The Relationship Between Primary Sleep Disorders and Temporomandibular Disorders: An 8-Year Nationwide Cohort Study in South Korea

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Introduction
Temporomandibular disorders (TMD) is a common musculoskeletal pain syndrome of the orofacial region with a prevalence as high as 8–15% in the general population, representing a significant public health issue. TMD is mainly known as a clinical dysfunction accompanied by pain and movement limitation of the temporomandibular joint (TMJ) and surrounding musculature. 1 It is a major cause of nonodontogenic pain in the orofacial region and is known to lower sufferers’ quality of life notably, especially when it is accompanied by various comorbidities such as chronic widespread pain, psychological, and gastrointestinal disorders. 2,3

Many physical and psychological factors, when repeatedly occurring, are known to trigger the initiation of TMD and affect its prognosis. Among those disturbed and

Background: While evidence is accumulating to propose a specific contribution of sleep disorders and low quality sleep in the pathogenesis of temporomandibular disorders (TMD), management of primary sleep disorders in the process of preventing and treating TMD still remains scientifically unsupported.

Objective: To investigate the association of primary sleep disorders with TMD risk in South Korea.

Patients and Methods: This study was based on the National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS) of South Korea with 468,882 participants. After excluding participants diagnosed in 2002, those with a diagnosis of a primary sleep disorder in 2003–2005 were recruited. All participants diagnosed with TMD between January 1, 2006 and December 31, 2013 received follow-up. Cox proportional hazards regression was performed to determine the adjusted hazard ratios (aHR) and 95% confidence interval (CI) for TMD according to the presence or absence of a primary sleep disorder diagnosis.

Results: After adjusting for all covariates, primary sleep disorder patients had a 44% higher risk for TMD compared with non-sleep disorder participants (aHR 1.44, 95% CI 1.02–2.04). The incidence rate of TMD was nearly twice as high in participants with sleep disorders compared with those without (6.08 vs 3.27, per 10⁴ person-years). In subgroup analysis, an association was observed with those over 60 years old or who frequently exercised physically.

Conclusion: Primary sleep disorders could be an important independent risk factor for the initiation and maintenance of TMD. Patients with sleep disorders should be monitored for possible co-occurrence of TMD-related symptoms that could aggravate sleep disorders in turn.

Keywords: sleep disorders, temporomandibular disorders, cohort studies, epidemiology

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unrefreshing sleep has also been reported as a major modulating factor. Restoration is necessary to maintain physiologic homeostasis, hence inadequate sleep, both qualitatively and quantitatively, has been associated with various adverse health outcomes encompassing cardiovascular, endocrinologic, psychological diseases and also cancer. Disturbed sleep is a common characteristic among pain disorders such as low back pain, fibromyalgia, and cancer pain. The relationship between pain and sleep is known to be bidirectional with poor sleep enhancing the perception of pain and pain resulting in disrupted sleep. The duration of pain is also known to influence the relationship, with this effect especially being prominent in chronic pain patients. Previous studies report sleep problems in 40–88% of patients depending on the specific chronic pain condition. As much as 90% of patients with TMD report poor sleep quality. Evidence that suggests the specific role of disturbed sleep as a causative factor in the pathogenesis of TMD is also accumulating. Several pathological processes may be involved in the interrelationship between sleep problems and TMD as in other pain disorders which include increased sympathetic nervous system activity, immune system dysregulation, and neuroendocrine dysfunction, however the exact mechanism is yet to be elucidated.

Despite evidence supporting the close relationship between TMD and sleep disorders only a limited number of previous studies have investigated the occurrence of primary sleep disorders in TMD patients based on objective measures of sleep and such studies were of a relatively small sample size. On the other hand, most studies are focused on assessing the sleep quality in TMD populations based on questionnaires or assessing its possible relationship with sleep bruxism, which is a single disease entity among the various sleep disorders that may be related to TMD.

