




Original Article



Long-term Effects of COVID-19 on Sleep Patterns

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Abstract

OBJECTIVE: To examine the long-term impact of Coronavirus disease-2019 (COVID-19) on sleep patterns and the prevalence of sleep disorders and to increase public health awareness of long-term COVID-19.

MATERIAL AND METHODS: Using the Massachusetts General Brigham Research Patient Data Registry, Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) positive patients were surveyed about their sleep patterns before and after the viral infection. Information related to comorbid conditions and medications was obtained through chart review.

RESULTS: Two hundred and forty-six completed surveys were analyzed. Average age was 53.3±16.3 years, and they were predominantly non-hispanic white (84.1%) and female (74.3%). The mean body mass index (kg/m²) was 29.9±6.9, and a greater proportion were non-smokers (63.2%). After COVID-19, there was an increase in the percentage of participants reporting difficulty initiating (39±49% vs. 31±46% prior to COVID-19 infection $P = 0.01$). Similarly, the participants reported difficulty in maintaining sleep after COVID infection (57% vs. 43% prior to infection $P < 0.001$). Additionally, there was an increase in the use of sleep aids (30% vs. 24% before the infection $P = 0.003$). The participants also reported a decrease in feeling rested and an increase in the need for napping (58% vs. 36%, $P < 0.0001$) and (27% vs. 40%, $P < 0.0001$) respectively. The sleep symptoms persisted beyond 12 months in 28% of the participants.

CONCLUSION: SARS-CoV-2 infection had negative effects on sleep, and a significant proportion of adults experienced insomnia and daytime sleepiness beyond 12 months after recovering from the initial infection.

KEYWORDS: Long Coronavirus disease-2019, insomnia, hypersomnia

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INTRODUCTION

The Coronavirus disease-2019 (COVID-19) pandemic has caused over 700 million cases and 7 million deaths globally.¹ However, a significant proportion of COVID-19 survivors experience a variety of ongoing symptoms characterized by persistence or recurrence of initial symptoms or emergence of new symptoms. Those so afflicted often refer to themselves as “long haulers” and the constellation of these symptoms is colloquially known as “long COVID-19”. In October 2021, the World Health Organization proposed to define these symptoms as “post-COVID-19 condition”, referring to any symptom(s) occurring in individuals with a probable or confirmed Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) infection within three months of infection and lasting for at least two months as long as there is no alternative diagnosis.² Similarly, in the United Kingdom, the National Institute for Health Excellence proposed a definition of “post-COVID-19 syndrome” for symptoms developing during or after infection with COVID-19 lasting for more than 12 weeks and after excluding alternative diagnoses.³ The syndrome is now formally known as post-acute sequelae of SARS-CoV-2 (PASC). It has been estimated that approximately 100 million people suffer from PASC globally, and the total economic burden is estimated to be approximately 2.6-3.7 trillion dollars.⁴ Estimates of the prevalence of PASC range from 7.5-41% in non-hospitalized adults depending on the criteria used to identify cases.⁵

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The most commonly reported symptoms of PASC are fatigue, brain fog, and sleep disturbance. Fatigue is a vague symptom that is difficult to separate from sleep disturbances. Although the prevalence of sleep disturbances in PASC is estimated to range from 18-40%,⁶ most reports of sleep disturbances in PASC are non-specific; there are few reports of the exact symptoms, prevalence, evolution, and ultimate outcomes of sleep disturbances in PASC.⁷⁻⁹ Nonetheless, a high prevalence of insomnia has been reported within the first six months after COVID-19 infection.¹⁰ A large cohort study in the UK demonstrated an increased risk of fatigue and sleep problems¹¹. Similarly, a recent study (the International COVID Sleep Study-II study)¹² demonstrated a high prevalence of insomnia (49.6%) and excessive daytime sleepiness (35.8%) among patients with PASC. Even if only 10% of those with PASC develop a sleep disorder, there would be an enormous social and economic impact. Therefore, documenting the time course of disturbed sleep related to COVID-19 may better prepare healthcare providers to manage and possibly mitigate the impact of PASC.

In this study, we report the incidence and prevalence rates of self-reported disturbed sleep symptoms and changes in sleep duration in a cohort of individuals with COVID-19 infection. In addition, we documented the persistence of these symptoms during the post-infection period. We hypothesized that symptoms of sleep disturbance related to COVID-19 will be heterogeneous and persist for an extended period after initial infection with SARS-CoV-2.

