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SCIENTIFIC INVESTIGATIONS

Associations between obstructive sleep apnea and COVID-19 infection and hospitalization among US adults

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Study Objectives: Medical comorbidities increase the risk of severe COVID-19 infection. In some studies, obstructive sleep apnea (OSA) has been identified as a comorbid condition that is associated with an increased prevalence of COVID-19 infection and hospitalization, but few have investigated this association in a general population. This study aimed to answer the following research question: In a general population, is OSA associated with increased odds of COVID-19 infection and hospitalization and are these altered with COVID-19 vaccination?

Methods: This was a cross-sectional survey of a diverse sample of 15,057 US adults.

Results: COVID-19 infection and hospitalization rates in the cohort were 38.9% and 2.9%, respectively. OSA or OSA symptoms were reported in 19.4%. In logistic regression models adjusted for demographic, socioeconomic, and comorbid medical conditions, OSA was positively associated with COVID-19 infection (adjusted odds ratio: 1.58, 95% CI: 1.39–1.79) and COVID-19 hospitalization (adjusted odds ratio: 1.55, 95% CI: 1.17–2.05). In fully adjusted models, boosted vaccination status was protective against both infection and hospitalization. Boosted vaccination status attenuated the association between OSA and COVID-19 related hospitalization but not infection. Participants with untreated or symptomatic OSA were at greater risk for COVID-19 infection; those with untreated but not symptomatic OSA were more likely to be hospitalized.

Conclusions: In a general population sample, OSA is associated with a greater likelihood of having had a COVID-19 infection and a COVID-19 hospitalization with the greatest impact observed among persons experiencing OSA symptoms or who were untreated for their OSA. Boosted vaccination status attenuated the association between OSA and COVID-19-related hospitalization.

Keywords: obstructive sleep apnea, COVID-19, hospitalization, infection, epidemiology

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Medical comorbidities increase susceptibility to COVID-19 infection and hospitalization. Whether obstructive sleep apnea (OSA) is associated with increased rates of infection and hospitalization is unclear.

Study Impact: In a large general population sample, OSA was associated with a greater likelihood of COVID-19 infection and hospitalization. Those with OSA symptoms or who were untreated were at higher risk; boosted vaccination status conferred lower risk of OSA-related hospitalization.

INTRODUCTION

As of September 25, 2022, the mortality estimates from COVID-19 worldwide and in the United States were 6,536,722 and 1,056,409, respectively.[1] Early in the COVID-19 pandemic, it became apparent that individuals who were older or had common medical conditions were at greater jeopardy for COVID-19-related hospitalization and death.[2,3] For example, among approximately 10,000 COVID-19 decedents during mid-February through mid-May 2020, nearly three-quarters had one or more underlying medical conditions (76.4%) or were aged ≥65 years (74.8%).[4] While these risk factors garnered considerable attention, in many[5–19] but not all studies,[20–22] obstructive sleep apnea (OSA) was identified as a risk factor as well. The degree to which OSA represents an independent risk factor for adverse COVID-19 outcomes is uncertain; in several investigations, the impact of OSA was observed to be partially or completely explained by the presence of obesity and/or other comorbidities.[2,11,13,23,24] Nevertheless, a meta-analysis of 13 studies found that OSA was associated with an increase in mortality from COVID-19.[25] Furthermore, most studies of the association between OSA and COVID-19 were

conducted in hospitalized populations,[5,8,12,15–17,20,23] introducing the possibility of collider bias[26]; there are relatively few studies in general population cohorts.[7,14]

Vaccination confers protection, albeit incomplete, against infection, hospitalization, and death from COVID-19.[27] However, vaccine-induced and postinfection immunity declines with time,[27] and therefore vaccine "boosters" are now recommended by the US Centers for Disease Control and Prevention and other international health authorities, particularly for those who are immunocompromised.[28,29] In a recent review, vaccination against COVID-19 was noted to be effective in those with common comorbidities.[30] However, whether vaccination alters risks of COVID-19 infection or hospitalization in persons with OSA has not been determined.