Considering the general lack of recognition and high percentage of undiagnosed cases leading to the undertreatment of sleep disorders, the current scarcity of data describing the co-occurrence of primary sleep disorders and TMD may have detrimental health consequences resulting from the untimely management of sleep disorders that can initiate and exacerbate TMD and its related symptoms. The relationship between the two should be examined to identify high-risk patients who are in need of sleep disorder management and provide accurate clinical guidelines for assessing sleep during the diagnostic and treatment process of TMD to prevent poor long-term prognosis from inappropriate levels of multidisciplinary approaches.

Therefore, the objective of this study was to characterize the incidence of well-defined TMD in a large-scale nationwide population-based sample of primary sleep disorder patients by examining the rate of TMD in comorbid sleep disorders relative to the general population as well as other socioeconomic and clinical factors that may have an association with their co-occurrence. We hypothesized that TMD would be substantive in the primary sleep disorder population even after controlling for well-known confounders of TMD.

**Patients and Methods**

**Study Design and Population**

This study was designed as a retrospective cohort study and utilized the National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS), a cohort of participants registered in the health screening program provided by NHIS of the Republic of Korea from 2002 to 2013. The NHIS-HEALS cohort was composed of 509,900 random samples of individuals aged 40 to 79, which accounted for 10% of all health screening participants between 2002 and 2003. The NHIS has been providing mandatory health insurance for all Koreans since 1989 with approximately 98% of all Koreans enrolled. This contains all insurance claim data as well as causes of death, which are identified using a national database and thorough healthcare data for admissions and outpatient visits. All participants are required to undergo standardized health examinations every two years. The health examination database included biological laboratory results such as blood pressure, fasting glucose, lipid profile, hemoglobin, body mass index and waist circumference as well as health-related behavioral variables.

Of the total 509,900 people, 1,620 participants who were diagnosed with a primary sleep disorder in 2002 were excluded to consider only the newly diagnosed cases since 2003. Among these included individuals, 246 participants were excluded because they were diagnosed with TMD before the outset of the follow-up (index date: January 1, 2006). A further 36,451 participants with missing screening data and 2,701 deaths were also excluded. The final study population consisted of 468,882 participants (shown in Figure 1). This study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital.
The IRB granted exemption of informed consent. The data accessed complies with relevant data protection and privacy regulations. All data were anonymized and maintained with confidentiality.

**Definition of Clinical Outcomes**

Primary sleep disorders and TMD were defined as a case respectively when the same diagnosis was given at least twice and such diagnoses occurred at intervals of 30 days or more based on the International Classification of Diseases, Tenth Revision (ICD-10). While this tends to underestimate the frequency of cases compared with other studies, it is a conservative approach to minimize the likelihood of misclassification. ICD-10 codes for primary sleep disorders including G47 sleep disorders (insomnia, hypersomnia, circadian rhythm sleep disorders, sleep apnea, narcolepsy, parasomnia, and sleep-related movement disorders), F51 sleep disorders not due to a substance or known physiological condition (insomnia not due to a substance or known physiological condition, hypersomnia not due to a substance or known physiological condition, sleepwalking, sleep terrors, and nightmare disorder), and G25.8 other specific extrapyramidal and movement disturbances were considered as exposure variables. Restless legs syndrome (G25.81) diagnoses were additionally included and analyzed because it is described as a primary sleep disorder in the International Classification of Sleep Disorders, Third Edition (ICSD-3). The outcome variable of this study was TMD defined as the existence of an outpatient visit record from January 1, 2006 to December 31, 2013. The ICD-10 code used to diagnose TMD was K07.6 (temporomandibular joint disorders). At the end of follow-up, the survival length was calculated until one of the following three results appeared: (1) diagnosis of TMD; (2) end of 2013; (3) death during follow-up period.

