Sleep Medicine 91 (2022) 253–261

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Sleep disorders and COVID-19

Sushanth Bhat [a,*], Sudhansu Chokroverty [b]

[a] Hackensack Meridian-Health JFK University Medical Center, 65 James Street, Edison, NJ, 08818, USA
[b] Sleep Medicine Research, and Co-Chair Emeritus of Neurology, Hackensack Meridian-Health JFK University Medical Center, 65 James Street, Edison, NJ, 08818, USA

ARTICLE INFO

Article history:
Received 2 July 2021
Accepted 7 July 2021
Available online 18 July 2021

Keywords:
Coronasomnia
COVIDsomnia
COVID-19 and sleep dysfunction
COVID-19 and obstructive sleep apnea
COVID-19 and nightmares

ABSTRACT

This chapter summarizes the known associations between COVID-19 and sleep dysfunction, including insomnia, excessive daytime sleepiness, restless legs syndrome and nightmares, and touches upon pandemic-related considerations for obstructive sleep apnea and continuous positive airway pressure treatment. Treatment strategies and management approaches are also briefly discussed.

1. Introduction

The global COVID-19 pandemic has had a serious and significant impact on all aspects of daily living. Caused by a novel coronavirus (SARS-CoV-2), which was first reported in Wuhan, China, in December 2019 [1], this public health crisis is still ongoing at the time of writing in mid-2021. As such, it is not surprising that sleep patterns, sleep quality, and the diagnosis and management of sleep disorders have all been affected in profound and somewhat unexpected ways. The fear and anxiety of potential infection, mandatory lockdowns and quarantine procedures have combined to cause a degree of sleep dysfunction in the general population as well as among healthcare workers (HCWs) whose full scope has yet to be fully assessed [2]. Additionally, research into sleep dysfunction in patients diagnosed with COVID-19 in both the acute and chronic phases of the illness is still being performed.

This article summarizes some of the findings that have emerged from research into the associations between COVID-19 and sleep dysfunction. Many of the topics discussed are expanded upon in greater detail elsewhere in this special issue.

Box 1 enumerates the types of sleep dysfunction associated with the COVID-19 pandemic.

2. COVID-19 related sleep dysfunction

The colloquial terms "coronasomnia" or "COVID-somnia" [3] have been proposed to encompass the constellation of symptoms of sleep dysfunction such as insomnia, disrupted sleep continuity, changes in sleep-wake cycle, feelings of non-restorative sleep and decreased sleep quality arising either due to stresses related to fear of the virus itself or the psychosocial impact on daily living (such as loss of employment, financial concerns, social isolation resulting from lockdowns and quarantine, or the actual medical and psychological sequalae of contracting COVID-19 infection). There is already a wealth of published information relating to changes in sleep among various populations in the context of the COVID-19 pandemic [2], although the long-term implications remain to be determined given that the global health crisis remains ongoing.

2.1. Factors contributing to sleep dysfunction in COVID-19

Several factors are likely responsible for sleep dysfunction related to COVID-19. A recent meta-analysis showed relatively high rates of symptoms of anxiety (ranging from 6.33% to 50.9%), depression (14.6%–48.3%), post-traumatic stress disorder (PTSD) (7%–53.8%), psychological distress (34.43%–38%), and stress (8.1%–81.9%) in the general population across the globe during the COVID-19 pandemic [4]. The reported risk factors including female gender, younger age group (less than 40 years), presence of chronic/psychiatric illnesses, unemployment, educational status, and frequent exposure to social media/news concerning COVID-19. Anxiety and

* Corresponding author.
E-mail addresses: sbhat2012@yahoo.com (S. Bhat), sudhansu.chokroverty@hmhn.org (S. Chokroverty).

https://doi.org/10.1016/j.sleep.2021.07.021
1389-9457/

Box 1
Types of Sleep Dysfunction in COVID-19.

- Insomnia: Acute and persistent.
- Effect of COVID-19 on obstructive sleep apnea.
- Circadian rhythm abnormalities.
- Excessive daytime sleepiness related to sleep-wake impairment (? central nervous system functional or structural dysfunction).
- Post-traumatic-like sleep dysfunction (new-onset or re-emergence of prior post-traumatic stress disorder).
- Abnormal dreams (nightmare disorder).
- Transient restless legs syndrome associated with insomnia.

depression are well known to have reciprocal relationships with insomnia [5,6], and it has been shown that the prevalence of all forms of psychological distress in the general population has been higher during the pandemic [7,8].

3. COVID-19 related sleep dysfunction in the general population

The concomitant COVID-related increase in sleep dysfunction in the general population has been confirmed by the work of many groups. Lin et al. [9] studied 5461 Chinese participants and found that, as with mood disorders, insomnia was more severe in women and young people, living in the epicenter and experiencing a high degree of threat from COVID-19. In another large Chinese study among nearly 12,000 adolescents and young adults [10], the prevalence of insomnia symptoms during part of the COVID-19 epidemic period was 23.2%, with female sex, depression and anxiety, and residing in the city being the greater risk factors; social support, both subjective and objective, was protective. Another group found the incidence of new onset COVID-19-related insomnia as high as 13.6% [11]. Studies among the general population in Europe suggest similar trends. An Italian study of 1989 young to middle-aged adults showed that during the pandemic, the prevalence of clinical insomnia was 18.6%, and insomnia severity was associated with poor sleep hygiene behaviors, dysfunctional beliefs about sleep, self-reported mental disorder, anxiety and depression [12]. A French study of 556 participants from the general population revealed that 19.1% met the diagnostic criteria of clinical insomnia and confirmed that COVID-19-related worries and loneliness were the major contributing factors to clinical insomnia, in addition to lower education status, being infected by the virus and pre-existing mental health illness [13]. Robillard et al. [14] surveyed 5525 Canadian respondents and found that relative to the pre-pandemic baseline, wake-up times were significantly delayed and occurrences of clinically meaningful sleep difficulties significantly increased, with female sex, chronic illnesses, being employed, family responsibilities, earlier wake-up times, higher stress levels, as well as heavier alcohol use and television exposure representing risk factors. A three-day online survey in Greece [15] studied 2363 individuals and found that 37.6% of the participants had COVID-19 related-insomnia; women and people in urban areas were more vulnerable to sleep problems. Fears of contracting COVID-19 (either self or loved ones), higher levels of intolerance to uncertainty, COVID-19 related worry, loneliness, as well as more severe depressive symptoms, were all predictive of insomnia, but age did not seem to be a significant factor. Additionally, a recent study by Musse found a nearly threefold increase in nightmare frequency compared to a pre-pandemic baseline, with dream content in about one-third of the participants including pandemic-related elements (fear, loneliness, being chased by infected patients, etc.) [16].

Thus, overall, the data from numerous studies in several countries suggests that among the general population, female gender, urban living, high-risk environment with regard to COVID-19 (eg., living in an epicenter), lower socioeconomic and educational status, pre-existing psychiatric conditions with poorer coping mechanisms, absence of social support structures, and high level of exposure to COVID-19 related news are risk factors for COVID-19 related insomnia, with age playing an uncertain role.

Notably, the above findings also suggest that, given well-known disparities in access to testing and health care among racial/ethnic minorities (many of whom suffer from chronic health conditions predisposing to COVID-19 infections as well as chronic sleep deprivation) [17,18] providers have an obligation to be sensitive and vigilant in providing sleep-related care to these particularly at-risk sections of the general population in the time of COVID-19 [19].