MATERIAL AND METHODS

The data used in this study were obtained from the Massachusetts General Brigham (MGB) Research Patient Data Registry (RPDR). This centralized clinical registry or data warehouse was established in 1991 and can be used to identify patients based on clinical and demographic information. Using this repository, we assembled a study cohort of patients who tested positive for SARS-CoV-2 at MGB hospitals between February 2020 and March 2021. After institutional review board approval, a RPDR query was run to identify patients aged above 18 years who were enrolled in the Research Opportunities Direct to You program. This outreach program allows patients to agree to be contacted directly by researchers without involvement from their clinicians.

The RPDR query included patients irrespective of gender and race who had a documented positive COVID-19 test. Patients with severe neurologic disease, those on chronic ventilatory support, pregnant women, or those in rehabilitation were excluded from this study. Using the Research Electronic Data

Capture (REDCap) HIPAA-compliant web-based application, patients meeting the defined criteria were sent a survey (Appendix Survey 1). The survey was sent in two languages (English and Spanish). A total of 1,090 invitations were sent, and 290 responses were received. Participants who provided incomplete surveys were excluded, leaving a total of 246 for final analysis (22.6%). Comparisons of the mean age (53.3 ± 16.3 vs. 51.0 ± 16.5 years, $P = 0.09$) and sex distribution (74.3% vs. 68.8% female, $P = 0.35$) of respondents to non-respondents were not significantly different.

In addition to demographic information, the survey included questions pertaining to the number of hours of sleep, difficulty initiating or maintaining sleep, daytime sleepiness, snoring, difficulty breathing while asleep, history of vivid dreams or hypnagogic hallucinations, and use of sleep aids before and after their diagnosis of COVID-19 (Appendix Survey 1). Information related to comorbid conditions and medications was obtained through chart review.

The study was approved by the Massachusetts General Brigham Institutional Review Board (protocol number: 2020P004011, date: 12.15.2020).

Statistical Analysis

Data are summarized as mean with standard deviation for continuous variables or frequency with proportions for categorical variables. Group comparisons before and after COVID-19 infection were examined using Student's paired sample t-test for continuous data or Pearson χ^2 test for categorical data. As the response categories for self-reported sleep duration were ordinal, changes in the distribution of responses were determined using the Stuart-Maxwell marginal homogeneity test. To examine whether symptoms persisted beyond 12 months, the data were stratified into two categories (≤ 12 months or > 12 months) according to the duration of time after their COVID-19 diagnosis. Each respondent completed the survey. The effects of hypertension, heart disease, anxiety/depression, diabetes, and smoking on changes in sleep characteristics were assessed using McNemar's test. In all analyses, the statistical significance was set as $P < 0.05$. All statistical tests were performed using STATA v18 (MP-parallel Edition; STATA Corp, College Station TX) or IBM Statistical Package for the Social Sciences v28 (Armonk, NY).

RESULTS

Table 1 shows the baseline characteristics of the 246 participants who responded to the sleep survey. The average age was 53.3 ± 16.3 years, and the respondents were predominantly non-hispanic white (84.1%) and female (74.3%). The mean BMI (kg/m^2) was 29.9 ± 6.9 , and a greater proportion were non-smokers (63.2%). College education and current employment were reported by 47.9% and 63.7% of respondents, respectively. Significant proportions of the cohort reported anxiety/depression (50.0%), hypertension (41.8%), heart disease (13.9%), and diabetes (13.7%). A previous sleep disorder diagnosis was noted in 37.0%. Hospital admission occurred in 11.3% of participants, and 7.9% of the patients had pneumonia as an admission diagnosis. Hospital admission, but not pneumonia, occurred more frequently in those with symptoms exceeding 12 months. Additionally, only one participant required mechanical ventilation.