This study aimed to evaluate whether persons with OSA have differential risk of COVID-19 outcomes (infection, hospitalization) and whether vaccinations attenuated such risk. To accomplish this, we used data from the first three 2022 waves of The COVID-19 Outbreak Public Evaluation Initiative (https://www.thecopeinitiative.org/), a program focused on accumulating data on public attitudes, behaviors, and beliefs related to the COVID-19 pandemic from large-scale, demographically representative samples.

METHODS

Study design and participants

From March 10, 2022, to June 2, 2022, the COVID-19 Outbreak Public Evaluation Initiative administered three successive waves of surveys focused on accumulating data on the prevalence and sequelae of COVID-19 infection. Dates of administration were Wave 1 (March 10–30, 2022), Wave 2 (April 4–May 1, 2022), and Wave 3 (May 4–June 2, 2022); each wave consisted of more than 5,000 unique participants who were recruited to approximate population estimates for age, sex, race, and ethnicity based on the 2020 US census. Surveys were conducted online by Qualtrics, LLC (Provo, Utah, and Seattle, Washington), using their network of participant pools with varying recruitment methodologies that include digital advertisements and promotions, word-of-mouth and membership referrals, social networks, television and radio advertisements, and offline mail-based approaches. Informed consent was obtained electronically. The study was approved by the Monash University Human Research Ethics Committee (Study #24036).

Survey items

Participants self-reported demographic, anthropometric, and socioeconomic information including age, race, ethnicity, sex, self-reported height and weight, education level, employment status, and household income. In addition, they reported information on several current and past medical conditions by answering the question "Have you ever been diagnosed with any of the following conditions?" In addition to OSA, opportunity was provided to endorse high blood pressure, cardiovascular disease (eg, heart attack, stroke, angina), gastrointestinal disorder (eg, acid reflux, ulcers, indigestion), cancer, chronic kidney disease, liver disease, sickle cell disease, chronic obstructive pulmonary disease, and asthma. Possible responses to each condition were "Never," "Yes I have in the past but don't have it now," "Yes I have, but I do not regularly take medications or receiving treatment," and "Yes I have, and I am regularly taking medications or receiving treatment."

Symptoms of OSA were obtained from responses to the Pittsburgh Sleep Quality Index, which was embedded into each survey and included items related to roommate or bedpartner reported "loud snoring" and "long pauses between breaths while you sleep."[31] In addition, sleepiness was assessed from the following item in the questionnaire: During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?" Possible responses to all three items were "not during the past month," "less than once a week," "once or twice a week," or "three or more times a week." Participants were considered to have symptoms of OSA if they had either of the following combination of symptoms: (1) snoring "three or more times a week" and witnessed apnea or sleepiness "once or twice a week"; (2) witnessed apnea and sleepiness "once or twice a week."

Each survey contained identical items related to COVID-19 infection status, COVID-19-related hospitalization, and the number of COVID-19 vaccinations participants had obtained. Ascertainment of past COVID-19 infection was obtained using responses from the following questions related to COVID-19 testing or the presence of loss of taste or smell:

1. "Have you ever tested positive?"
2. "Despite never testing positive, are you confident that you have had COVID-19?"
3. "Despite never testing positive, have you received a clinical diagnosis of COVID-19?"
4. "Have you experienced a problem with decreased sense of smell or taste at any point since January 2020?"

History of hospitalization for COVID-19 was assessed with an affirmative response to the following statement: "I have been hospitalized for symptoms related to COVID-19." COVID-19 vaccination status was ascertained by asking "How many COVID-19 vaccine doses have you received? (If you have had two doses of one brand and one of another, please select three)." Participants were allowed to respond from 0 to 4.

Statistical analyses

Summary data for continuous or ordinal variables are reported as their respective means and standard deviations and for categorical variables as their percentages. After preliminary analyses, we defined a positive history of COVID-19 infection as an affirmative response to having tested positive for COVID-19, a confident assumption of having had COVID-19, or a clinical diagnosis of COVID-19. Participants were considered to have OSA if they endorsed currently having the condition whether treated or not or if they had two or more symptoms of OSA. Vaccination status was dichotomized as boosted (>2 vaccinations) or not boosted (≤2 vaccinations). Comorbid medical conditions were defined as currently having the condition whether treated or untreated. The effect of comorbid medical conditions was evaluated by summing the number of conditions reported by the participant (minimum value 0, maximum value 9). The number of comorbid medical conditions was also assigned

into terciles. Body mass index was calculated using self-reported height and weight as kg/m^2. Socioeconomic covariates were dichotomized as follows: employment (retired vs not retired), education (high school or less vs some college), and income in US dollars (<$100,000 vs ≥$100,000).