3.1. Effects of lockdown on COVID-19 related sleep dysfunction

While most studies among the general population, by their very nature, include individuals in lockdown (which was essentially the norm in most countries around the world during the pandemic), some researchers have attempted to study the effects of lockdown and/or quarantine periods in particular on sleep dysfunction. A large Spanish study [20] conducted in over 15,000 subjects in the early phase of the lockdown showed high rates of difficulty initiating or maintaining sleep (23.9%), associated with higher age, female sex, reduction in income, having elderly dependents, alcohol use, depression, anxiety and stress; conversely, indulging in hobbies such as painting or listening to music were protective factors. A web-based study among 1908 individuals in lockdown in six different countries (Greece, Switzerland, Austria, Germany, France, and Brazil) showed that sleep duration increased by a small amount (0.31 h); 15% of participants characterized their sleep as bad and 37.9% as average during the lockdown week, and a third of individuals reported worse quality of sleep during the lockdown week than under normal conditions [21]. An Italian study conducted among 400 university students and administrative staff workers [22] found later bedtimes, increased time in bed, increased sleep latency, and later wake-up times; prevalence of insomnia increased from 24% pre-pandemic to 40% during the pandemic, and 27.8% showed depressive symptoms, while 34.3% showed anxiety symptoms. Kocevska et al. [23] studied 667 Dutch individuals in lockdown and found that a quarter of people with pre-pandemic insomnia paradoxically experienced a meaningful improvement in sleep quality, whereas 20% of pre-pandemic good sleepers experienced worse sleep during the lockdown measures, and that changes in sleep quality throughout the pandemic were associated with negative affect and worry.

Use of electronic devices and social media has also increased during the lockdown [24] and it has been previously demonstrated that social media use is a risk factor for sleep dysfunction [25]; while this needs further exploration in the specific context of COVID-19, this would presumably be a factor that may cause additional sleep dysfunction, especially as much of the content on social media sites would likely relate to (often unregulated and possibly misleading) information relating to COVID-19, which may cause additional anxiety and stress.

Thus, overall, the effect of lockdown on the sleep of non-infected individuals seems to be varied and there may be additional cultural and geographic factors at play, which require further research for better delineation.

An additional factor for practitioners to bear in mind is weight gain occurring as a result of lockdown (so-called “covibesity” or COVID-obesity) [26], due to more sedentary lifestyles, increased snacking and overeating, increased alcohol use, and decreased opportunity for physical activities due to closure of parks, gymnasiums and hiking trails [27]. While there is not yet any reliable data in this regard, weight gain during lockdown can lead to worsening of underlying obstructive sleep apnea (OSA), whether previously diagnosed or undiagnosed, which may be an overlooked additional factor in sleep dysfunction, about which providers should be vigilant.

3.2. Treatment strategies for COVID-19 associated sleep dysfunction in the general population

The optimal treatment strategy for treating sleep dysfunction related to COVID-19 remains unclear. Cognitive behavioral therapy (CBT) [28] has been shown to have long-term efficacy in cases of primary insomnia or insomnia precipitated by stressors; COVID-19 would certainly qualify for this label, but CBT has yet to be studied in this particular context. There may be a role for short-term prescription of a sleep aid, but the best medication has yet to be determined. Drug therapy may have a role in acute COVID-19 related insomnia whereas CBT-I is recommended for chronic insomnia. Though not formally studied, it has been suggested that sleep aids that do not have drug–drug interactions with medications that are used to treat COVID-19, that do not cause significant respiratory depression, and that are not extensively metabolized by the liver, such as temazepam or quazepam, should be considered first choice [29]. Social and family support mechanisms will likely help sufferers cope and should be encouraged where available. It is hoped that as the pandemic begins to recede, vaccinations become more widespread and lockdowns are lifted, many stressors may be eliminated and sleep dysfunction may improve.

Box 2 summarizes treatment strategies for COVID-19 related sleep dysfunction.

Box 2

Principles of Treatment of Sleep Dysfunction During COVID-19 Pandemic.

- General measures specific to COVID-19.
  - Preventative measures (vaccinations, masking and gloving, social distancing, etc.)
  - Treatment of co-morbidities (medical, psychiatric and neurological).
  - Supportive measures in patients with respiratory distress (oxygen, ventilatory support).
  - Disease-specific treatments (eg., remdesivir, monoclonal antibodies [eg., tocilizumab], corticosteroids, etc.), although efficacy has not been established.
- Specific Measures to Combat Sleep Dysfunction.
  - Short-term pharmacotherapy for acute insomnia.
  - Cognitive-behavioral therapy for chronic persistent insomnia.
  - Melatonin for ICU-related delirium and sleep dysfunction.
  - Positive airway pressure therapy for obstructive sleep apnea (using special precautions to prevent aerosolization, see text).

4. COVID-19 related sleep dysfunction in healthcare workers

HCWs represent a particularly vulnerable section of the population for pandemic-related sleep dysfunction. In addition to the psychosocial stressors that affect the general population, they are subject to unique additional sources of stress, such as the higher potential for contracting the virus (whether or not they are actively exposed to patients with COVID-19 infections) by virtue of working in the inpatient or outpatient setting and being exposed to a large volume of patients. In addition, while they are generally exempt from mandatory lockdowns and may have greater job security than non-healthcare personnel, they are often called upon to perform additional shifts or work longer hours during health crises, contributing to burnout, mood disorder and sleep dysfunction [30]. Availability of facilities for proper hand hygiene and adequate personal protective equipment (PPE) is also often an issue. Some identified risk factors for negative impact on HCWs include working in a high-risk environment, diagnosed family member, inadequate hand hygiene, improper or inadequate PPE use, close contact with patients (greater than 12 times a day), long shifts (greater than 15 h) and unprotected exposure [31]. Early evidence suggests that a considerable proportion of HCWs have been experiencing mood and sleep disturbances during this outbreak, and reports of insomnia are significantly higher among HCWs than the general population [32,33]. In a Turkish study of the 939 HCWs [34], 77.6% participants exhibited depression, 60.2% exhibited anxiety, 50.4% exhibited insomnia, and 76.4% distress symptoms, all of which were significantly greater among women, individuals with a history of psychiatric illness, and individuals receiving psychiatric support during the COVID-19 pandemic; female gender, being a nurse (as opposed to a physician), working on the frontline, history of psychiatric illness, and being tested for COVID-19 were identified as risk factors for mental health problems. One US-based study conducted among 587 hospital nurses and nursing assistants [35] showed subthreshold insomnia, moderate-to-high chronic fatigue, high acute fatigue and low-to-moderate intershift recovery, with nurses who cared for COVID-19 patients scoring significantly worse on almost all measures than other HCWs. Symptoms were significantly predictive in those with longer work hours and less frequent 30-minute breaks. A study conducted among 421 HCWs in Spain [36] showed that the COVID-19 pandemic generated symptoms of stress, anxiety, depression and insomnia, with higher levels among women and older professionals. Factors associated with insomnia among HCWs include female gender, working experience, chronic diseases, midday nap duration, direct participation in rescue of patients with COVID-19, frequency of night shifts, professional psychological assistance during the pandemic, negative experiences (such as family, friends, or colleagues being seriously ill or dying due to COVID-19), the degree of fear of COVID-19, fatigue, and perceived stress [37].

At particular risk for COVID-19-related stressors are frontline health care workers (FHCWs), defined as medical personnel (doctors, nurses, medical students, technicians, respiratory therapists, etc.) involved in the assessment, quarantine, isolation, and treatment of established COVID-19 cases. Barua et al. [38] studied 370 Bangladeshi frontline physicians and found that 18.6% had insomnia; additionally, 36.5% had anxiety, 38.4% had depression, and 31.9% had fear of COVID-19, with inadequate resources in the workplace being the single most significant predictor for all psychological outcomes. A study conducted among 528 Chinese FHCWs [39] found that frequent nightmares (thought to be a maker for potential PTSD) were found in 27.3% of subjects, and that reduced sleep duration and reduced sleep efficiency were independently associated with frequent nightmares after adjustment for age, sex, poor mental health, and regular sleep aid use.

