the analysis not reported Exclusion rates in subgroups not reported	–	–	Low risk of bias
Lam et al., 2001 [40]	*Minor flaw*: Random sampling restricted to geographic area *Major flaw*: Medical records based sampling frame (they used medical records for dataextraktion)	*Minor flaw*: Data obtained from medical records	–	Low risk of bias
Lee et al., 2016 [33]	*Poor reporting*: Aim of study not reported *Minor flaw*: Random sampling restricted to geographic area *Major flaw*: insurance claims based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence obtained from administrative database. Frequency can be relevant but not assessed in the study	–	Low risk of bias
Maciel et al., 2018 [52]	*Minor flaw*: Sampling of the subjects by the investigators *Poor reporting*: Estimate bias not reported Exclusion rate from the analysis not reported	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases: proxy reported *Poor reporting*: Validation of outcomes not reported measurements Reliability of the estimates not reported	–	Some risk of bias
Manfredini et al., 2015 [20]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Poor reporting*: Assessment of sampling bias not reported Estimate bias not reported Address Bias not reported *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias

(*Continued*)

Table 2. (Continued).

Author, year	*External validity*	*Internal validity*	*Comments*	*Risk of bias*
Michiels et al., 2019 [54]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Poor reporting*: Estimate bias not reported Exclusion rate from the analysis not reported	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	–	Some risk of bias
Oliveira et al., 2023 [48]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias
Parker & Chole, 1995 [56]	*Minor flaw*: Random sampling restricted to geographic area. self selection- based sampling method. *Major flaw*: Health care-based sampling frame	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Pavaci et al., 2019 [53]	*Minor flaw*: Sampling of the subjects by the investigators *Poor reporting*: Estimate bias not reported Exclusion rate from the analysis not reported	–	–	Some risk of bias
Peleg et al., 2022 [4]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method Assessment of sampling bias *Poor reporting*: Estimate bias not reported Exclusion rate from the analysis not reported *Major flaw*: Healthcare-based sampling frame	Source of measure incidence/ prevalence of chronic diseases: minor flaw	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Riga et al., 2010 [59]	*Poor reporting*: General population based sampling not reported Nongeneral population based sampling frame not reported Assesment of sampling bias not reported Response rate in total sample not reported Exclusion rate from the analysis not reported Sampling bias not reported Number screened not reported Number eligible not reported. *Major flaw*: Healthcare-based sampling frame	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Ren & Isberg, 1995 [57]	*Minor flaw*: Random sampling restricted to geographic area the authors did not assess sampling bias *Major flaw*: Healthcare-based sampling frame *Poor reporting*: Response rate in total sample not reported Exclusion rate from the analysis not reported	–	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Rubinstein et al., 1990 [55]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Some risk of bias
Saldanha et al., 2012 [43]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population-based sampling method *Major flaw*: Healthcare-based sampling frame	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	Healthcare-based sampling frame is accepted since the research area makes it impossible to exclude such studies	Low risk of bias

(*Continued*)

Table 2. (Continued).

Author, year	*External validity*	*Internal validity*	*Comments*	*Risk of bias*
Song et al., 2018 [34]	*Minor flaw*: Sampling of the subjects by the investigators	*Minor flaw*: Source of measure incidence/ prevalence of chronic diseases	–	Low risk of bias
Tuz et al., 2003 [58]	*Major flaw*: Medical records based sampling frame *Minor flaw*: Random sampling restricted to geographic area *Poor reporting*: Response rate in total sample not reported Response rate in other subgroups not reported Exclusion rate from analysis not reported Exclusion rate from analysis in subgroups not reported Sampling bias not addressed in analysis Number screened not reported Number eligible not reported	*Minor flaw*: Data obtained from medical records	–	Some risk of bias
Yap et al., 2022 [21]	*Minor flaw*: Sampling of the subjects by the investigators Nongeneral population based sampling method Assessment of sampling bias	–	–	Some risk of bias

Table 3. The prevalence ratios of the presence of tinnitus among patients with temporomandibular disorders as well as the presence of temporomandibular disorders in patients with tinnitus are presented in this table both in number of patients as well as in percentage.