Comparisons of continuous or ordinal variables stratified by COVID-19 infection status or history of COVID-19 hospitalization were performed using Student's unpaired *t* test. Bivariate comparisons of categorical variables stratified by COVID-19 infection or history of COVID-19 hospitalization were completed using χ^2.

Multivariable modeling using logistic regression was utilized to determine whether OSA was associated with COVID-19 infection and hospitalization and whether boosted vaccination status attenuated any association. For both COVID-19 infection and COVID-19-related hospitalization, a baseline model was constructed using only OSA, boosted vaccination status, and their interaction. We then developed increasingly complex models by sequentially including demographic factors, comorbidities, and socioeconomic factors. We also assessed whether the association with COVID-19 infection or hospitalization was different for participants who were treated for OSA by further stratifying these individuals as treated or untreated in fully adjusted logistic regression models. Inasmuch as sleepy individuals with OSA may be a phenotype at greater risk for cardiovascular morbidity, a similar analysis was performed after classifying OSA as asymptomatic or symptomatic (*vide supra* for definition of OSA symptoms) to determine whether OSA symptoms were associated with greater risk of COVID-19 infection or hospitalization. Results of the logistic regression models are presented as adjusted odds ratios (aOR) and their 95% confidence intervals (95% CI).

To determine whether our definition of COVID-19 infection status influenced our results, we performed sensitivity analyses with stricter (ie, using COVID-19 infection as a positive test only) and broader (ie, our original definition plus loss of taste or smell as an indicator of a past COVID-19 infection).[32] Additional sensitivity analyses were conducted with an OSA definition that omitted participants with OSA symptoms but did not self-report of a diagnosis of OSA.

All analyses were conducted using IBM SPSS version 28 (Armonk, NY). A $P < .05$ was considered statistically significant.

RESULTS

Table 1 shows the bivariate associations between COVID-19 infection status; OSA; and comorbid medical, demographic, and social characteristics of the cohort. Of the 15,057 respondents, 5,857 (38.9%) had at least one COVID-19 infection and 2,926 (19.4%) had OSA. The prevalence of OSA among COVID-19 respondents was substantially higher than those negative for COVID-19 (29.6% vs 13.0%, $P \leq .001$). COVID-19-positive in comparison to COVID-19-negative participants were younger (39.3 ± 15.3 vs 50.3 ± 18.1 years, $P \leq .001$), slightly higher body mass index (28.6 vs 28.3 kg/m^2, $P < .05$), had more comorbidities (1.7 ± 2.4 vs 0.7 ± 1.2, $P \leq .001$), and were less likely to have received a COVID-19 booster vaccination (26.2% vs 46.8%, $P \leq .001$). COVID-19 positive participants also were more likely to be non-White, not retired, and have an income less than $100,000 per year (all $P < .05$ or .01).

Table 2 displays the bivariate associations between COVID-19-related hospitalizations; OSA; and medical, demographic, and social characteristics of the cohort. There were 432 participants with at least one COVID-19-related hospitalization The prevalence of OSA in individuals who had been hospitalized was higher than in those not hospitalized (38.2% vs 18.9%, $P \leq .001$). Those who had been hospitalized were younger (40.3 vs 46.2 years, $P \leq .001$), had a greater number of comorbidities (2.5 vs 1.1, $P \leq .001$), were more likely to be male (56.1% vs 48.7%, $P \leq .001$), and were less likely to have received a COVID-19 booster vaccination (26.2% vs 39.1%, $P \leq .001$). Hospitalized patients also were more likely to be non-White, not retired, have an income greater than $100,000 per year, and be more educated.