**Covariates**

Covariates included age, sex, household income (quartile), smoking (never, < 10, 10–29, and ≥30 years), alcohol consumption (< 3, and ≥3 times per week), physical exercise frequency (< 3, and ≥ 3 times per week), hypertension, diabetes mellitus, hyperlipidemia, body mass index (BMI) (< 25, and ≥ 25), and the Charlson Comorbidity Index (CCI) as of before the index year. “How many times a week do you exercise enough to sweat?” was used as a question to verify the frequency of physical exercise. Hypertension was defined as a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg. Diabetes mellitus was defined as a fasting blood glucose ≥126 mg/dL. Hyperlipidemia was defined as a total cholesterol level ≥200 mg/dL or low density lipoprotein level ≥140 mg/dL.
survival time was significantly shorter for the sleep dis-

Data Analyses

To compare the characteristics of the two groups according
to the exposure variable, the categorical variable was
expressed as a percentage of the population using
Pearson chi-square tests, and the continuous variable was
expressed as a mean with standard deviation using inde-
pendent t-tests. We used the Cox proportional hazards
regression model after hierarchically adjusting potential
confounding factors to compute the hazard ratio (HR) and
95% confidence interval (95% CI) for TMD. Subgroup analysis was done with sex, age, and physical
exercise frequency groups to identify potential subgroups
with possible associations between sleep disorders and
TMD. Statistical significance was defined as a P-value
<0.05. All data collection and statistical analysis were
performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

3,638,524 person-years were analyzed. Table 1 shows
descriptive characteristics of the study population. The
number of participants with and without primary sleep
disorders were 6,999 (1.5%) and 461,883 (98.5%), respec-
tively. The mean age was higher for participants with sleep
disorders than for those without. Women had significantly
more sleep disorders than men. The incidence rate of TMD
was almost twice as high in primary sleep disorder patients
compared with participants without sleep disorders.

Figure 2 shows the Kaplan–Meier survival curves with
Log rank tests for crude causal association of TMD
according to the presence of primary sleep disorders. The
survival time was significantly shorter for the sleep dis-
group (mean survival time, 7.972; 95% CI, 7.963–
7.981) than the non-sleep disorder group (mean survival
time, 7.986 years; 95% CI, 7.986–9.987) by Log rank test
(P<0.001).

The risk of TMD according to the presence of sleep
disorders is shown in Table 2. When all covariates were
adjusted as possible confounders of TMD, the participants
with sleep disorders had a higher risk for TMD than the
non-sleep disorders (aHR 1.44, 95% CI 1.02–2.04).

Discussion

The results of this nationwide, population-based cohort
study showed that primary sleep disorders act as an inde-
pendent risk factor for TMD and this increased incidence
remained significant even after adjusting for well-known
confounding factors of TMD including demographic char-
acteristics such as age and sex, and environmental factors
such as household income, smoking, alcohol consumption,
and physical exercise level. The impact of sleep disorders
on TMD was more critical at an older age (age ≥60 years)
and for those who exercised above a certain exertion level
more often. This is the first large-scale study to demon-
strate the prevalence of TMD in a primary sleep disorder
population and analyze its effect on TMD occurrence.

Although primary sleep disorders encompass a wide
variety of distinct disease entities with different pathophy-
siologic mechanisms, the most evident consequence shared
by all sleep disorders is the disruption and lowering of sleep
quality. Sleep is universal to all species, taking up to one-
third of a human’s lifespan, and is critical for recovery and
overall well-being.39 Low quality sleep has been associated
with a wide range of dysfunctions throughout the whole
body system including increased risk of coronary heart
disease,40 diabetes,41 neurological disorders,42 and psycho-
logical disorders such as depression and anxiety.43 Increased pain sensitivity is also a well-known phenomenon
commonly identified with sleep disruption. It is known that
around 50% of people who report low quality sleep suffer
from chronic pain.44 Patients with primary insomnia, the
most common type of primary sleep disorder, showed lower
pain thresholds and attenuated pain inhibition compared
with healthy controls.45 Sleep apnea, the second most com-
mon primary sleep disorder, is also frequently associated
with heightened pain sensations46 and its treatment through

≥130 mg/dL or triglyceride level ≥150 mg/dL. BMI was
calculated as weight (kg) divided by the square of height
(meter). CCI was used to reflect overall morbidity and
calculated by weighting and scoring for comorbid