Main Points

- A significant proportion of Coronavirus disease-2019 (COVID-19) survivors suffer from ongoing symptoms, referred to as long-term COVID-19.
- Severe acute respiratory syndrome-Coronavirus-2 infection has negative effects on sleep.
- COVID-19 survivors may experience increased insomnia and daytime sleepiness beyond 12 months after the infection

Tables 2, 3 presents the effect of COVID-19 diagnosis on various sleep characteristics. Results for all participants are presented in Table 2. After the infection, a significantly greater number of participants reported difficulty initiating (31 vs. 39%, $P = 0.016$), and maintaining sleep (43 vs. 57%, $P < 0.001$), and increased use of sleep aids (24 vs. 30% $P = 0.006$) with incidence rates of 24%, 37%, and 12%, respectively. In addition, feeling unrested and the need for napping were greater (58 vs. 36%, $P < 0.001$) and (27 vs. 40% $P < 0.001$) with an incidence of 7.9% and 22.6%, respectively. Interestingly, a large number of participants reported having vivid dreams and hypnagogic hallucinations during the post-COVID-19 period. The incidence rate of vivid dreams was 31% after recovery

from COVID-19. Although shortness of breath while sleeping increased slightly, the prevalence of snoring did not change. Figure 1 illustrates the distribution of self-reported sleep duration before and after COVID-19. There was a substantial shift in the distribution toward shorter sleep as well as a less perceptible change toward greater sleep ($P = 0.009$).

Table 3 shows the prevalence of sleep symptoms before and after COVID-19 after excluding individuals with pre-existing anxiety or depression. The patterns of change in the prevalence rates of COVID-19 were similar to those observed in the full cohort, although some symptoms were no longer statistically significant.

Table 1. Baseline characteristics

	All participants	<12 months	≥12 months	P value
	246	176	70	
Age (yrs)	53.3±16.3	52.2±15.5	56.1±17.9	0.09
Sex (M/F %)	25.7/74.3	27.8/72.2	20.3/79.7	0.22
Hispanics (%)	6.9	6.3	8.6	0.52
Caucasians (%)	84.4	84.0	85.5	0.89
Employed (%)	63.7	65.5	60.0	0.42
Education (% college)	47.9	49.4	44.3	0.76
BMI (kg/m ²)	29.9±6.9	29.8±6.4	30.2±8.2	0.77
Smoking history (%):				
Never	63.2	64.1	60.4	
Current	6.2	5.5	8.3	0.70
Past	30.6	30.3	31.3	
Hypertension (%)	41.8	42.6	39.6	0.72
Anxiety/depression (%)	50.0	50.0	50.0	1.0
Diabetes (%)	13.7	12.0	19.0	0.25
Heart disease (%)	13.9	12.4	18.6	0.31
Duration between infection and survey (months)	7.4±3.9	5.4±1.9	13.3±0.8	0.00
Hospitalized (%)	11.3	8.5	19.1	0.02
Pneumonia (%)	7.9	6.8	11.1	0.27

BMI: body mass index, yrs: years, M: male, F: female

Table 2. Sleep symptoms before and after COVID-19 infection (n = 246)

	Pre-COVID-19 (%)	Post-COVID-19 (%)	P value
Difficulty falling asleep	31	39	0.016
Difficulty staying asleep	43	57	<0.001
Use of sleep aids	24	30	0.006
Rested	58	36	<0.001
Napping	27	40	<0.001
Snoring	48	49	0.454
Difficulty breathing	10	14	0.049
Vivid dreams	44	56	<0.001
Hypnagogic hallucinations	3	10	<0.001

COVID-19: Coronavirus disease-2019

To evaluate the impact of COVID-19 infection severity, analyses were performed after stratification by hospital admission history and COVID-19 pneumonia. As shown in Appendix Tables 1, and 2, the number of participants who were hospitalized or who developed pneumonia was small. Nonetheless, the pattern of change in prevalence rates after COVID-19 infection were qualitatively similar in those with a history of hospital admission as well as those with a history of pneumonia. A previous diagnosis of a sleep disorder was noted in 37% of respondents (Appendix Table 3). Although some symptoms were not statistically significant, the pattern of change in

these individuals was generally similar to that in individuals without a sleep disorder diagnosis. In particular, there was a marked increase in feeling unrested and a need to nap, both of which were noted in the overall cohort.