There has been some preliminary research into whether the sleep dysfunction in FHCWs differs from that seen in non-FHCWs, but the results are somewhat contradictory. A Chinese study [40] of 1306 subjects (801 FHCWs vs 505 non-FHCWs) showed that FHCWs complained of significantly poorer sleep quality and higher prevalence of sleep disturbances, insomnia and depression than non-FHCWs. Similarly, a study of 2737 Chinese HCWs [41] showed that the prevalence of sleep disorders was higher among FHCWs compared to non-FHCWs and non-medical staff, while anxiety and depression were prevalent in all groups; medical occupation, family burden, bereavement, anxiety, and depression were significantly predictive of poor sleep quality. Another study [42] found that FHCWs had higher prevalence of insomnia compared to non-FHCWs (47.8% vs. 29.1%). On the other hand, a study comparing FHCWs to non-FHCWs in Bahrain [43] showed no significant difference in subjective sleep quality between the two groups; for FHCWs vs non-FHCWs, the proportion of poor sleepers (75% vs 76%), those moderate-to-severe stress (85% vs 84%) and both (61% vs 62%) were similar, but female sex and professional background were the predictors of poor sleep quality and stress. A study conducted among Chinese frontline nurses [44] during two separate periods (the "outbreak period" and the subsequent "stable period" of the pandemic) showed that while overall over a third of nurses suffered from depression, anxiety, and insomnia during the pandemic, all symptoms except insomnia significantly declined to equal that in the non-frontline nurses group in the stable period, suggesting that sleep dysfunction among FHCWs may outlast psychological symptoms. However, long-term longitudinal studies are needed to better explore this possibility.

4.1. Treatment of sleep dysfunction in HCWs

Among HCWs, few specific interventional studies exist; however, it has been suggested that implementation strategies to reduce the chance of infection (including adequate hand hygiene and adequate supply of PPE), shorter shift lengths and institutional mechanisms for social and mental support during the pandemic may be helpful in mitigating adverse outcomes, including sleep dysfunction [31].

5. Sleep dysfunction in COVID-19 sufferers (short and long term)

At this time, there remains limited data regarding sleep dysfunction in patients who have been diagnosed with COVID-19, whether asymptomatic or symptomatic, whether requiring hospitalization or not, and among those hospitalized, whether requiring intensive care (ICU) admission due to respiratory failure or not. Huang et al. [45] compared adults infected with COVID-19 to uninfected adults in three Chinese provinces and found that in symptomatic patients, risk of severe infection was six to eightfold higher in the presence of decreased sleep status and reduced sleep hours in the week prior to the diagnosis. In one study among 572 patients hospitalized for COVID-19 [46], the prevalence of insomnia was 11%; notably, these authors also found that the prevalence of OSA in this group was 19.8% and that of restless legs syndrome (RLS, recently renamed Willis-Ekbom disease) or periodic limb movements of sleep was 3.9%. Akıncı and Melek Başar [47] found that among 189 patients hospitalized for COVID-19 who later required mental health and clinical interventions, the duration of hospitalization and the depression rate were higher in the group exhibiting poor sleep quality. Zhang et al. [48] divided a group of Chinese patients hospitalized for COVID-19 into good and poor sleepers based on a subjective scale and found that compared to the good sleepers, the poor sleepers had lower absolute lymphocyte count and increased neutrophil-to-lymphocyte ratio; 12% of poor sleepers required ICU care while none of the good sleepers did. Poor sleepers had increased duration of hospital stay compared to good sleepers (33 days vs 25 days). Overall, thus, there is a suggestion that poor sleep is associated with greater susceptibility to COVID-19 infection and worse clinical course among hospitalized patients, however, the cause-and-effect relationship remains undefined. It is well known that the quality and quantity of sleep in hospitalized patients is often suboptimal and negatively associated with many hospital-related factors, thus, what degree of sleep dysfunction in patients hospitalized for COVID-19 is specific to the viral illness is similarly unclear [49]. Among patients hospitalized for COVID-19, some authors [50] have suggested that melatonin in doses up to 10 mg may be considered in the prevention and treatment of sleep disturbances and delirium.

5.1. Sleep dysfunction in post-acute COVID-19 syndrome ("long-haulers")

There has recently been a lot of interest in the phenomenon of Post-Acute Covid-19 Syndrome (PACS), variously called "chronic COVID", "long COVID" or "COVID-19 long haulers" [51], a loosely-defined, still evolving concept describing the clinical sequelae and other medical complications that last weeks to months after initial recovery from the index infection. It is unclear why only a subset of patients suffer from PACS; there is speculation that factors such as viral load, angiotensin converting enzyme (ACE)-2 density in tissues, vascular permeability, coagulation, and cytokine activation cascade may favor a prolonged less lethal but more incapacitating clinical picture [52], and a role for oxidative stress and mitochondrial dysfunction has also been proposed [53]. As with several other chronic conditions thought to have a post-viral etiology, such as post-influenza syndrome and chronic fatigue syndrome (myalgic encephalomyelitis), there are no clear biomarkers, standardized diagnostic criteria or well-defined clinical course. Patients suffering from the condition typically did not need critical care but on social media platforms and in interviews with journalists report a myriad of vague and non-specific "rolling waves of symptoms", including fatigue, hallucinations, "brain fog", delirium, memory loss, subjective tachycardia, numbness and tingling, and shortness of breath, often with a waxing and waning course [54,55]. A significant number of patients with PACS complain of persistent dyspnea, which has been shown to be associated with greater restriction on spirometry, lower diffusion capacity for carbon monoxide (DL_{CO}), reduced functional capacity, and increased exertional oxygen desaturations [56].

Although sleep complaints in COVID long-haulers are frequent, detailed data in this regard are currently lacking. In one large study conducted in a hospital in Wuhan, China [57], 1733 patients discharged after hospitalization for COVID-19 were followed up (median follow-up time after symptom onset was 186 days). Fatigue or muscle weakness (seen in 63%) and sleep difficulties (seen in 26%) were the most common symptoms, with anxiety or depression reported among 23% of patients; of 94 patients with blood antibodies tested at follow-up, the seropositivity (96.2% vs 58.5%) and median titers (19·0 vs 10·0) of the neutralizing antibodies were significantly lower compared with at the acute phase. The optimal treatment strategy in these patients, including for sleep complaints, remains to be elucidated.

6. COVID-19 related circadian rhythm abnormalities

(See also Chapter on "Circadian Disturbance, Sleep Quality and the COVID-19 Pandemic" by Salehinijad in this volume).

With its resulting lockdowns, alterations in employment situations and trend towards working from home (WFH), the COVID-19 pandemic has provided researchers with a unique opportunity to study evolutions in circadian rhythms when less encumbered by traditional environmental and societal constraints [58,59]. In many circumstances, WFH (or in those less fortunate, loss of employment), as well as online rather than in-person classes, allow individuals to eliminate their commute to their school or workplace and therefore wake up later, in some cases significantly so. Many individuals are able to maintain a self-selected sleep-wake cycle during lockdown conditions. Recently, a large study conducted among 3787 healthy volunteers during lockdown [60] showed that the most significant changes occurred during the first ten days, when the differences between weekday and weekend sleep-wake cycles ("social jetlag") disappeared and there was a tendency towards eveningness and daytime napping; those who exhibited desynchronized alternating sleep rhythms tended to be male participants over the age of 50 years. In another study among university students during a lockdown period [61], sleep duration increased on both weekdays and weekends by 25–30 min (greater on weekdays), bedtimes became more regular and were delayed by approximately 50 min during weekdays and approximately 25 min on weekends (decreased social jetlag) and the percentage of participants that reported 7 h or more sleep per night increased from 84% to 92% for weekdays. This trend towards delayed bedtimes, reduced social jetlag and greater time in bed during lockdown periods has been confirmed by other investigators as well [62,63] and in one study among adolescents, also translated into better subjective sleep quality and less daytime sleepiness [64], although other investigators found sleep quality reduced in older adults, suggesting a possible effect of age [65]. The perception of poorer sleep quality despite later bedtimes and wake-up times and longer hours in bed appears to be related to a higher symptomatic level of depression, anxiety and stress [24]. Overall, these findings seem to suggest a massive sleep deficit under pre-pandemic social time pressure and indicate potential avenues to explore better sleep health once the COVID-19 pandemic has passed.