Figure 3 shows the results of subgroup analysis stratify-
ing participants by sex, age, and frequency of physical
exercise. Although women had more sleep disorders than
men, the risk of TMD according to sleep disorders was not
statistically different between the sexes. At age 60 and
older, participants who had a sleep disorder had a 1.64
times higher risk than participants without a sleep disorder
for TMD. In addition, among the participants who exer-
cised three or more times a week, those who suffered from
sleep disorders had a twice higher risk for TMD. Sleep
disorders were associated with an increased risk of TMD
as the participants’ age and frequency of physical exercise
per week increased.

43Age was treated as a continuous variable
and all other variables as categorical variables.
Table 1 Demographic and Clinical Characteristics of the Study Population According to the Presence of Primary Sleep Disorders

|                                      | No Sleep Disorder | Sleep Disorder | P value |
|--------------------------------------|------------------|----------------|---------|
| Number of subjects, n, (%)           | 461,883 (98.5)   | 6,999 (1.5)    |         |
| Number of TMD cases, n, (%)          | 1,171 (97.3)     | 33 (2.7)       |         |
| Incidence rate, (95% CI)             | 3.3 (2.9–3.8)    | 6.1 (5.4–7.1)  | < 0.001 |
| Age, years, mean (SD)                | 55.4 (9.5)       | 61.0 (10.1)    | < 0.001 |
| Sex, %                               |                  |                | < 0.001 |
| Male                                 | 53.5             | 41.6           |         |
| Female                               | 46.5             | 58.4           |         |
| Household income, quartile, %        |                  |                | < 0.001 |
| 1st (highest)                        | 15.3             | 16.7           |         |
| 2nd                                  | 21.8             | 22.7           |         |
| 3rd                                  | 29.0             | 27.4           |         |
| 4th (lowest)                         | 33.9             | 33.2           |         |
| Smoking status, %                    |                  |                | < 0.001 |
| Never                                | 69.5             | 77.1           |         |
| < 10 years                           | 3.9              | 2.9            |         |
| 10–29 years                          | 7.2              | 4.3            |         |
| ≥ 30 years                           | 19.4             | 15.7           |         |
| Alcohol consumption, per week, %     |                  |                | < 0.001 |
| Never                                | 58.7             | 71.0           |         |
| < 3 times                            | 30.4             | 20.6           |         |
| ≥ 3 times                            | 10.9             | 8.4            |         |
| Physical exercise, per week, %       |                  |                | < 0.001 |
| Never                                | 54.1             | 58.5           |         |
| < 3 times                            | 24.7             | 18.4           |         |
| ≥ 3 times                            | 21.2             | 23.1           |         |
| Hypertension, %                      |                  |                | < 0.001 |
| No                                   | 70.0             | 67.0           |         |
| Yes                                  | 30.0             | 33.0           |         |
| Diabetes mellitus, %                 |                  |                | < 0.001 |
| No                                   | 92.0             | 91.0           |         |
| Yes                                  | 8.0              | 9.0            |         |
| Hyperlipidemia, %                    |                  |                | < 0.001 |
| No                                   | 53.4             | 50.7           |         |
| Yes                                  | 46.6             | 49.3           |         |
| BMI, %                               |                  |                | 0.315   |
| < 25                                 | 65.3             | 65.8           |         |
| ≥ 25                                 | 34.7             | 34.2           |         |
| CCI, %                               |                  |                | < 0.001 |
| 0                                    | 14.5             | 3.3            |         |
| 1                                    | 21.7             | 8.6            |         |
| 2                                    | 20.8             | 13.7           |         |
| ≥ 3                                  | 43.0             | 74.4           |         |

Notes: Continuous variables are expressed as mean (SD), and categorical variables as %. Analysis of variance for continuous variables and Chi-square test for categorical variables. *per 104 person-years.

Abbreviations: SD, standard deviation; BMI, body mass index; CCI, Charlson Comorbidity Index; TMD, temporomandibular disorders; CI, confidence interval.