The long-term effects of COVID-19 on sleep are presented in Table 4. Overall, 64 participants (26%) experienced sleep symptoms after more than 12 months of COVID-19 treatment. The symptom pattern did not differ between those with a shorter vs. longer duration of past infection. As shown in Figure 2, sleep duration decreased similarly in those who were less than 12

Table 3. Sleep symptoms before and after COVID-19 infection, excluding pre-existing anxiety or depression (N = 92)

	Pre-COVID-19 (%)	Post-COVID-19 (%)	P value
Difficulty falling asleep	22	33	0.021
Difficulty staying asleep	39	53	0.011
Use of sleep aids	16	24	0.039
Rested	66	46	<0.001
Napping	23	28	0.508
Snoring	53	51	1.0
Difficulty breathing	8	13	0.063
Vivid dreams	41	54	0.019
Hypnagogic hallucinations	1	3	0.625

COVID-19: Coronavirus disease-2019

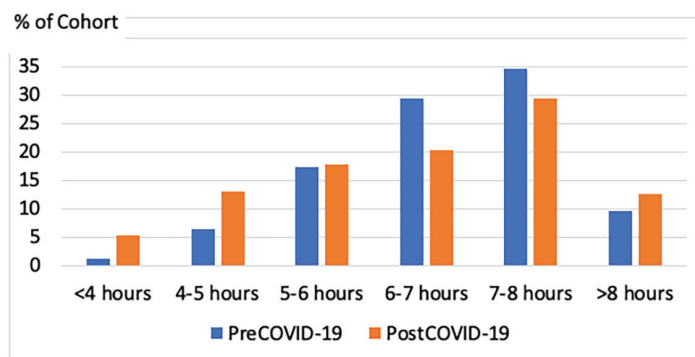


Figure 1. Distribution of self-reported sleep duration before and after COVID-19 infection. $P = 0.009$, pre-COVID-19 vs. post-COVID-19

COVID-19: Coronavirus disease-2019

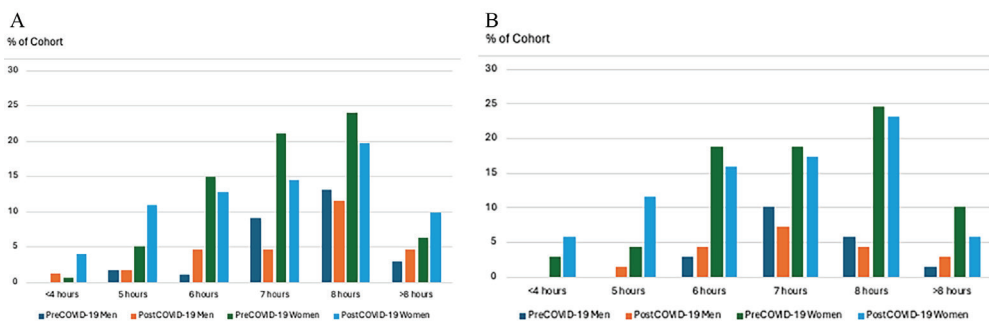


Figure 2. Distribution of self-reported sleep duration before and after COVID-19 infection stratified by sex for participants A) who were less than 12 months removed from infection (N = 183). $P = 0.007$, pre vs. post-COVID-19; $P = 0.208$, men pre vs. post-COVID-19; $P = 0.017$, women pre vs. post-COVID-19; B) for participants who were >12 months removed from infection (N = 64). $P = 0.044$, pre vs. post-COVID-19; $P = 0.527$ for men, pre vs. post-COVID-19; $P = 0.056$, women pre vs. post-COVID-19

COVID-19: Coronavirus disease-2019

Table 4. Sleep impairment associated with COVID-19 infection before and after 12 months

	<12 months		≥12 months	
	N = 183		N = 63	
	Pre-COVID-19	Post-COVID-19	Pre-COVID-19	Post-COVID-19
Difficulty falling asleep (%)	30±46	36±48	33±47	48±50
<i>P</i>	0.14		0.01	
Difficulty staying asleep (%)	43±49	55±49	43±49	61±49
<i>P</i>	0.001		0.009	
Use of sleep aids (%)	24±43	29±46	23±43	32±47
<i>P</i>	0.03		0.03	
Rested (%)	58±49	34±48	60±49	41±49
<i>P</i>	<0.001		0.002	
Napping (%)	29±45	41±49	23±42	38±49
<i>P</i>	<0.001		0.006	
Snoring (%)	50±50	50±50	43±49	47±50
<i>P</i>	0.74		0.26	
Difficulty breathing (%)	9±29	13±33	13±34	17±38
<i>P</i>	0.11		0.08	
Vivid dreams (%)	43±49	55±49	46±50	60±49
<i>P</i>	<0.001		0.006	
Hypnagogic hallucinations (%)	2±15	9±28	4±21	15±36
<i>P</i>	0.007		0.007	

COVID-19: Coronavirus disease-2019

months removed from the infection and those with 12 months or more removed from the infection. Furthermore, changes in sleep duration were primarily attributable to women.