6.1. COVID-19 related sleep dysfunction in shift workers

Previously published data suggest that shift work is associated with greater risks of cancer, metabolic syndrome, obesity and diabetes [66], many of which are also associated with higher risk of COVID-19 infection. Several mechanisms have been proposed, including sleep deprivation, diminished immunological responses due to disruption of circadian rhythms and inhibition of melatonin secretion, which may hamper DNA repair and upregulation of *Bmal1*, which in turn inhibits certain viruses like herpes simplex and influenza [67]. Therefore, there is concern as to whether shift workers are more vulnerable to contracting COVID-19. Unfortunately, there is little data in this regard, although some early work does suggest that night shifts are associated with increased risk for COVID-19 infection [68].

Box 3 summarizes factors predisposing to sleep dysfunction in specific populations vulnerable to COVID-19.

Box 3
Factors Predisposing to COVID-19 related Sleep Dysfunction in Specific Populations.

- General population during the pandemic (predisposing factors: female gender, poor sleep hygiene and dysfunctional beliefs about sleep, pre-existing mood disorders, lower socioeconomic status, urban living, poor coping mechanisms and social support, exposure to COVID-19 related news).
- Individuals in special situations.
  - Lockdown Mode/self-isolation, and
  - Quarantine/forced isolation (predisposing factors: female gender, increased age, reduced income, elderly dependents, alcohol use, pre-existing mood disorders, potentially weight gain and increased electronic media use).
  - Shift workers.
- Patients hospitalized with COVID-19 (with or without ICU admissions).
  - Acute stage (predisposing factors: duration of hospitalization, pre-existing mood disorders, lower absolute lymphocyte count and increased neutrophil-to-lymphocyte ratio).
  - Long-term course after discharge ("long-haulers") (predisposing factors: all speculative, viral load, cytokine activation, tissue angiotensin converting enzyme (ACE)-2 density, mitochondrial dysfunction and oxidative stress have all been proposed).
- Health Care Workers (HCWs) (physicians, nurses, technologists, etc.) (predisposing factors: female gender, nursing occupation, high-risk environment, inadequate hand hygiene and personal protective equipment use, close contact with patients, long shifts with reduced break time, unprotected exposure).
  - Frontline HCWs (directly involved in the care of COVID-19 patients).
  - Non-frontline HCWs (not directly involved in the care of COVID-19 patients).

7. RLS and COVID-19

While RLS has been described in hospitalized COVID-19 patients [46], it is based on a retrospective review of electronic medical records and diagnostic codes, with no clear indication as to whether the patients fulfilled all the essential diagnostic criteria for RLS, or if RLS had been present before contracting the virus. There has been no reliable prospective study exploring the relationship between RLS and COVID-19. A recent case report [69] described transient apparent new-onset RLS (fulfilling all clinical criteria for the disease) in a 49-year-old female HCW with confirmed COVID-19 and several medical co-morbidities (hypertension, diabetes mellitus and ischemic heart disease); all RLS symptoms and sleep dysfunction resolved when she was discharged after a five-day admission. However, even in this report there is considerable uncertainty regarding a relationship between contracting the SARS-CoV-2 virus and RLS.

Despite the lack of strong evidence of a cause-and-effect relationship, there are a large number of pandemic-related factors such as anxiety, stress and depression, as well as medications taken to treat these conditions, that could theoretically worsen symptoms in patients with RLS or trigger them de novo in susceptible individuals, causing sleep initiation and maintenance insomnia [70]. Furthermore, RLS is a disease of quiescence relieved by distraction, and the immobility imposed by self-isolation and quarantine, as well as lack of social interaction, would be expected to worsen RLS symptoms. As such, during the COVID-19 pandemic, patients with RLS would be recommended to avoid immobility as much as possible, participate in light to moderate exercise and practice good sleep hygiene measures, including maintaining a regular sleep-wake cycle to minimize exacerbation of symptoms.

8. COVID-19 and obstructive sleep apnea

8.1. Proposed common mechanisms

OSA is a condition characterized by recurrent mechanical narrowing and collapse of the upper airway in sleep [71] resulting in intermittent arterial oxygen desaturations and hypoxemia, arousals from sleep and sympathetic hyperactivity. Untreated or sub-optimally treated OSA is associated with increased prevalence of serious medical conditions which are also associated with poor outcomes in patients with COVID-19 infections, such as hypertension, hyperlipidemia, diabetes mellitus, as well as cardiac arrhythmias [72], all of which increase morbidity and mortality and elevate the risk of cardiovascular events such as myocardial infarction and cerebrovascular accidents [73]. As with COVID-19 infections [74], obesity is a risk factor for OSA [75], and co-existent pulmonary pathology such as chronic obstructive pulmonary disease (COPD) and bronchial asthma may worsen clinical outcomes in both COVID-19 pneumonia [76] and OSA [77]. Advancing age and male gender are associated with greater severity of both OSA and COVID-19 infections [78].

Several common mechanisms have been proposed in the pathogenesis of both OSA and COVID-19 infections, including massive mobilization of pro-inflammatory monocytes and neutrophils due to elevated interleukin, tumor necrosis factor and cytokine levels [79]. Sleep deprivation is thought to be a causative factor for this phenomenon in OSA (and possibly in COVID-19 infection as well) [80]. Additionally, intermittent hypoxia and sleep fragmentation, as seen in patients with OSA, are associated with a less robust response to a septic and viral inflammatory challenge in animal models [81]. This pro-inflammatory environment may lead to severe pulmonary infiltration and acute respiratory distress, with increased risk of significant morbidity and possibly death in patients with COVID-19 infections. Another proposed area of interplay is dysregulation of the renin–angiotensin–aldosterone axis due to the hypoxemia associated with OSA leading to upregulation of ACE-2 receptors independent of hypertension, which facilitates SARS-CoV-2 virus entry into cells [82,83].

8.2. Association between COVID-19 and OSA

These shared risk factors and proposed common underlying mechanisms raise the question as to whether patients with OSA may be more susceptible to and likely to suffer more severe outcomes from COVID-19 infections. There have been several recently published studies evaluating patients diagnosed with COVID-19 that have explored this relationship. The presence of OSA in patients hospitalized with COVID-19 has been estimated in various studies to be between 8 and 21% [46,84–87]. There have been contradictory findings with regard to whether the presence of OSA increases the likelihood of contracting COVID-19, but most published data suggest that OSA is a risk factor for hospitalization, ICU admission, mechanical ventilation and death in patients infected with COVID-19. Some authors have reported that patients with severe OSA had a greater than double risk of contracting COVID-19 compared to those with mild disease [87]. While Maas et al. found that patients with OSA experienced an approximately eight-fold greater risk for COVID-19 [84], a contemporaneous study conducted among 445 Finnish patients [85] showed that OSA was not a risk factor for contracting COVID-19. However, these authors found that OSA presented an almost three-fold increased risk for hospitalization among patients with COVID-19, controlling for age, sex, body mass index (BMI) and co-morbidities (hypertension, diabetes mellitus, asthma, COPD and congestive heart failure). Another large US healthcare system-based study of 4668 patients with positive reverse transcriptase RNA polymerase chain reaction (RT-PCR) diagnostic results revealed that the 443 participants (9.5%) with previously diagnosed OSA had an increased all-cause mortality rate compared with controls, with a significant association between OSA and death related to COVID-19 (that attenuated somewhat after adjusting for BMI), as well as for hospitalization, ICU admission and mechanical ventilation [88]. Along the same lines, a multicenter observational French study suggested that hospitalized diabetic patients with COVID-19 and previously diagnosed and treated OSA had a nearly three-fold higher risk of death [89], and a Turkish study found that patients hospitalized with COVID-19 who were determined to be at moderate risk for OSA based on Berlin questionnaire scores had poorer clinical outcomes than those at low risk [90]. Najafi et al. [87] reported that the risk of developing COVID-19 was more than double in those patients whose OSA was untreated compared to those accepting definitive treatment (with lower sleep time and sleep efficiency also conferring increased risk). For the most part, however, very few studies have investigated the impact of the level of previous adherence to continuous positive airway pressure (CPAP), if any, and therefore this remains an area that needs to be studied in more detail.

