Self-Reported Migraine and Chronic Fatigue Syndrome Are More Prevalent in People with Myofascial vs Nonmyofascial Temporomandibular Disorders

Haissam Dahan, DMD, PhD
PhD Student
Division of Oral Health and Society
Faculty of Dentistry
McGill University
Montreal, Quebec, Canada

Yoram Shir, MD
Director
Alan Edwards Pain Management Unit
McGill University Health Centre
Montreal General Hospital Campus
Montreal, Quebec, Canada

Belinda Nicolau, DDS, PhD
Associate Professor
Division of Oral Health and Society
Faculty of Dentistry
McGill University
Montreal, Quebec, Canada

David Keith, DMD, BDS
Professor
Department of Oral and Maxillofacial Surgery
Massachusetts General Hospital
Boston, Massachusetts, USA

Paul Allison, BDS, FDSRCS, DMD
Professor
Division of Oral Health and Society
Faculty of Dentistry
McGill University
Montreal, Quebec, Canada

Correspondence to:
Dr Haissam Dahan
Division of Oral Health and Society
Faculty of Dentistry
McGill University
2001 McGill College
Montreal, Quebec, H3A 1G1, Canada
Email: haissam.dahan@mail.mcgill.ca

Aims: To compare the number of comorbidities and the prevalence of five specific comorbidities in people who have temporomandibular disorders (TMD) with or without myofascial pain. **Methods:** This cross-sectional study included 180 patients seeking TMD treatment in Boston and Montreal hospitals. A self-administered questionnaire was used to collect information on sociodemographic and behavioral factors, as well as the presence of the following five comorbidities: migraine, chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis, and restless leg syndrome. TMD was diagnosed using the Research Diagnostic Criteria for TMD. Chi-square and Student *t* tests were used for categorical and continuous variables, respectively, to test for differences between myofascial (n = 121) and nonmyofascial (n = 59) TMD groups. Multiple logistic regression analysis was used to compare the type and number of self-reported comorbidities in both groups, controlling for confounding variables. **Results:** The following were found to be significantly higher in the myofascial TMD group than in the nonmyofascial TMD group: self-reported migraine (55% vs 28%, $P = .001$), chronic fatigue syndrome (19% vs 5%, $P = .01$), and the mean total number of comorbidities (1.30 vs 0.83, $P = .01$). **Conclusion:** Individuals with myofascial TMD had a higher prevalence of self-reported migraine and chronic fatigue syndrome than those with nonmyofascial TMD. *J Oral Facial Pain Headache 2016; 30:7–13. doi: 10.11607/ofph.1550*

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Temporomandibular disorders (TMD) is a collective term comprising heterogeneous conditions of dysfunction or pain in the temporomandibular joint, disc, and surrounding muscles.[1] Individuals with TMD have a high prevalence of comorbidities, with reported totals averaging from 3.5 to 4.5 comorbidities per person.[2,3] Burris et al found that the top five comorbidities in individuals with TMD were severe headaches (40.9%), earache/tinnitus (39.4%), allergies/hives (32.1%), gastric acid reflux (20.1%), and high blood pressure (19.7%).[3] Pain conditions, such as fibromyalgia, are some of the comorbidities found in individuals with TMD.[4,5] A growing body of literature suggests that the link between these pain conditions could be in part a manifestation of a central sensitivity syndrome.[6] Central sensitivity syndromes comprise overlapping and similar syndromes without structural pathologic findings that are bound by the common mechanism of central sensitization.[7] Besides TMD, central sensitivity syndromes include migraine, chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), interstitial cystitis (IC), and restless leg syndrome (RLS). Currently, data are limited on the degree of overlap between these conditions and TMD. Furthermore, most studies investigating comorbidities in the TMD population have estimated comorbidities using questionnaires that simply asked participants "do you have a condition?" This method can overestimate prevalence by introducing recall and social desirability biases.[8,9] A more accurate assessment of the presence of comorbidities could be made by using validated diagnostic questionnaires that probe disease symptoms.