In **Table 3** are logistic regression models displaying aORs for having had a COVID-19 infection in association with OSA and having received a COVID-19 booster vaccination. In a baseline model adjusting for age, sex, and combined race and ethnicity, OSA was associated with nearly three times higher odds of reporting one or more COVID-19 infections (aOR: 2.95, 95% CI: 2.65–3.28). This association was attenuated but remained statistically significant in subsequent additive models adjusting for demographic factors, medical comorbidities, and socioeconomic variables. In the final model, there was a 58% higher probability of COVID-19 infection among persons with OSA (aOR: 1.58, 95% CI: 1.39–1.79). Boosted vaccination status was protective against COVID-19 infection in the baseline model adjusting for age, sex, and combined race and ethnicity (aOR: 0.42, 95% CI: 0.39–0.46), and this association was maintained in the fully adjusted model (aOR: 0.58, 95% CI: 0.53–0.64). There was a significant interaction between OSA and boosted vaccination status in the demographic model (aOR: 0.81, 95% CI: 0.68–0.98). However, this finding was not significant in the fully adjusted model.

Table 4 displays logistic regression models evaluating the relationships between COVID-19-related hospitalization, OSA, and boosted vaccination status. In the baseline model, which adjusted for age, sex, and combined race and ethnicity, OSA was positively associated with COVID-19 hospitalization (aOR: 2.22, 95% CI: 2.34–3.65). This relationship was attenuated but remained significant in the final model, which adjusted for demographic factors, comorbidities, and socioeconomic variables (aOR: 1.55, 95% CI: 1.17–2.05). Boosted vaccination status was protective against COVID-19-related hospitalization both in the baseline (aOR: 0.48, 95% CI: 0.36–0.63) and the final fully adjusted model (aOR: 0.53: 95% CI: 0.39–0.72). The interaction between OSA and boosted vaccination status was significant in the baseline model (aOR: 0.59, 95% CI: 0.36–0.63) and in the final fully adjusted model (aOR: 0.53, 95% CI: 0.33–0.85).

In **Table 5** are fully adjusted logistic regression models illustrating the associations between COVID-19 infection or hospitalization and participants who were treated or untreated for their OSA and participants who were OSA asymptomatic or OSA symptomatic. Both treated and untreated OSA were positively associated with COVID-19 infection, but those who were untreated were at slightly greater risk (aOR: 1.67 vs 1.33, $P < .001$ for comparison

Table 1—Associations between COVID-19 infection status and OSA, comorbid medical, demographic, and social characteristics.

		COVID-19 Negative (n = 9,200)		COVID-19 Positive (n = 5,857)		Overall (n = 15,057)	
	n	Mean	SD	Mean	SD	Mean	SD
Age (y)*	15,048	50.3	18.1	39.3	15.3	46.0	17.9
Body mass index (kg/m^2)†	14,807	28.3	7.8	28.6	10.5	28.4	8.9
No. comorbidities*	15,057	0.7	1.2	1.7	2.4	1.1	1.8
		n	%	n	%	n	%
Sex	14,952						
Male		4,455	48.7	2,864	49.4	7,319	48.9
Female		4,701	51.3	2,932	50.6	7,633	51.1
Race/Ethnicity*	15,057						
White		6,124	66.6	3,466	59.2	9,590	63.7
Black		937	10.2	647	11.0	1,584	10.5
Hispanic		1,099	11.9	1,236	21.1	2,335	15.5
Other		1,040	11.3	508	8.7	1,548	10.3
Employment*	15,057						
Retired		2,827	30.7	634	10.8	3,461	23.0
Not retired		6,873	69.3	5,223	89.2	11,596	77.0
Education	15,057						
High school or less		2,499	27.2	1,624	27.7	4,123	27.4
Some college		6,701	72.8	4,233	72.3	10,934	72.6
Income (yearly)*	14,402						
< $100,000		6,684	76.5	4,009	70.8	10,693	74.2
≥ $100,000		2,052	23.5	1,657	29.2	3,709	25.8
Vaccination dose*	15,057						
0		1,994	21.7	1,344	22.9	3,338	22.2
1		556	6.0	982	16.8	1,538	10.2
2		2,348	25.5	1,999	34.1	4,347	28.9
3		3,653	39.7	1,369	23.4	5,022	33.4
4		649	7.1	163	2.8	812	5.4
Vaccination boosted	15,057						
No (≤ 2 vaccinations)		4,898	53.2	4,325	73.8	9,223	61.3
Yes (> 2 vaccinations)		4,302	46.8	1,532	26.2	5,834	38.7
Any comorbidity*	15,057						
None		5,540	60.2	2,931	50.0	8,471	56.3
Any		3,660	39.2	2,926	50.0	6,586	43.7
Comorbidity tertiles*	15,057						
0–3		8,892	96.7	4,656	79.5	13,548	90.0
4–6		246	2.7	811	13.8	1,057	7.0
6–9		62	.7	390	6.7	452	3.0
OSA*	15,057						
No OSA		8,008	87.0	4,123	70.4	12,131	80.6
Diagnosed or symptoms		1,192	13.0	1,734	29.6	2,926	19.4
Diagnosed		948	10.3	1,220	20.8	2,167	14.4
Symptoms only		244	2.7	514	8.8	758	5.0
Treated		540	5.9	532	9.1	1,072	7.1