Continuous positive airway pressure therapy was shown to reduce pain sensitivity.47 The direct relationship between circadian rhythm sleep disorders and pain sensitivity has not yet been investigated, however, a previous study reported that night shift workers exhibited an increased sensitivity to experimentally induced pain.48 Interestingly, most studies on the relationship between sleep disorders and pain are focused on the restriction of sleep and less sleep duration while there are no studies that investigate the correlation between hypersomnia and pain. Based on the reports that show idiopathic hypersomnia patients exhibit high levels of sleep fragmentation,49 and long sleep time (≥9 hours) is associated with increased risk of musculoskeletal pain,50 we could assume that more sleep of a lower quality is also a risk factor for increased pain sensitivity. Restless leg syndrome is another primary sleep disorder that has only recently been investigated in relation to pain disorders and the results suggest a common pathophysiology involving disturbed supraspinal pain modulation of the basal ganglia and dopaminergic pathways.51

The impact of sleep disorders has already been investigated specifically in the TMD population in previous studies. However, most studies focus on the influence of bruxism as a contributing factor to TMD pain aggravation52 and more recently have investigated the relationship between TMD and sleep-related breathing disorders as a single disease entity stating obstructive sleep apnea as a risk factor of developing TMD.53,54 The only other primary sleep disorder to be analyzed in relation to TMD is insomnia although the existing literature is scarce in spite of the fact that insomnia disorder is the most frequently diagnosed sleep disorder in TMD patients.29 One study reported that insomnia was associated with reduced mechanical and thermal pain thresholds in myofascial TMD patients29 and another study showed that the increases in insomnia symptoms were succeeded by increases in average daily TMD pain in the next month.55 However, the current literature lacks an accurate characterization of the relationship between primary sleep disorders as a whole and TMD. The results of our analysis support the need to investigate the possibility of TMD and orofacial pain in any primary sleep disorder population that could be experiencing sleep disruption. Such an anticipatory diagnostic approach could take place even before a definitive diagnosis of a specific sleep disorder is given to a patient if the patient complains of low quality sleep. Early diagnosis and active
treatment is known to result in better long-term prognosis with pain disorders.\textsuperscript{56,57} Studies on the reciprocal bidirectional relationship between sleep and pain once again highlight the importance of appropriate TMD diagnosis and symptom control since chronic pain could impair sleep quality in turn.\textsuperscript{58} Also some studies suggest the close relationship between the TMJ and systemic conditions.\textsuperscript{59}

The presence of a primary sleep disorder may affect the initiation and maintenance of TMD-related symptoms through various mechanisms. Restricted and disturbed sleep is known to cause systemic inflammation. Sleep restriction has been associated with elevated levels of interleukin-1\textbeta\textsuperscript{60} while sleep disturbance was correlated to increased circulatory levels of interleukin (IL)-6 and C-reactive protein.\textsuperscript{61} Obstructive sleep apnea patients

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Temporomandibular Disorders} & \textbf{Presence of Sleep Disorder} & \\
\hline
 & No & Yes & \\
Model 1 & aHR (95% CI) & 1.00 (reference) & *1.55 (1.09–2.19) & \\
Model 2 & aHR (95% CI) & 1.00 (reference) & *1.56 (1.10–2.20) & \\
Model 3 & aHR (95% CI) & 1.00 (reference) & *1.56 (1.10–2.21) & \\
Model 4 & aHR (95% CI) & 1.00 (reference) & *1.44 (1.02–2.04) & \\
\hline
\end{tabular}
\caption{Hazard Ratios for Temporomandibular Disorders According to the Presence of Primary Sleep Disorders}
\end{table}

Notes: Model 1 was adjusted for age and sex; model 2 was adjusted for variables included in model 1 and household income; model 3 was adjusted for variables included in model 2 and smoking status, alcohol consumption, and physical exercise; model 4 was adjusted for variables included in model 3 and hypertension, diabetes mellitus, hyperlipidemia, body mass index, and Charlson comorbidity index. * indicates a significant difference.