Individuals with TMD can be divided on the basis of the presence of myofascial TMD pain (m-TMD) or nonmyofascial TMD pain (n-TMD).[10–13] The prevalence of m-TMD, which includes muscular pain conditions such as myospasms and myogenous pain, is more chronic, results in more dysfunction, and is more debilitating than n-TMD, which includes disc dysfunction, joint pain, and arthritis.[10] When compared with individuals with n-TMD, those with m-TMD have a higher prevalence of depression, anxiety, and mood disorders.[10,14] Furthermore, m-TMD patients more frequently have headaches, chronic fatigue syndrome, and fibromyalgia, with one study suggesting that these differences still exist after controlling for emotional distress in acute TMD.[15] A search of the literature revealed no studies that examined whether a difference exists in the mean number of comorbidities between individuals with chronic m-TMD and those with n-TMD.

Given the aforementioned limited work on comorbidities associated with TMD, the aim of the present study was to compare the total number of comorbidities and the prevalence of five specific comorbidities in individuals with m-TMD vs n-TMD. Specifically, this study had three objectives: *(1)* to identify the prevalence of five self-reported comorbidities associated with central sensitivity syndrome (ie, migraine, CFS, IBS, IC, and RLS) in a TMD population; *(2)* to compare the prevalence of these five self-reported comorbidities between m-TMD and n-TMD groups; and *(3)* to compare the mean total number of self-reported comorbid conditions between m-TMD and n-TMD groups. It was hypothesized that patients with m-TMD would have a higher prevalence of the five comorbidities and a higher mean total number of comorbidities than patients with n-TMD.

Materials and Methods

Participants, Study Design, and Setting

This cross-sectional, multicenter study included patients with TMD treated at the Division of Dentistry at Montreal General Hospital in Quebec, Canada, the Department of Oral and Maxillofacial Surgery at Massachusetts General Hospital in Boston, and the Orofacial Pain Clinic at Massachusetts General Hospital.

Interested participants were included in the study if they had chronic TMD. TMD was diagnosed using the Research Diagnostic Criteria for TMD, and pain lasting longer than 6 months was considered chronic.[16,17] Exclusion criteria were history of acute or subacute pain, other types of orofacial pain conditions (eg, neuropathic, burning mouth syndrome, atypical), and history of temporomandibular joint surgery.

At Massachusetts General Hospital, current TMD patients attending the clinics were screened for eligibility. Information was gathered from interested participants after their current appointment or by having the patients completing the questionnaire at home and bringing it to their next scheduled appointment. At Montreal General Hospital, inactive patients of a TMD clinic that had closed and who were deemed eligible by a medical record review were invited to join the study by a letter mailed to their last known address.

The sample size calculation was based on a significance level of .05, a power at 80%, and a 20% prevalence difference in each comorbidity between m-TMD and n-TMD groups. A sample of 100 participants per group was deemed necessary to fulfill these criteria. Ethical approval for this study was granted from the institutional review boards of McGill University and Massachusetts General Hospital before the start of data collection. A written informed consent form was obtained from all patients before they joined the study.

Data Collection

The study assessed the association of type and number of comorbidities with the TMD subgroups, which were defined as follows: *(1)* m-TMD group: participants reported myofascial pain, whether alone or in combination with other forms of TMD (joint or disc disorders); and *(2)* n-TMD group: participants were free of myofascial pain but had other forms of TMD (joint or disc disorders). For the purpose of this study, the presence of myofascial pain during clinical examination was sufficient, regardless of whether it was primary, secondary, or tertiary. TMD was diagnosed by dentists with expertise in TMD (H.D. at Montreal General Hospital and H.D. and D.K. at Massachusetts General Hospital). To test the interrater agreement of the two examiners, 19 participants were randomly chosen and examined separately by both. The kappa score of interrater agreement was 0.88, with 95% confidence intervals (CIs) of 0.65 to 1.00, which is considered substantial.[18]

To identify the presence of the five comorbidities (ie, migraine, CFS, IBS, IC, and RLS), each participant was asked to fill out five diagnostic questionnaires:

1. The ID-Migraine questionnaire: a 3-item validated instrument that has 81% sensitivity, 75% specificity, and 94% positive predictive value.[19] It provides a "yes/no" diagnosis for migraine.
2. The Schedule of Fatigue and Anergia questionnaire: a 10-item validated instrument that has 93% sensitivity, 95% specificity, and 94% positive predictive value.[20] It provides a "yes/no" diagnosis for CFS.