			Tinnitus		
			No	Yes	Total
TMD	No	cases	17160	14908	32068
		% in TMD	53.5%	46.5%	100.0%
	Yes	cases	2156	2915*	5071
		% in TMD	42.5%	57.5%*	100.0%
Total		cases	19316	17823	37139
		% in TMD	52.0%	48.0%	100.0%
			TMD		**Total**
			No	Yes	
TINNITUS	No	cases	2172	9994	12166
		% in TINNITUS	17.9%	82.1%	100.0%
	Yes	cases	134	1763*	1897
		% in TINNITUS	7.1%	92.9%*	100.0%
Total		cases	2306	11757	14063
		% in TINNITUS	16.4%	83.6%	100.0%

*= $p < .05$ (Chi-square test).
TMD = temporomandibular disorders.

of the patients also have a diagnosis of tinnitus (Table 1). Further, there is a strong association of having tinnitus if the patient also has a diagnosis of TMD (Chi-square value: [$X^2(1) = 212.075$; $p < .001$]) as well as the opposite (Chi-square value: [$x^2(1) = 139.354$; $p < .001$]). This association was strong for both groups (Phi value for TMD in tinnitus is 0.076; $p < .001$, and Phi value for tinnitus in TMD is 0.100; $p < .001$). The odds ratio for TMD is 1.556 ($p < .05$) and for tinnitus 2.859 ($p < .05$).

Narrative description of painful TMD vs non-painful TMD

In this article search 7 articles that clearly differed between painful and non-painful TMD were revealed. In one study by Henderson et al.. (1992) there was no significant difference in the prevalence of tinnitus among patients with painful TMD and non-painful TMD [38]. However, in the other six studies there were two-eight times more patients with painful TMD also having tinnitus (range between 65% and 93% of the patients with tinnitus) than those with non-painful TMDs (range between 7% and 35% of the patients with tinnitus) [20,43–45,58,60].

Psychosocial findings of Tinnitus and TMD

Six of the studies included in the analysis examined the psychological status of individuals with tinnitus and TMD, with a primary focus on depression, assessed through validated tools. Among these, four studies revealed that individuals with both tinnitus (mild or severe) and TMD experienced higher levels of depression compared to those with tinnitus alone, as per their severity [4,36,37,44]. In a study by Hilgerberg et al.. (2012), it was found that the presence of tinnitus was associated with significantly elevated levels of depression when compared to a control group (no tinnitus) [49]. Furthermore, a study identified a positive relationship between the severity of tinnitus, chronic pain, and depression, highlighting a significant correlation between chronic pain intensity and tinnitus [43].

Discussion

This study aimed to investigate potential associations between the presence of tinnitus and TMD or vice versa, but also the strength of this association. Secondarily, it aimed to distinguish between the associations of tinnitus with painful and/or non-painful TMD. Our results revealed a strong bi-directional association between TMD and tinnitus, with the highest prevalence of tinnitus reported in patients diagnosed with painful TMD.

A clinically interesting finding that was revealed was that 92.9% of the patients with tinnitus displayed a TMD diagnosis, which is a significantly higher prevalence when compared to the general population where literature suggests that only about 5–31% has a TMD diagnosis [3,4]. Furthermore, while tinnitus is represented by 12–30% in the general population [61], our meta-analysis showed that 57.5% of the patients with TMD also suffered from tinnitus. This indicates that the presence of TMD is 3 to 15 times higher among tinnitus patients than in a non-TMD population, while the increase of the prevalence of TMD – 2 to 5 times higher – is not that distinct in a healthy population when compared to patients suffering from tinnitus. This finding is in line with a recent cross-sectional study reporting that 67% of tinnitus population presented TMD [62]. In contrast to previous systematic reviews, our study reported a higher bi-directional prevalence of TMD and tinnitus. This could be explained

by different factors. One is because of the higher number of studies included in the analysis that could be a contributing factor only by time. However, when analyzing the previous ones, this was not the fact. Another reason was that the present study used broader and more inclusive search terms than the previous [23–25]. One of the previous reviews did not do any odds-ratio, risk-ratio and chi-square analysis, but only reported the findings [24]. Further, the studies assessing odds-and-risk ratios just included studies using clinically diagnosed TMD, resulting in only five [23] and eight studies [25] for their analysis, respectively. Taken together, the results from this study further contribute to knowledge about the potential cause-relationship, where tinnitus seems rather to be a consequence of TMD instead of TMD being a consequence of tinnitus.