Additional analyses (data not shown) demonstrated that changes in sleep characteristics after COVID-19 infection occurred irrespective of comorbid conditions, such as hypertension, heart disease, diabetes, and anxiety/depression.

DISCUSSION

In this study, we documented that after COVID-19 infection, there is a high incidence and prevalence of self-reported symptoms of sleep disturbance. In addition, these symptoms persist for over 12 months in many individuals. In addition, self-reported sleep duration changes were observed in many individuals, with most experiencing a decline but with an increase apparent in a few.

A bidirectional relationship exists between sleep and immunity, and sleep disturbances have been reported as consequences of infections, particularly viral infections.¹³⁻¹⁵ Several sleep symptoms, including difficulties with sleep initiation and maintenance, reduced sleep time, prolonged sleep time, and daytime napping, have been reported. Prior studies on the neuropsychiatric consequences of COVID-19 showed that the most prevalent symptoms were sleep disturbances (27%) followed by fatigue (24%)¹⁰ although another study found that fatigue (40%) was more common than sleep disturbances (29.4%).¹⁶ However, reports of sleep disturbances in other studies were undifferentiated. Our findings demonstrate that symptoms of sleep disturbance associated with insomnia are common and increase after COVID-19 infection. In contrast, symptoms indicative of sleep-disordered breathing, such as snoring, did not increase. Our results are consistent with those of previous studies in confirming that disturbed sleep is highly prevalent after COVID-19 and but extend them by

demonstrating that it is a result of a high incidence of symptoms suggestive of insomnia.

Our cohort of COVID-19 survivors reported insomnia symptoms that persisted beyond 12 months following COVID-19 infection. Insomnia is a fairly well documented post-COVID-19 sequelae¹⁷⁻²⁰ and is one of the symptoms attributed to PASC. The average prevalence of post-COVID-19 insomnia is estimated at approximately 24%.²¹ However, few studies document its time course. A previous study demonstrated persistence of insomnia for up to 30 days after COVID-19 infection.²² A recent study of sailors on an aircraft carrier noted that over 50% of the participants reported at least one symptom of long-lived COVID-19 at 6, 9, and 12 months.¹⁷ Our study extends the findings from previous studies by demonstrating that 28% of individuals with COVID-19 from a community can experience disturbed sleep for more than 12 months. Consistent with our findings, a high prevalence of sleep disturbances (67%) was reported among COVID-19 survivors in a recent uncontrolled prospective observational study.²³

We observed that sleep duration decreased in many of our cohort and that it was present for 12 months or more after COVID-19 infection. However, in a small number of individuals, sleep duration has been shown to increase. These changes are similar to those observed in uninfected persons in the general population during the COVID-19 pandemic and have been associated with anxiety and depression.²⁴ It is possible that a similar relationship exists with individuals who have had COVID-19 infection, as there was a high prevalence of anxiety or depression in our cohort.

Fatigue is one of the most common persistent symptoms following COVID-19^{16,25} and can last up to a year after infection.^{26,20} It has been shown to occur concurrently with insomnia in some patients.²⁷ Post-infection fatigue syndrome has also been reported following infectious mononucleosis²⁸⁻³⁰ suggesting that fatigue in these two conditions may share the same pathogenetic mechanism. Our analysis also revealed increased fatigue and the need for daytime napping among COVID-19 survivors, confirming previous reports. In a recent study using data from the German National Pandemic Cohort Network, the researchers found fatigue and cognitive deficits as the most prevalent long-term COVID-19 symptoms, and these symptoms improved over two years in more than half of the participants who recovered from post-COVID-19 syndrome.^{31,25}

Vivid dreaming and hypnagogic hallucinations, which can be features of narcolepsy, occurred post-COVID-19 in our cohort, and these symptoms persisted for 12 months or more. Although COVID-19 has not been associated with an increased risk of narcolepsy³², infection with SARS-CoV-2 may provide an opportunity to investigate the mechanisms related to the development of narcolepsy.³³ In a previous study examining the interaction between COVID-19 and multiple health behaviors (sleep, diet, and physical activity), the authors demonstrated increased vivid dreams and nightmares among 12% of participants, and the majority were linked to increased stress and anxiety (75%).³⁴ These symptoms were predominantly reported by women. To our knowledge, this is the first study to report vivid dreams and hypnagogic hallucinations as part of

the neuropsychiatric consequences of COVID-19 infection and the persistence of these symptoms beyond 12 months.