3. The ROME III questionnaire: a 10-item validated instrument that has 82% sensitivity and 70% specificity.[21] It provides a "yes/no" diagnosis for IBS.
4. The Pain, Urgency, and Frequency Symptom Scale: an 8-item validated instrument that has 83% sensitivity, 88% specificity, and 77% positive predictive value.[22] It provides a "yes/no" diagnosis for IC.
5. The Cambridge-Hopkins Restless Leg Syndrome Questionnaire-short form: a 13-item validated instrument that has 87% sensitivity, 94% specificity, and 87% positive predictive value.[23] It provides a "yes/no" diagnosis for RLS.

Each participant was also asked to fill out a questionnaire to assess and control for the following potential confounding variables:

- TMD pain duration: Participants were asked, "How long have you had pain in the face?" and they were allowed to write their answer in months and years.
- TMD pain intensity: Participants were asked to identify their pain on a scale from 0 to 10, with 0 indicating "no pain" and 10 indicating "worst possible pain."
- Socioeconomic information: Participants were asked to provide information such as sex, age, marital status, employment status, and level of education.
- Past history of anxiety and depression: Participants were asked to answer "yes" or "no" to the question, "Have you ever been treated for anxiety and/or depression?"
- Study site and patient status: Information about the site of recruitment and whether patients were new, active, or inactive was also gathered.

All questionnaires were originally in English but translated into French for the participants at Montreal General Hospital. Participants had the choice of completing questionnaires in either English or French.

Data Analysis

Simple descriptive statistics were used to compare sociodemographic information and self-reported comorbidity differences between m-TMD and n-TMD groups. Means, standard deviations (SDs), and proportions were generated, and chi-square[2] and Student *t* tests were used for categorical and continuous variables, respectively, to test differences between the two groups.

For the first study objective, to identify the prevalence of the five self-reported comorbid conditions associated with central sensitivity syndrome in a TMD population (migraine, CFS, IBS, IC, and RLS), descriptive statistics were used with means and proportions. For the second study objective, to compare the prevalence of the five self-reported comorbidities between m-TMD and n-TMD groups, five separate multivariate logistic analyses were completed, one for each of the five comorbid conditions as the exposure and the TMD subgroups as the outcome variable, taking into account the confounding variables. For each comorbidity, three regression models were performed: *(1)* a crude model with only the exposure and outcome variables; *(2)* a complete model including all comorbidities and potential confounders; and *(3)* a simple model including all comorbidities and only those confounders that displayed a statistically significant association with the study outcomes. For the complete model, the following confounders were chosen because of the overwhelming evidence of their influence on both outcome and exposure variables: sex, age, employment status, marital status, and history of depression or anxiety.[24–27] For the simple model, a backward elimination process was used to keep confounders in the model, where only covariates that exhibited a P value $\leq .25$ were included: sex, age, and employment status.[28,29] For the third study objective, to compare the mean number of self-reported comorbid conditions between individuals in the m-TMD and n-TMD groups, a multivariate logistic analysis was completed, using the same modeling strategy described previously. Because of the small sample size, participants with four and five comorbidities were placed into one group. All statistical analyses were performed using Stata statistical software (version 10). Odds ratios (ORs) and 95% CIs were reported.

Results

A total of 224 participants agreed to partake in the study: 16 from Montreal General Hospital, 153 from the Massachusetts General Hospital Department of Oral Surgery, and 55 from the Massachusetts General Hospital Orofacial Pain Clinic. A total of 44 participants were excluded from the study: 31 for not fulfilling the inclusion criteria and 13 for not completing all questionnaires (Fig 1). The final sample included 180 participants, including 121 in the m-TMD group and 59 in the n-TMD group. Table 1 shows that the mean age (± SD) of all participants was 42.8 ± 1.2 years and that the majority of participants were female (82.8%), married (51.1%), and working full time (51.1%). Of all participants, 55.6% had a history of depression, anxiety, or both. The mean ± SD duration of TMD pain was 6.33 ± 0.60 years. Among all participants, the prevalence of migraine, CFS, IBS,