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval.
present with increased levels of inflammatory cytokines including tumor necrosis factor-α, IL-6, and IL-8. Higher plasma levels of inflammatory cytokines were found in TMD patients with lower sleep quality. Inflammatory cytokines can directly elicit pain through activation of specific receptors on nociceptive sensory neurons and also indirectly through other mediators such as prostanoids and amines. Another mechanism to consider is the effect of sleep disturbance on psychological conditions. Sleep disturbance is a well-known symptom of depression and more recent studies have identified insomnia as a risk factor of developing depression. Sleep disturbance has been suggested as an exacerbating factor of anxiety symptoms. Depression and anxiety are both prominent features of chronic TMD and are fully established contributors to TMD symptom aggravation with studies showing poor sleep quality increasing the level of depression and anxiety in TMD patients. Interestingly depression and anxiety have also been investigated in regards of chronic systemic inflammation. High pro-inflammatory cytokine levels predicted the risk of developing depression and anti-inflammatory medication was effective in controlling depressive symptoms. IL-6 is known to cause increased anxiety levels in mice. Another pathway to consider in the relationship between primary sleep disorders and TMD is the hypothalamic-pituitary-adrenal (HPA) axis. This mechanism is also involved in the mediation of psychological disorders. Altered HPA axis function has been associated with chronic pain disorders such as fibromyalgia while its normal activity is crucial for maintaining and modulating normal sleep. Evidence supports increased HPA axis activity in TMD patients with psychological factors such as anxiety and depression contributing to its upregulation. Another minor mechanism to consider could be sleep bruxism. The role of sleep bruxism has been handled in numerous studies as a risk factor of TMD with conflicting results. On the other hand increased episodes of bruxism were associated with more apneic events in mild to moderate obstructive sleep apnea patients and insomnia increased the risk of sleep bruxism. However, due to the lack of sufficient scientific data on both the causality between sleep disorders and TMD with bruxism it is difficult to establish a conclusive relationship and further studies are necessary to investigate common mechanisms.

Another interesting finding of our study is the significant impact of physical exercise frequency on the association between primary sleep disorders and TMD. Those who were diagnosed with a primary sleep disorder and regularly exercised 3 or more times a week were exposed to a significantly increased risk of TMD. The results are in line with a recent study that first explored the relationship between general physical activity and TMD with the results showing that moderate-intensity exercise compared

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**Figure 3** Subgroup analysis of the association between primary sleep disorders and temporomandibular disorders by sex (A), age (B), and physical exercise (C). Bold indicates $P < 0.05$. 

| Subgroup | Hazard ratio (95% CI) |
|----------|-----------------------|
| A Sex    |                       |
| Men      | 1.56 (0.86-2.83)      |
| Women    | 1.39 (0.91-2.13)      |
| B Age    |                       |
| 40-49 years old | 0.74 (0.19-2.99)      |
| 50-59 years old | 1.22 (0.58-2.59)      |
| ≥ 60 years old  | **1.64 (1.09-2.47)**  |
| C Physical exercise |        |
| Never    | 1.21 (0.76-1.94)      |
| < 3 times | 1.51 (0.67-3.41)      |
| ≥ 3 times | **2.16 (1.10-4.22)**  |
with low-intensity exercise was associated with a significantly higher risk of TMD pain while low-intensity exercise significantly decreased such a risk. The interaction between physical activity and sleep is complex with numerous factors including sex, age, exercise type, duration, and compliance moderating the relationship. Generally, poor sleep quality is associated with low physical activity level. However due to the lack of a standardized approach in defining and measuring physical activity level and the heterogeneity among studies related to the age, sex, and psychological status of the study group it is difficult to directly compare the results from distinctive studies. A previous study that sought the role of sleep disturbance in the association between physical activity and prospectve pain onset showed that those that experienced sleep disturbance with a high frequency did not benefit from increased physical activity suggesting that the frequency of sleep disturbance is a decisive factor in the interrelationship between physical activity and pain. In our study a primary sleep disorder was defined as a case when the same diagnosis was given at least twice and such diagnoses occurred at intervals of 30 days or more to avoid possible misclassification. This could have resulted in a study population with a relatively more severe level of sleep disorders which could explain the harmful effect of higher exercise levels observed in the results. Several studies on pain disorders including low back pain and fibromyalgia report the deleterious effect of high levels of physical exercise on pain exacerbation. Fatigue could be the factor that is related to the increased incidence of TMD in primary sleep disorder patients with higher physical activity levels. Fatigue was reported as a significant mediator of the relationship between sleep disturbance and musculoskeletal pain severity and naturally fatigue is independently associated with high-intensity exercise in patients with widespread pain.