Further, the results from the meta-analysis also indicate that the strong bi-directional association between both conditions points towards the fact that patients presenting tinnitus are more likely to have TMD (odds ratio = 2.85) than TMD patients having tinnitus (odds ratio = 1.55). Even though an exact cause for this association is not yet fully understood, some hypotheses can be raised. TMD and tinnitus may be linked due to the close proximity of the middle ear and TMJ [1,19,43]. This close anatomical and functional relationship between these two structures is mediated by the anterior malleolar ligament (AML), the sphenomandibular ligament (SML), and the discomallear ligament (DML). In addition, DML, distinct from AML, is a key player in the mobility of the malleus, a bone in the middle ear, with its structure potentially affecting outcomes in TMJ surgery and conditions leading to anterior displacement of the articular disc. These ligaments can be stretched during TMJ use affecting middle ear structures like the eardrum and malleus [63]. The relationship between the TMJ and the middle ear depends on which ligament is present, the structure of the ligament (whether collagenous or elastic), and the width of the petrotympanic fissure. Also, the overactivity of masticatory muscles could influence the association between tinnitus and TMD, since these muscles which are involved in TMD share the trigeminal nerve with muscles involved in the function of the eustachian tube, which indeed includes the lateral and medial pterygoids muscles [64]. Disruption of the pressure regulation of the auditory tube may be an important factor contributing to the increased risk of developing tinnitus risk [64]. Furthermore, this association could also be explained by the somatosensory theory, in which chronic pain or impaired psychosocial status like depression or anxiety induce changes in the central nervous system, producing a sensorial hypersensitivity and an altered perception of the auditive stimuli [43,65,66]. A recent review also imposes that this link can be contributed by an increased gut permeability, a disturbed gut microbiome and disturbed metabolism of tryptophan – a well-known biomarker for chronic musculoskeletal pain. This is a substrate for serotonin and melatonin, that both play a key role in microglia activation (e.g. gastrointestinal tract) and regulation of chronic orofacial pain that leads to an increased sensibility to pain and depression, which in turn could affect both TMD and tinnitus [67]. In addition, another study found an association between depression and TMDs as well as tinnitus [4]. Finally, TMJ herniation – even though it is rare – could also be the cause of tinnitus [68].

The present systematic review also investigated if the associations differ between painful and non-painful TMDs among patients with tinnitus. However, due to an insufficient number of studies distinguishing between painful and non-painful TMDs, a meta-analysis was not feasible. Notwithstanding, when the prevalence was compared there was a higher prevalence of tinnitus among patients with painful TMDs than in patients with non-painful TMDs. In addition, one of the included studies reported that the severity of tinnitus was correlated with the severity of chronic pain, which could be explained by the influence that the central nervous system exerts on these two symptoms [43].

In this direction, since the complexity of chronic pains such as TMDs and their multifactorial biopsychosocial etiology are well known [69,70], and that tinnitus could be triggered by psychosocial distress [71], the assessment of the psychosocial status in patients suffering of TMD and/or tinnitus is of main importance. However, it is often neglected. In the present study, only 13 of the included studies assessed the psychosocial status, mainly focusing on depression symptoms and severity; however, only six studies used validated tools for this assessment. These studies found that the single presence of tinnitus is associated with higher levels of depression and that there is a relationship between the presence of chronic pain such as TMDs, tinnitus and depression (43,49). In addition, it has been reported that tinnitus could be associated with periods of stress and anxiety, as a result of enhanced activity in the limbic and autonomic nervous systems [71]. These variables are also usually impaired in TMD patients [72,73], fact that could strengthen the relationship between psychosocial impairment, TMD and tinnitus.