8.3. Impact of COVID-19 on CPAP adherence

Given the pervasive and all-encompassing impact of COVID-19 on health and hygiene practices globally, there has also been great interest in the evolution of adherence patterns to CPAP treatment during the pandemic. A recent small study conducted among patients of a New York City sleep practice [91] showed that a majority of patients (88%) continued to use CPAP during the early stages of the pandemic, when they were located in the epicenter, and among the 38% who expressed concern that their underlying OSA would make them susceptible to COVID-19, several expressed the sentiment that use of CPAP more often and for longer periods of time would be of clinical benefit, despite absence of clear data in this regard. With regard to adherence to CPAP use, it could be expected that factors such as government-mandated lockdown, social distancing, feelings of isolation, worsening sleep patterns and reduced access to physicians and sleep medicine clinics would have deleterious effects. Indeed, there have been case reports showing reduced CPAP adherence during the pandemic, even among those patients who have not been exposed to COVID-19 [92]. However, this does not appear to be a universal trend, as one large prospective cohort of patients with OSA showed a significant increase in adherence to CPAP during a lockdown period [93]. Batool-Anwar et al. [94] found that compared to the 12 months prior, CPAP adherence in a group of US patients with OSA in the month following the announcement of the national shutdown did not change, nor did self-reported sleep duration, whereas insomnia was reported to have increased (though only among women). Thus, there appear to be multiple factors in play and further studies to identify those subsections of patients with OSA who are likely to exhibit worsening CPAP adherence in the context of COVID-19 are needed to allow for early intervention and appropriate corrective measures.

One area of concern for patients, caregivers and practitioners is the theoretical risk of spreading the virus to family members in the household due to the high-risk aerosol generating nature of CPAP devices. Some authors have gone so far as to advocate cessation of CPAP use and other forms of non-invasive ventilation except where necessary for life support purposes [95]. However, given the lack of data to support this concern and the significant impact on quality of life as well as the increased morbidity and mortality from untreated OSA, especially in the context of an ongoing pandemic, and the unpredictability of the time course of the current COVID-19 pandemic, other groups have argued against this [96] and most international medical societies recommend continuing use of CPAP in patients with OSA, albeit with measures taken to avoid potential spread of the virus such as sleeping in a separate room and diligent cleaning and disinfecting of equipment.

9. The impact of COVID-19 on the practice of sleep medicine

9.1. Role of telemedicine

During the pandemic, as in many other fields of medicine, physician visits, both for new and established patients in a sleep medicine practice, have often been conducted via telemedicine [97,98]. The American Academy of Sleep Medicine (AASM) has issued an updated position paper [99] on the use of telemedicine for assessment of patients with sleep disorders (particularly during the pandemic), suggesting that telemedicine visits may be performed in lieu of live in-person office visits if they mirror live visits in quality and process and comply with all licensing, state, federal and HIPAA regulations for both originating and distant sites, even when both sites are located outside of the traditional office. The AASM position paper also recommends special consideration for both the physical and psychological safety of the patient at the time of the telemedicine visit. Patient satisfaction, acceptability and CPAP adherence rates in of sleep telemedicine clinics have been favorable [100,101]. Recent data suggests that autoCPAP pressures may need to be adjusted higher in patients who have had COVID-19 [102], possibly due to upper airway inflammation and edema in symptomatic patients leading to further narrowing and also as a result of weight gain as a result of decreased mobility during quarantine periods. Therefore, adequate time to review compliance downloads and discuss patients' response to treatment during telemedicine visits, similar to the practice during in-person visits, is imperative. This often requires access during the telemedicine visit to patient compliance data through online wireless portals.

9.2. COVID-19 and sleep testing

Furthermore, the highly contagious nature of COVID-19 and the unique environment of the sleep laboratory have necessitated specific precautionary measures to control the spread of the virus. In-laboratory sleep studies, including polysomnography (PSG) and CPAP titration studies require intimate physical contact between the technologist and the patient, and social distancing measures are impossible to follow in this setting. Additionally, during CPAP titration studies, there is the potential for aerosolization of the virus. These factors have led to unforeseen challenges and complications and have impacted the practice of sleep medicine and the diagnosis of sleep disorders in significant ways [103]. In the wake of the pandemic and with the announcement of shutdowns and suspension of elective medical procedures, many sleep laboratories remained closed for several months. During this time, access to sleep testing was severely limited [98,103].

The trend toward home ambulatory sleep testing (HSAT), also known as out-of-center sleep testing (OCST), which had initially arisen out of insurance-mandated guidelines, has accelerated during the pandemic, as most patients have been reluctant to enter the sleep laboratory. However, the issue of proper disinfection of HSAT equipment to prevent cross-contamination is also a matter of concern. Manufacturers of HSAT equipment recommend quaternary alcohol-based cleaning following Centers for Disease Control and Prevention (CDC) guidance, which is not specific to HSAT equipment. No specific changes in the disinfection process for HSAT devices has been recommended by manufacturers [104]. The AASM recommends waiting 72 h between the reuse of HSAT devices based on data for SARS-CoV-2 surface stability on plastic surfaces [105]. Disposable peripheral arterial tonometry (PAT) based HSAT devices are also being increasingly used, which are shipped directly to the patient's home and results uploaded to cloud networks and made immediately available for physician review, thereby eliminating the need for the patient to travel and risk exposure.

Similarly, the prescription of auto-CPAP devices in lieu of in-laboratory titration studies would avoid unnecessary patient and technologist exposure, although may not be feasible in patients who require bilevel PAP, specialized devices such as assisted servo ventilation (ASV) or volume-assured pressure support (VAPS), or those in whom the need for supplemental oxygen is anticipated, such as patients with concomitant pulmonary, cardiac or neuromuscular pathology. Other sleep study testing that requires a full array of electroencephalogram (EEG) electrodes and extensive technologist oversight, such as maintenance of wakefulness (MWT) and multiple sleep latency testing (MSLT), also cannot be performed in the ambulatory setting. In those cases where in-laboratory testing is considered necessary, strict protocols to prevent the spread of COVID-19 are recommended. These include screening for symptoms and travel history while making appointments, regular temperature measurements on arrival, SARS-CoV-2 PCR testing of all patients and staff, fewer patients studied each night to limit the number of personnel, use of full PPE by technologists, utilization of non-vented masks (lacking exhalation ports), proper disposal, sanitation and cleaning of equipment and negative pressure rooms where feasible [106]. Additionally high-efficiency particulate (HEPA) filters, used in the prevention of spread of other aerosolized contaminants, have been discussed as an adjunctive means for decontamination of SARS-CoV-2 aerosols in health care settings including sleep laboratories [107], although direct studies for SARS-CoV-2 have not been performed and no guidelines in this regard have yet been issued by the CDC.

Box 4 lists methods to assess sleep dysfunction related to the pandemic.