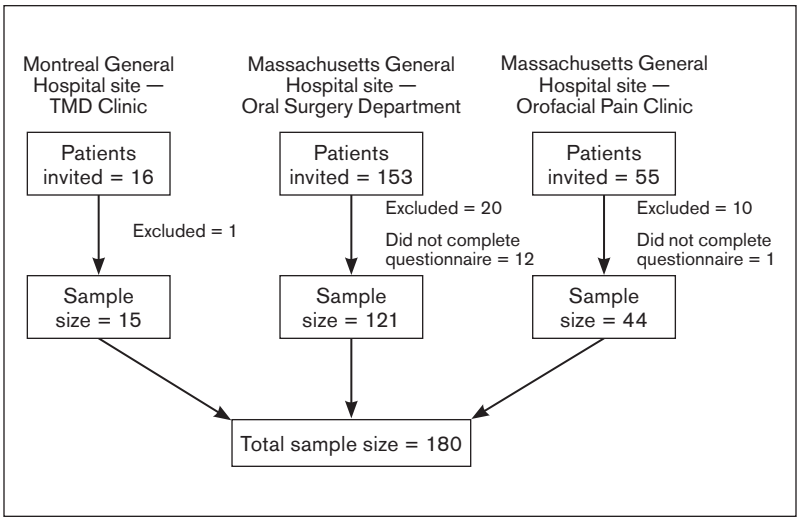

Fig 1 Study sample flowchart. TMD = temporomandibular disorder.

Table 1 Sociodemographic Characteristics of Study Participants with Temporomandibular Disorders (TMD)

Characteristic	All TMD patients (n = 180)[a]	Nonmyofascial TMD patients (n = 59)[a]	Myofascial TMD patients (n = 121)[a]	*P* value
Mean age + SD (y)	42.8 ± 1.2	43.4 ± 2.1	42.5 ± 1.4	.71
Females, n (%)	149 (82.8)	47 (79.7)	102 (84.3)	.44
Marital status, n (%)				.10
Single	63 (35.0)	16 (27.1)	47 (38.8)	
Married	92 (51.1)	37 (62.7)	55 (45.5)	
Divorced	20 (11.1)	6 (10.2)	14 (11.6)	
Widowed	5 (2.8)	0 (0.0)	5 (4.1)	
Work status, n (%)				.11
Unemployed	44 (24.4)	19 (32.2)	25 (20.7)	
On disability	12 (6.7)	1 (1.7)	11 (9.1)	
Part-time work	32 (17.8)	11 (18.6)	21 (17.4)	
Full-time work	92 (51.1)	28 (47.5)	64 (52.9)	
History of depression or anxiety, n (%)	100 (55.6)	30 (50.9)	70 (57.9)	.38
No. of self-reported comorbidities, n (%)				.01
0	68 (37.7)	31 (52.5)	37 (30.6)	
1	54 (30.0)	16 (27.1)	38 (31.4)	
2	30 (16.7)	4 (6.8)	26 (21.5)	
3	19 (10.5)	7 (11.9)	12 (9.9)	
≥ 4	9 (5.0)	1 (1.7)	8 (6.6)	
Type of self-reported comorbities, n (%)[b]				
Migraine	83 (46.1)	17 (28.8)	66 (54.6)	< .01
Chronic fatigue syndrome	26 (14.4)	3 (5.1)	23 (19.0)	.01
Irritable bowel syndrome	51 (28.3)	14 (23.7)	37 (30.6)	.34
Interstitial cystitis	22 (12.2)	5 (8.5)	17 (14.1)	.28
Restless leg syndrome	30 (16.7)	10 (16.9)	20 (16.5)	.94
Total number of comorbidities (mean ± SD)	1.15 ± 1.2	0.83 ± 1.1	1.30 ± 1.2	.01
Mean pain duration ± SD (y)	6.33 ± 0.6	5.86 ± 1.1	6.55 ± 0.7	.58
Mean pain intensity ± SD[c]	5.10 ± 0.2	4.53 ± 0.4	5.38 ± 0.2	.03

[a]Percentages do not total 100 because of rounding.
[b]Participants could report more than one comorbidity.
[c]Measured on a scale from 0 ("no pain") to 10 ("worst possible pain").

IC, and RLS was 46%, 14%, 28%, 12%, and 17%, respectively. In addition, 38% had no comorbidities, 30% had one self-reported comorbidity, and 32% had two or more self-reported comorbidities.

When the m-TMD and n-TMD groups were compared, no sociodemographic differences were observed. Also, no between-group differences were noted for site of recruitment or patient status (ie, new, active, or inactive) (data not shown). However, a significantly higher level of pain was observed in the m-TMD group than in the n-TMD group (mean score, 5.38 vs 4.53 on a 0- to 10-point scale, respectively, $P = .03$).