Our study results indicated that women were more likely to experience a reduction in sleep duration after COVID-19. These findings are consistent with our previous research in a large general population, which demonstrated that sleep decline during the pandemic was more likely to occur in women.²⁴ In addition, studies from the Middle East and the West have demonstrated an increased risk of developing mental health problems among women during the COVID-19 pandemic,^{35,36} mental health issues during the pandemic were major factors associated with changes in sleep duration.²⁴ In contrast, several studies from China have found no gender difference.^{37,38} Further investigation is required.

Given the heterogeneity of PASC symptoms and, in particular, associated sleep disturbances, multispecialty collaboration is needed to treat afflicted individuals. However, due to the lack of specialists and long wait times, primary care providers are responsible for early recognition of sleep disorders in patients with PASC. Our study results emphasize that sleep disturbances are common and enduring in PASC and therefore require as much attention as other PASC-related symptoms. The World Health Organization, in its document "Support for rehabilitation self-management after COVID-19 related illness"³⁹ has published simple recommendations for improving sleep, which can be a useful tool for clinicians.

To our knowledge, this is the first study to examine the long-term effects of COVID-19 on disturbed sleep symptoms. However, we acknowledge some limitations. First, the response rate for our study was very low, which is concerning for non-response bias. However, we found no statistical difference between the age and sex distribution of respondents and non-respondents, suggesting that the two groups were not meaningfully different. Furthermore, some studies have explored the relationship between low response rates and non-response bias and found little relationship between the two.⁴⁰⁻⁴² Nevertheless, some degree of non-response bias cannot be excluded and should be considered when interpreting our results. Second, the study participants were contacted using the REDCap portal, and it is likely that patients without access to technology were not represented in this study, thereby causing sampling bias and skewing the interpretation. Third, the results of this study were based on self-reported sleep impairment, which may have caused reporting bias. Fourth, the majority of the study participants were women. Therefore, our findings related to sex differences should be interpreted with caution. Fifth, the cohort was comprised mainly of Caucasians and English-speaking participants despite our efforts to recruit Spanish speakers. Thus, our sample is not representative of the United States population, and the results may not be generalizable. Lastly, measures of sleep disturbance were self-reported; future studies using objective sleep measures are needed to better assess the long-term effects of COVID-19.

CONCLUSION

In this observational study, infection with SARS-CoV-2 had a negative effect on sleep, with a high proportion of adults experiencing difficulty initiating and maintaining sleep, feeling

unrested, and other symptoms of disturbed sleep lasting beyond 12 months after recovering from the initial infection. Future studies with a more diverse population and using objective sleep measures are needed to examine these relationships and to determine whether interventions can improve sleep health in individuals with PASC.

Ethics

Ethics Committee Approval: The study was approved by the Massachusetts General Brigham Institutional Review Board (protocol number: 2020P004011, date: 12.15.2020).

Informed Consent: Waived [patients who were enrolled in the Research Opportunities Direct to You (RODY) program were contacted]. This outreach program allows researchers to directly contact patients. Eligible patients were sent recruitment letters via secure email, and only after they agreed to participate, were the REDCAP sleep surveys sent.

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Footnotes

Authorship Contributions

Concept: S.B-A., O.S.F., S.F.Q., Design: S.B-A., O.S.F., S.F.Q., Data Collection or Processing: S.B-A., Analysis or Interpretation: S.B-A., S.F.Q., Literature Search: S.B-A., O.S.F., S.F.Q., Review and Editing: S.B-A., S.F.Q., Writing: S.B-A.

Conflict of Interest: SFQ has served as a consultant for Best Doctors, Bryte Foundation, Jazz Pharmaceuticals, and Whispersom. The remaining authors declare no conflict of interest.

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