10. Conclusions and summary

- The ongoing COVID-19 pandemic has had a profound impact on sleep quality and the practice of sleep medicine.
- Insomnia, sleep fragmentation, nightmares, anxiety and depression have become more common among the general population in the context of COVID-19 (“coronasomnia/COVID-somia”). Female gender, pre-existing psychiatric conditions, urban living, exposure to COVID-19 related news and lack of

Box 4
Methods to Assess Sleep Dysfunction During COVID-19 Pandemic.

- Scales, questionnaires and Internet surveys for subjective symptom evaluation.
- Actigraphy for assessment of sleep/wake rhythms.
- For patients with suspected obstructive sleep apnea (OSA): polysomnography (PSG) or Home Sleep Apnea Testing (HSAT) with special precautionary measures during testing (see text).
- For patients with established OSA: remote adherence data analysis to determine adequacy of treatment of positive airway pressure (PAP) therapy in obstructive sleep apnea.

social support are the main drivers. The appropriate management strategy remains unclear.
- Sleep dysfunction is more common among HCWs than the general community and is related to factors such as number and duration of shifts, volume of patient exposure, access to PPE and adequate hand hygiene.
- Lockdown has resulted in certain notable trends in sleep-wake cycles (decreased social jetlag, later bedtimes, increased time in bed, emergence of napping).
- The presence of OSA worsens clinical course and outcomes for patients hospitalized with COVID-19.
- During the pandemic, sleep laboratories have shifted to practice models minimizing physical contact with patients, including telemedicine visits, HSAT and prescription of auto-CPAP devices.

Conflict of interest

None declared.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2021.07.021.

References

[1] Borges do Nascimento IJ, Cacic N, Abdulazeem HM, et al. Novel coronavirus infection (COVID-19) in humans: a scoping review and meta-analysis. J Clin Med 2020;9(4):941.
[2] Jahrami H, BaHammam AS, Bragazzi NL, et al. Sleep problems during the COVID-19 pandemic by population: a systematic review and meta-analysis. J Clin Sleep Med 2021;17(2):299–313.
[3] Gupta R, Pandi-Perumal SR. COVID-somnia: how the pandemic affects sleep/wake regulation and how to deal with it? Sleep Vigil 2020:1–3. https://doi.org/10.1007/s41782-020-00118-0 [published online ahead of print, 2020 Dec 3].
[4] Xiong J, Lipsitz O, Nasri F, et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. J Affect Disord 2020;277:55–64.
[5] Oh CM, Kim HY, Na HK, et al. The effect of anxiety and depression on sleep quality of individuals with high risk for insomnia: a population-based study. Front Neurol 2019;10:849.
[6] Cutler AJ. The role of insomnia in depression and anxiety: its impact on functioning, treatment, and outcomes. J Clin Psychiatr 2016;77(8):e1010.
[7] Lakhan R, Agrawal A, Sharma M. Prevalence of depression, anxiety, and stress during COVID-19 pandemic. J Neurosci Rural Pract 2020;11(4):519–25.
[8] Wu T, Jia X, Shi H, et al. Prevalence of mental health problems during the COVID-19 pandemic: a systematic review and meta-analysis. J Affect Disord 2021;281:91–8.
[9] Lin LY, Wang J, Ou-Yang XY, et al. The immediate impact of the 2019 novel coronavirus (COVID-19) outbreak on subjective sleep status. Sleep Med 2021;77:348–54.
[10] Zhou SJ, Wang LL, Yang R, et al. Sleep problems among Chinese adolescents and young adults during the coronavirus-2019 pandemic. Sleep Med 2020;74:39–47.
[11] Li Y, Qin Q, Sun Q, et al. Insomnia and psychological reactions during the COVID-19 outbreak in China. J Clin Sleep Med 2020;16(8):1417–8.
[12] Bacaro V, Chiabudini M, Buonanno C, et al. Insomnia in the Italian population during covid-19 outbreak: a snapshot on one major risk factor for depression and anxiety. Front Psychiatr 2020;11:579107.
[13] Kokou-Kpolou CK, Megalakaki O, Laimou D, et al. Insomnia during COVID-19 pandemic and lockdown: prevalence, severity, and associated risk factors in French population. Psychiatr Res 2020;290:113128.
[14] Robillard R, Dion K, Pennestri M-H, et al. Profiles of sleep changes during the COVID-19 pandemic: demographic, behavioural and psychological factors. J Sleep Res 2021;30:e13231.
[15] Voitsidis P, Gliatas I, Bairachtari V, et al. Insomnia during the COVID-19 pandemic in a Greek population. Psychiatr Res 2020;289:113076.
[16] Musse FCC, Castro LS, Sousa KMM, et al. Mental violence: the COVID-19 nightmare. Front Psychiatr 2020;11:579289.
[17] Jackson CL, Johnson DA. Sleep disparities in the era of the COVID-19 pandemic highlight the urgent need to address social determinants of health like the virus of racism. J Clin Sleep Med 2020;16(8):1401–2.
[18] Nayak A, Islam SJ, Mehta A, et al. Impact of social vulnerability on COVID-19 incidence and outcomes in the United States. medRxiv 2020;2020. https://doi.org/10.1101/2020.04.10.20060962. 04.10.20060962. Published 2020 Apr 14.
[19] Egede LE, Walker RJ. Structural racism, social risk factors, and covid-19 - a dangerous convergence for black Americans. N Engl J Med 2020;383(12):e77.
[20] Dal Santo F, González-Blanco L, Rodríguez-Revuelta J, et al. Early impact of the COVID-19 outbreak on sleep in a large Spanish sample. Behav Sleep Med 2021:1–16.
[21] Trakada A, Nikolaidis PT, Andrade MDS, et al. Sleep during "lockdown" in the COVID-19 pandemic. Int J Environ Res Publ Health 2020;17(23):9094.
[22] Marelli S, Castelnuovo A, Somma A, et al. Impact of COVID-19 lockdown on sleep quality in university students and administration staff. J Neurol 2021;268:8–15.
[23] Kocevska D, Blanken TF, Van Someren EJW, et al. Sleep quality during the COVID-19 pandemic: not one size fits all. Sleep Med 2020;76:86–8.
[24] Cellini N, Canale N, Mioni G, et al. Changes in sleep pattern, sense of time and digital media use during COVID-19 lockdown in Italy. J Sleep Res 2020;29(4):e13074.
[25] Bhat S, Pinto-Zipp G, Upadhyay H, et al. "To sleep, perchance to tweet": in-bed electronic social media use and its associations with insomnia, daytime sleepiness, mood, and sleep duration in adults. Sleep Health 2018;4(2):166–73.
[26] Khan MA, Moverley Smith JE. "Covibesity," a new pandemic. Obes Med 2020;19:100282.
[27] de Luis Román DA, Izaola O, Primo Martín D, et al. Effect of lockdown for COVID-19 on self-reported body weight gain in a sample of obese patients. Nutr Hosp 2020;37(6):1232–7.
[28] Edinger JD, Wohlgemuth WK, Radtke RA, et al. Cognitive behavioral therapy for treatment of chronic primary insomnia: a randomized controlled trial. J Am Med Assoc 2001;285(14):1856–64.
[29] Rismanbaf A. Insomnia drug therapy in COVID-19 patients; a letter to editor. Caspian J Intern Med 2020;11(Suppl 1):583–4.
[30] Aydin Sayilan A, Kulakaç N, Uzun S. Burnout levels and sleep quality of COVID-19 heroes. Psychiatr Care 2020 Nov 4. https://doi.org/10.1111/ppc.12678 [Epub ahead of print].
[31] Shaukat N, Ali DM, Razzak J. Physical and mental health impacts of COVID-19 on healthcare workers: a scoping review. Int J Emerg Med 2020;13(1):40.
[32] Pappa S, Ntella V, Giannakas T, et al. Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: a systematic review and meta-analysis. Brain Behav Immun 2020;88:901–7.
[33] Cénat JM, Blais-Rochette C, Kokou-Kpolou CK, et al. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: a systematic review and meta-analysis. Psychiatr Res 2021;295:113599. https://doi.org/10.1016/j.psychres.2020.113599.
[34] Şahin MK, Aker S, Şahin G, et al. Prevalence of depression, anxiety, distress and insomnia and related factors in healthcare workers during COVID-19 pandemic in Turkey. J Community Health 2020;45(6):1168–77.
[35] Sagherian K, Steege LM, Cobb SJ, et al. Insomnia, fatigue and psychosocial well-being during COVID-19 pandemic: a cross-sectional survey of hospital nursing staff in the United States [published online ahead of print, 2020 Nov 20]. J Clin Nurs 2020. https://doi.org/10.1111/jocn.15566.
[36] Dosil Santamaría M, Ozamiz-Etxebarria N, Redondo Rodríguez I, et al. Psychological impact of COVID-19 on a sample of Spanish health professionals. Rev Psiquiatía Salud Ment 2020;S1888–9891(20):30060–4.
[37] Zhan Y, Liu Y, Liu H, et al. Factors associated with insomnia among Chinese front-line nurses fighting against COVID-19 in Wuhan: a cross-sectional survey. J Nurs Manag 2020;28(7):1525–35.
[38] Barua L, Zaman MS, Omi FR, et al. Psychological burden of the COVID-19 pandemic and its associated factors among frontline doctors of Bangladesh: a cross-sectional study. F1000Res 2020;9:1304.
[39] Lin YQ, Lin ZX, Wu YX, et al. Reduced sleep duration and sleep efficiency were independently associated with frequent nightmares in Chinese front-line medical workers during the coronavirus disease 2019 outbreak. Front Neurosci 2021;14:631025.
[40] Qi J, Xu J, Li BZ, et al. The evaluation of sleep disturbances for Chinese frontline medical workers under the outbreak of COVID-19. Sleep Med 2020;72:1–4.
[41] Wang W, Song W, Xia Z, et al. Sleep disturbance and psychological profiles of medical staff and non-medical staff during the early outbreak of COVID-19 in hubei province, China. Front Psychiatr 2020;11:733.
[42] Cai Q, Feng H, Huang J, et al. The mental health of frontline and non-frontline medical workers during the coronavirus disease 2019 (COVID-19) outbreak in China: a case-control study. J Affect Disord 2020;275:210–5.
[43] Jahrami H, BaHammam AS, AlGahtani H, et al. The examination of sleep quality for frontline healthcare workers during the outbreak of COVID-19 [published online ahead of print, 2020 Jun 26]. Sleep Breath 2020:1–9. https://doi.org/10.1007/s11325-020-02135-9.
[44] Cai Z, Cui Q, Liu Z, et al. Nurses endured high risks of psychological problems under the epidemic of COVID-19 in a longitudinal study in Wuhan China. J Psychiatr Res 2020;131:132–7.
[45] Huang B, Niu Y, Zhao W, et al. Reduced sleep in the week prior to diagnosis of COVID-19 is associated with the severity of COVID-19. Nat Sci Sleep 2020;12:999–1007. https://doi.org/10.2147/NSS.S263488. Published 2020 Nov 12.
[46] Goldstein CA, Rizvydeen M, Conroy DA, et al. The prevalence and impact of pre-existing sleep disorder diagnoses and objective sleep parameters in patients hospitalized for COVID-19. J Clin Sleep Med 2021 Feb 9. https://doi.org/10.5664/jcsm.9132 [Online ahead of print].