Table 1 shows that the m-TMD group had a significantly higher prevalence of migraine ($P = .001$) and CFS ($P = .01$). Prevalence rates for IBS and IC were also higher in this group, but the differences were not statistically significant. RLS prevalence was the same for both groups. The mean total number of comorbidities was statistically significantly higher in the m-TMD group than in the n-TMD group ($P = .01$).

Table 2 shows results of the logistic regression analysis of the associations of type and number of comorbidities with TMD subgroups by using n-TMD as a reference. Participants with self-reported migraine were three times more likely to have m-TMD than n-TMD (OR [95% CI], 3.00 [1.41–6.40]). Those with self-reported CFS were also more likely to have m-TMD (OR [95% CI], 3.25 [0.86–12.26]). However, statistical significance was not reached because the CI included 1; therefore, it is possible that there is no association between CFS and m-TMD. Between-group differences in the prevalence of the three other self-reported comorbidities (IBS, IC, and RLS) were not statistically significant. Participants with a higher number of comorbidities were 1.5 times more likely to have m-TMD than n-TMD (OR [95% CI], 153 [1.13–2.08]).

Table 2 Crude and Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for the Association of Type and Number of Self-Reported Comorbidities with Type of TMD

Self-reported comorbidity	Crude model OR (95% CI)	Complete model[a] OR (95% CI)	Simple model[b] OR (95% CI)
Migraine	2.96 (1.52–5.78)	2.98 (1.40–6.36)	3.00 (1.41–6.40)
Chronic fatigue syndrome	4.38 (1.26–15.25)	3.22 (0.85–12.30)	3.25 (0.86–12.26)
Irritable bowel syndrome	1.42 (0.69–2.89)	1.15 (0.52–2.55)	1.15 (0.52–2.55)
Interstitial cystitis	1.76 (0.62–5.04)	1.03 (0.30–3.60)	1.06 (0.31–3.59)
Restless leg syndrome	0.97 (0.42–2.23)	0.66 (0.25–1.75)	0.66 (0.25–1.75)
Total comorbidities	1.46 (1.08–1.95)	1.51 (1.10–2.08)	1.53 (1.13–2.08)

[a]Variables included in the model: sex, age, employment status, marital status, and history of depression or anxiety.
[b]Variables included in the model: sex, age, and employment status.

Discussion

To the best of the authors' knowledge, this study is the first to use logistic regression to investigate the association of type and number of comorbidities with m-TMD or n-TMD. It is also, to their knowledge, the first TMD study to estimate the prevalence of RLS in a TMD sample.

Similar to previous studies showing an association between headaches and m-TMD,[11,30,31] the results of the present study showed that self-reported migraine is associated with m-TMD but not with n-TMD. The association between self-reported CFS and m-TMD was statistically significant in the crude model analysis. However, the OR for this finding remained above 3 in the other models, suggesting that this association may be significant. Other studies have observed an association between CFS and m-TMD when compared with n-TMD.[11,32] A higher number of self-reported comorbidities was observed in the m-TMD sample compared with the n-TMD sample, which is consistent with literature.[11]

An association was also observed between m-TMD and the self-reported comorbidities of IBS and IC; however, the association did not reach statistical significance. Between-group differences in the prevalence of these comorbidities were less than 10%. Associations between m-TMD and self-reported IBS and m-TMD and self-reported IC may exist, but they may have been underpowered by this study's small sample size. A post hoc sample size calculation revealed that for the overlap present in the study, the sample size would need to be 503 and 664 to observe a statistical difference for self-reported IC and IBS, respectively.

The association between m-TMD and painful self-reported comorbidities adds to the body of evidence suggesting that m-TMD is part of a widespread pain condition, whereas n-TMD is part of a localized dysfunction.[7,11,13] Yunus has suggested that m-TMD, but not n-TMD, may be one of the other central sensitivity syndromes, with migraine, CFS, IC, IBS, and fibromyalgia.[7] Evidence of bilateral widespread mechanical pain sensitization in women with m-TMD has given rise to a theory that these patients have impairment in the central nociceptive processing pathway.[33] Other studies have shown that m-TMD patients have a generalized hyperexcitability of central nociceptive processing compared with healthy control participants.[34,35] In addition, emotional distress, depression, anxiety, and somatization may increase, prolong, or perpetuate the pain symptoms in m-TMD patients.[15,36]