Study strengths and limitations

One limitation is the diversity in the system used for TMD diagnostics in the included articles. Only a few used a standardized and validated clinical protocol; most used questionnaires or did not even specify how TMD was diagnosed. Based on this, there is an uncertainty about the TMD group, what TMD condition is elaborated, i.e. it could be a painful condition, or just an internal derangement of the temporomandibular joint. However, both types of TMD could be associated with tinnitus, but with different cause-relationships. Therefore, even though there is a strong reported association in the present study, the outcome might have been different if only validated systems would have been used and the different TMDs analyzed separately. As for TMD, the same accounts for tinnitus. Even though patient-history/anamnesis remains the easiest and most cost-effective method for assessing tinnitus, there are instrumental examinations available to assess the presence and severity of tinnitus [74]. Another limitation could be that only adults were included in this review. However, this was chosen since children are growing and therefore growth itself could be a possible confounding factor. Further, the present validated diagnostic criteria for TMD (DC/TMD) [75], as well as the previous one (research diagnostic criteria for TMD; RDC/TMD) [76] are not validated for children which therefore would be a confounding factor itself. Even though, the Axis I of the DC/TMD was adapted for children and recently published in a Delphi study, there is still no validation of this tool [77]. RDC/TMD is validated for adolescents, but not children. A third limitation was that this study could not investigate if there are any gender differences when it comes to frequency of both TMD and tinnitus. This could be relevant since the vast majority of TMD patients are women, and sex itself seems to be one of the important etiological factors [3,4]. Based on this, a deeper understanding on possible sex differences would also contribute to the knowledge of the TMD-tinnitus cause-relationship. However, when it comes to sex differences, present knowledge is inconsistent. For instance, one of the included studies reported that there are no significant differences between men and women according to either TMD or tinnitus [4]. On the other hand, another study reported that the prevalence of tinnitus is more frequent among men than women [61]. Therefore, in future studies a possible gender difference needs to be investigated, since it would have a great clinical implication once the vast majority of the patients with TMD are women [78]. This would also contribute to a deeper understanding of the connection and causality of both conditions.

One of the strengths of this study is the inclusion of a relatively large number of full texts ($n = 32$). Another strength is that most included studies showed a low risk of bias and high quality, which indicates that the outcome of the present study is valid and reliable.

Clinical implications and generalizability

The results of this study indicate that it is important to identify patients with tinnitus and TMD by health care professionals, since both conditions seem to be comorbid. This could lead to the fact that these patients will receive individualized treatments that affect both conditions. However, the available literature is inconclusive about the effects of treating one condition on the improvement of the other condition, which should be a matter of assessment for future researches [79,80]. This would lead to less patient suffering, less costs for the society and increased quality of life in these two common patient-groups (10–20%) [78,81]. Thus, based on our results, the authors suggest that health care professionals in clinical practice that have patients that suffer from either tinnitus or TMD should also consider assessing the respective condition by for instance the validated 3Q-TMD [82] in patients with tinnitus or the questionnaires FiveQ, THI, THQ etc. in patients with TMD complaining of ear symptoms [74] or the PHQ-4 in both patients, since anxiety and depression could increase both conditions [83]. This screening would then help clinicians to individualize and choose the treatment-approach based on both conditions.

Additionally, as tinnitus could be a red flag of other potentially life-threatening diseases, assessing tinnitus in clinical practice is of main importance, since comorbidities other than TMD like, multiple sclerosis, vestibular schwannoma, meningitis, syphilis, Lyme disease and medications like salicylates, nonsteroidal anti-inflammatory drugs, chemotherapy agents between others are associated with it [71]. Therefore, the orofacial pain specialist should be aware of these other associations, in order to make differential diagnosis and consequently to refer the patient to a proper health care provider.

Future applications

Based on this review, one could recommend that future studies investigate not just the prevalence but also the biopsychosocial aspects among these patients in order to find common etiological factors. Further, there is a need for studies based on the validated diagnostic system, dividing the patients in the specified sub-

groups of DC/TMD in order to present associations based on cause-relationships and not only the TMD group as an entity. The same accounts for tinnitus. Anamnesis remains the easiest and most cost-effective method for assessing tinnitus. However, instrumental examinations are also available to assess its severity, which then also could be used to correlate tinnitus severity with the presence of TMD. Then, studies could also specify whether tinnitus was bilateral or unilateral and if it is present on the same side of each specific TMD diagnosis. When common etiological factors are presented, then randomized, controlled clinical treatment studies are warranted with for instance standard treatments of TMD and tinnitus compared to combination of treatments looking at both pain reduction, physical functioning, and reduction in tinnitus. In addition, since conservative treatments for TMD include cognitive behavioral therapies, it would be interesting to investigate the role of these therapies in tinnitus related to TMD. It would also be intriguing to distinguish if there could be gender-specific causes or treatment approaches.

Conclusion

It can be concluded that there is a strong significant association between tinnitus and TMD and that the prevalence of TMD among patients with tinnitus is significantly higher than the prevalence of tinnitus among patients with TMD. Further research is needed to unravel the nature of this association and its clinical implication.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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