[47] Akıncı T, Melek Başar H. Relationship between sleep quality and the psychological status of patients hospitalised with COVID-19 [published online ahead of print, 2021 Jan 28]. Sleep Med 2021;80:167–70.
[48] Zhang J, Xu D, Xie B, et al. Poor-sleep is associated with slow recovery from lymphopenia and an increased need for ICU care in hospitalized patients with COVID-19: a retrospective cohort study. Brain Behav Immun 2020;88:50–8.
[49] Wesselius HM, van den Ende ES, Alsma J, et al. Nanayakkara PWB; "onderzoeks consortium acute geneeskunde" acute medicine research consortium. Quality and quantity of sleep and factors associated with sleep disturbance in hospitalized patients. JAMA Intern Med 2018 Sep 1;178(9):1201–8.
[50] Zambrelli E, Canevini M, Gambini O, et al. Delirium and sleep disturbances in COVID-19: a possible role for melatonin in hospitalized patients? Sleep Med 2020;70:111.
[51] Baig AM. Chronic COVID syndrome: need for an appropriate medical terminology for long-COVID and COVID long-haulers. J Med Virol 2021;93(5):2555–6.
[52] Baig AM. Deleterious outcomes in long-hauler COVID-19: the effects of SARS-CoV-2 on the CNS in chronic COVID syndrome. ACS Chem Neurosci 2020;11(24):4017–20.
[53] Wood E, Hall KH, Tate W. Role of mitochondria, oxidative stress and the response to antioxidants in myalgic encephalomyelitis/chronic fatigue syndrome: a possible approach to SARS-CoV-2 'long-haulers'? [published online ahead of print, 2020 Nov 21]. Chronic Dis Transl Med 2020. https://doi.org/10.1016/j.cdtm.2020.11.002. 10.1016/j.cdtm.2020.11.002.
[54] Honigsbaum M, Krishnan L. Taking pandemic sequelae seriously: from the Russian influenza to COVID-19 long-haulers. Lancet 2020;396(10260):1389–91.
[55] Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in adults at 6 Months after COVID-19 infection. JAMA Netw Open 2021;4(2):e210830.
[56] Cortés-Telles A, López-Romero S, Figueroa-Hurtado E, et al. Pulmonary function and functional capacity in COVID-19 survivors with persistent dyspnoea. Respir Physiol Neurobiol 2021:103644.
[57] Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021;397(10270):220–32.
[58] Bryson WJ. Circadian rhythm sleep-wake disorders and the COVID-19 pandemic. J Clin Sleep Med 2020;16(8):1423.
[59] Morin CM, Carrier J, Bastien C, et al. Sleep and circadian rhythm in response to the COVID-19 pandemic. Can J Public Health 2020;111(5):654–7.
[60] Roitblat Y, Burger J, Vaiman M, et al. Owls and larks do not exist: COVID-19 quarantine sleep habits. Sleep Med 2021;77:177–83.
[61] Wright Jr KP, Linton SK, Withrow D, et al. Sleep in university students prior to and during COVID-19 Stay-at-Home orders. Curr Biol 2020;30(14):R797–8.
[62] Leone MJ, Sigman M, Golombek DA. Effects of lockdown on human sleep and chronotype during the COVID-19 pandemic. Curr Biol 2020;30(16):R930–1.
[63] Korman M, Tkachev V, Reis C, et al. COVID-19-mandated social restrictions unveil the impact of social time pressure on sleep and body clock. Sci Rep 2020;10(1):22225.
[64] Gruber R, Saha S, Somerville G, et al. The impact of COVID-19 related school shutdown on sleep in adolescents: a natural experiment. Sleep Med 2020;76:33–5.
[65] Blume C, Schmidt MH, Cajochen C. Effects of the COVID-19 lockdown on human sleep and rest-activity rhythms. Curr Biol 2020;30(14):R795–7.
[66] Kecklund G, Axelsson J. Health consequences of shift work and insufficient sleep. BMJ 2016;355:i5210.
[67] Galano A, Tan DX, Reiter RJ. Melatonin: a versatile protector against oxidative DNA damage. Molecules 2018;23(3):530.
[68] Rizza S, Coppeta L, Grelli S, et al. High body mass index and night shift work are associated with COVID-19 in health care workers. J Endocrinol Invest 2020:1–5.
[69] Tony AA, Tony EA, Ali SB, et al. COVID-19-associated sleep disorders: a case report. Neurobiol Sleep Circadian Rhythms 2020;9:100057.
[70] Franco B, Morais MA, Holanda ASS, et al. Impact of Covid-19 on the restless legs syndrome. Sleep Sci 2020;13(3):186–90.
[71] Korson R, Guilleminault C. Obstructive sleep apnea syndrome. In: Chokroverty S, editor. Sleep disorders medicine: basic science, technical considerations and clinical aspects. 4th ed. New York: Springer; 2017.
[72] Bonsignore MR, Baiamonte P, Mazzuca E, et al. Obstructive sleep apnea and comorbidities: a dangerous liaison. Multidiscip Respir Med 2019;14:8.
[73] Kohli P, Balachandra JS, Malhotra A. Obstructive sleep apnea and the risk for cardiovascular disease. Curr Atherosclerosis Rep 2011;13(2):138–46.
[74] Popkin BM, Du S, Green WD, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. Obes Rev 2020;21:e13128. https://doi.org/10.1111/obr.13128.
[75] Schwartz AR, Patil SP, Laffan AM, et al. Obesity and obstructive sleep apnea: pathogenic mechanisms and therapeutic approaches. Proc Am Thorac Soc 2008;5(2):185–92.
[76] Hansen ESH, Moeller AL, Backer V, et al. Severe outcomes of COVID-19 among patients with COPD and asthma. ERJ Open Res 2021;7:594–2020. https://doi.org/10.1183/23120541.00594-2020.
[77] Owens RL, Malhotra A. Sleep-disordered breathing and COPD: the overlap syndrome. Respir Care 2010;55(10):1333–46.
[78] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020 Feb 15;395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-5. Epub 2020 Jan 24. Erratum in: Lancet. 2020 Jan 30.