It is important to note that in the combined TMD population, the majority of participants had at least one of the five examined self-reported comorbidities, with a mean comorbid count of 1.15. This finding suggests that TMD can overlap with other common painful comorbidities, especially in individuals seeking treatment.[4,5,37] The number of comorbidities has been observed to be strongly associated with increased pain severity scores, longer pain duration, disability, and psychosocial variables in individuals with chronic pain.[38–40] A strong, almost linear relationship seems to exist between the number of pain sites and multiple aspects of functionality, including daily activity, physical activity, social activity, and overall health in individuals with chronic pain.[38–41]

The prevalence of the five comorbidities in the current study agrees with past studies, which have reported prevalence rates of 22% to 58% for migraine,[30,42,43] 15% to 25% for IBS,[5,37] 4% to 41% for CFS,[5,32] and 17% for IC.[5] The current study confirms and strengthens these results with its use of validated diagnostic questionnaires and control of confounders. Furthermore, this study appears to be the first to look at RLS prevalence in individuals with TMD. RLS is considered a sensorimotor disorder characterized by abnormal sensations in the limbs that are both dependent on activity and time of day.[44] In this study, 17% of the whole TMD population reported symptoms of RLS, similar to RLS prevalence in the general population (5% to 15%).[45] Thus, the present findings suggest that RLS is not more prevalent in individuals with TMD, consistent with the findings of Neblett et al.[46] In addition, the equal distribution of RLS between the m-TMD and n-TMD groups suggests that RLS does not share central sensitivity

syndrome characteristics like the other four conditions in this study. This finding is in agreement with a previous study showing that RLS prevalence in migraine patients is the same as in the general population.[47] However, other studies have noted a higher overlap between RLS and fibromyalgia and headache.[48,49]

Some caution is necessary in the interpretation of these results. Because of its cross-sectional design, the current study cannot provide information regarding the direction of association between m-TMD and the self-reported comorbidities. Also, although the study took place at three tertiary hospital sites, the majority of patients came from Massachusetts General Hospital, where patients typically have private health insurance. Therefore, a sampling bias may have been introduced, where more affluent, educated patients were involved in the study. However, the large multicenter OPPERA study found that individuals with TMD were more educated and earn a higher income than healthy control participants.[25] The present study might have had a measurement bias,[50] as emotional distress and psychological status may not have been adequately assessed and controlled for all participants. To assess psychological variables, patients were asked about history of depression and anxiety, with "yes" and "no" as possible answers. Past studies have shown that TMD patients with muscle pain have more psychological symptoms, including depression, anxiety, hostility, somatization, and obsessive-compulsive disorder.[10,51] However, the current study showed no difference in history of depression or anxiety between those with m-TMD and n-TMD. It is possible that the questionnaire used did not adequately capture psychological symptoms, and a validated survey should have been used.[50] A second possible measurement bias is the use of French-translated diagnostic questionnaires at Montreal General Hospital. These French-translated questionnaires were not validated and may not have been identical to the English-language validated versions. Finally, the sample size was smaller than necessary to achieve 80% power. A sample of 100 in each group was needed, but only 59 participants were recruited for the n-TMD group. A post hoc power analysis revealed that the current study could detect only the difference in prevalence of migraine between the m-TMD and n-TMD groups. Therefore, for the other four comorbidities, a type II error was introduced, where some results did not reach statistical significance although the trend was evident. It is possible that a larger sample size could enable demonstration of an association between m-TMD and these other comorbidities.

Conclusions

The current study found that individuals with m-TMD have a higher prevalence of self-reported migraine and CFS and have a higher total number of self-reported comorbidities than those with n-TMD. These differences may be a result of the central sensitization changes in individuals with m-TMD; however, more research is necessary to explore this possibility. The results of the current study could have clinical ramifications for patients with m-TMD, who might need more detailed screening and more complex therapy from a multidisciplinary pain team. The study results show that the natural history of singular TMD is complex and is a part of a comorbid, overlapping condition. A cohort study following TMD participants that have no comorbidities is recommended to identify risk factors, such as the presence of m-TMD, associated with developing comorbidities. Once risk factors have been identified, these clinical and biomedical variables can be tested to determine which ones best predict the development of painful comorbidities.

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