The results of our study showed that older age was another factor that increased the risk of TMD in primary sleep disorder patients. This is interesting considering the fact that the prevalence of TMD peaks in young adults (20–40 years old). However, a previous study showed that peak subgroup incidence of TMD differs according to the specific subgroup diagnosis of TMD with inflammatory degenerative joint disorders appearing more frequently at an older age. Unfortunately, TMD subgroup diagnosis information was not obtainable in this study hindering the evaluation of its effect on age-related differences in primary sleep disorder and TMD associations. The prevalence and severity of common sleep disorders including insomnia and obstructive sleep apnea are known to increase with age and suggests the possibility that higher levels of sleep disorders increase the risk of TMD more significantly. Disordered sleep is also known to have a physical and psychological impact in adolescents. This age range was not included in this study and requires additional investigations.

There are several limitations of this study that need to be considered. First, uncontrolled factors could exist due to the lack of information in the database. Second, this study was based on major diagnoses and was unable to differentiate with dual diagnoses that could affect TMD. Third, the stringent criteria for primary sleep disorder and TMD diagnoses could have resulted in underestimation of each disease, thus influencing the final results. Despite such limitations, there are several strengths of this study. The large sample size representative of Koreans was sufficient to provide accurate results. Selection bias was minimized by using a cohort consisting of a general population randomly selected for 10% of all health screening results without matching cases and controls. In addition, many known confounding factors were controlled and primary sleep disorder and TMD were strictly defined and screened. Furthermore, the long-term follow-up period provides evidence for a possible causal relationship between primary sleep disorders and TMD. It is noteworthy that this investigation was based on definitive diagnoses of primary sleep disorders and not sleep disturbance per se as in the majority of studies analyzing the relationship between sleep related problems and TMD. Such a real-life approach provides a more clinically oriented picture of the close association between primary sleep disorders and TMD and supports the need for active investigations of TMD and orofacial pain in the primary sleep disorder population.

**Conclusion**

This large population-based cohort study showed a significantly higher incidence of TMD in those diagnosed with primary sleep disorders. The results suggest the need to actively screen for TMD and orofacial pain-related issues in primary sleep disorder patients to prevent the adverse effect of uncontrolled sleep disorder prognosis on pain. An interdisciplinary approach should be taken to properly manage combined issues of TMD and sleep disorder along with their comorbid conditions.
Further clinical studies of a prospective longitudinal design are needed to clearly elucidate the relationship and causality between primary sleep disorders and TMD. The effect of early diagnosis and control of TMD and orofacial pain on long-term prognosis of sleep disorders should also be investigated to truly understand the value of recognizing TMD problems in the primary sleep disorder population. Additionally, studies based on specific sleep disorder diagnoses such as insomnia and obstructive sleep apnea are necessary to further elucidate the causal relationship between independent sleep disorders and TMD and suggest more detailed clinical guidelines.

Ethics Approval
The Institutional Review Board (IRB) of Seoul National University Hospital approved this study (IRB Number: 1801-019-912), which is in compliance with the World Medical Association Declaration of Helsinki of 1975, as revised in 2008. The IRB granted exemption of informed consent. The data accessed complies with relevant data protection and privacy regulations. All data were anonymized and maintained with confidentiality.

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