[79] McSharry D, Malhotra A. Potential influences of obstructive sleep apnea and obesity on COVID-19 severity. J Clin Sleep Med 2020;16(9):1645.
[80] Salles C, Barbosa HM. COVID-19 and obstructive sleep apnea. J Clin Sleep Med 2020;16(9):1647.
[81] Davis CJ, Dunbrasky D, Oonk M, et al. The neuron-specific interleukin-1 receptor accessory protein is required for homeostatic sleep and sleep responses to influenza viral challenge in mice. Brain Behav Immun 2015;47:35–43.
[82] Ekiz T, Köseoğlu HI, Pazarl AC. Obstructive sleep apnea, renin-angiotensin system, and COVID-19: possible interactions. J Clin Sleep Med 2020;16(8):1403–4.
[83] Barceló A, Elorza MA, Barbé F, et al. Angiotensin converting enzyme in patients with sleep apnoea syndrome: plasma activity and gene polymorphisms. Eur Respir J 2001;17(4):728–32.
[84] Maas MB, Kim M, Malkani RG, et al. Obstructive sleep apnea and risk of COVID-19 infection, hospitalization and respiratory failure [published online ahead of print, 2020 sep 29]. Sleep Breath 2020:1–3. https://doi.org/10.1007/s11325-020-02203-0.
[85] Strausz S, Kiiskinen T, Broberg M, et al. Sleep apnoea is a risk factor for severe COVID-19. BMJ Open Respir Res 2021;8:e000845. https://doi.org/10.1136/bmjresp-2020-000845.
[86] Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region - case series. N Engl J Med 2020;382:2012–22.
[87] Najafi A, Sadeghniiat-Haghighi K, Akbarpour S, et al. The effect of apnea management on novel coronavirus infection: a study on patients with obstructive sleep apnea. Sleep Health 2021;7(1):14–8.
[88] Cade BE, Dashti HS, Hassan SM, et al. Sleep apnea and COVID-19 mortality and hospitalization. Am J Respir Crit Care Med 2020;202(10):1462–4.
[89] Cariou B, Hadjadj S, Wargny M, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. Diabetologia 2020;63(8):1500–15.
[90] Karataş F, Uzel FI, Tabak L, et al. Effect of high-risk obstructive sleep apnea on clinical outcomes in adults with coronavirus disease 2019: a multicenter, prospective, observational cohort study. Ann Am Thorac Soc 2021 Feb 17. https://doi.org/10.1513/AnnalsATS.202011-1409OC [Epub ahead of print].
[91] Thorpy M, Figuera-Losada M, Ahmed I, et al. Management of sleep apnea in New York City during the COVID-19 pandemic. Sleep Med 2020;74:86–90.
[92] Naime S, Weiss M, Nino G. Effects of COVID-19 pandemic on adherence to obstructive sleep apnea therapy: a case report. Clin Case Rep 2020;9(1):12–4. https://doi.org/10.1002/ccr3.3363 [Epub ahead of print].
[93] Attias D, Pepin JL, Pathak A. Impact of COVID-19 lockdown on adherence to continuous positive airway pressure by obstructive sleep apnoea patients. Eur Respir J 2020;56(1):2001607.
[94] Batool-Anwar S, Omobomi OS, Quan SF. Impact of the novel coronavirus disease on treatment adherence and sleep duration in patients with obstructive sleep apnea treated with positive airway pressure. J Clin Sleep Med 2020;16(11):1917–20.
[95] Barker J, Oyefeso O, Koeckerling D, et al. COVID-19: community CPAP and NIV should be stopped unless medically necessary to support life. Thorax 2020;75(5):367.
[96] Baker JG, Sovani M. Case for continuing community NIV and CPAP during the COVID-19 epidemic. Thorax 2020;75(5):368.
[97] Voulgaris A, Ferini-Strambi L, Steiropoulos P. Sleep medicine and COVID-19. Has a new era begun? Sleep Med 2020;73:170–6.
[98] Kanchan S, Saini LK, Daga R, et al. Status of the practice of sleep medicine in India during COVID-19 pandemic. J Clin Sleep Med 2021. https://doi.org/10.5664/jcsm.9172.
[99] Shamim-Uzzaman QA, Bae CJ, Ehsan Z, et al. The use of telemedicine for the diagnosis and treatment of sleep disorders: an American Academy of Sleep Medicine update. J Clin Sleep Med 2021. https://doi.org/10.5664/jcsm.9194. Epub ahead of print.
[100] Parikh R, Touvelle MN, Wang H, et al. Sleep telemedicine: patient satisfaction and treatment adherence. Telemed J e Health 2011;17(8):609–14.
[101] Murphie P, Mills B, Little S. Telemedicine sleep clinic review - patient acceptability survey. Eur Respir J 2015;46(suppl 59):PA3377. https://doi.org/10.1183/13993003.congress-2015.PA337.
[102] Fidan V, Koyuncu H, Akin O. Alteration of Auto-CPAP requirements in obstructive sleep apnea patients with COVID-19 history. Am J Otolaryngol 2021;42(3):102919.
[103] Grote L, McNicholas WT, Hedner J. Sleep apnoea management in Europe during the COVID-19 pandemic: data from the European sleep apnoea database (ESADA). Eur Respir J 2020;55(6):2001323.
[104] Kole A. Home sleep testing in the era of COVID-19: a community perspective. J Clin Sleep Med 2020;16(9):1633.
[105] Summary of CDC recommendations relevant for sleep practices during COVID-19. 2021. Updated January 18, 2021. Accessed, https://aasm.org/covid-19-resources/covid-19-mitigation-strategies-sleep-clinics-labs/. [Accessed 21 April 2021].
[106] Johnson KG, Sullivan SS, Nti A, et al. The impact of the COVID-19 pandemic on sleep medicine practices. J Clin Sleep Med 2021;17(1):79–87.
[107] Christopherson DA, Yao WC, Lu M, et al. High-efficiency particulate air filters in the era of COVID-19: function and efficacy. Otolaryngol Head Neck Surg 2020 Dec;163(6):1153–5.