Significant differences in means or proportions: *$P \leq .001$; †$P < .05$. OSA = obstructive sleep apnea, SD = standard deviation.

Table 2—Associations between COVID-19-related hospitalization and obstructive sleep apnea, comorbid medical, demographic, and social characteristics.

		Never Hospitalized (n = 14,625)		Hospitalized (n = 432)		Overall (n = 15,057)	
	n	Mean	SD	Mean	SD	Mean	SD
Age (y)*	15,048	46.2	17.9	40.3	14.7	46.0	17.9
Body mass index (kg/m^2)	14,807	28.4	8.9	27.8	9.3	28.4	8.9
No. comorbidities*	15,057	1.1	1.8	2.5	2.7	1.1	1.8
		n	%	n	%	n	%
Sex†	14,952						
Male		7,079	48.7	240	56.1	7,319	48.9
Female		7,445	51.3	188	43.9	7,633	51.1
Race/Ethnicity†	15,057						
White		9,332	63.8	258	59.7	9,590	63.7
Black		1,522	10.4	62	14.4	1,584	10.5
Hispanic		2,257	10.4	78	18.1	2,335	15.5
Other		1,514	15.4	34	7.9	1,548	10.3
Employment*	15,057						
Retired		3,420	23.4	41	9.5	3,461	23.0
Not retired		11,205	76.6	391	90.5	11,596	77.0
Education†	15,057						
High school or less		4,032	27.6	91	21.1	4,123	27.4
Some college		10,593	72.4	341	78.9	10,934	72.6
Income (yearly)*	14,402						
< $100,000		10,428	74.6	265	62.1	10,693	74.2
≥ $100,000		3,547	25.4	162	37.9	3,709	25.8
Vaccination dose*	15,057						
0		3,254	22.2	84	19.4	3,338	22.2
1		1,451	9.9	87	20.1	1,538	10.2
2		4,199	28.7	148	34.3	4,347	28.9
3		4,920	33.6	102	23.6	5,022	33.4
4		801	5.5	11	2.5	812	5.4
Vaccination boosted							
No (≤ 2 vaccinations)	15,057	8,904	60.9	319	73.8	9,223	61.3
Yes (> 2 vaccinations)		5,721	39.1	113	26.2	5,834	38.7
Any comorbidity*	15,057						
None		8,314	56.8	157	36.3	8,471	56.3
Any		6,311	43.2	275	63.7	6,586	43.7
Comorbidity tertiles*	15,057						
0–3		13,247	90.6	301	69.7	13,548	90.0
4–6		977	6.7	80	18.5	1,057	7.0
6–9		401	2.7	51	11.8	452	3.0
Obstructive sleep apnea*	15,057						
Never		11,864	81.1	267	61.8	12,131	80.6
Diagnosed or symptoms		2,761	18.9	165	38.2	2,926	19.4
Diagnosed		2,061	14.1	107	24.8	2,168	14.4
Symptoms only		700	4.8	58	13.4	758	5.0
Treated		1,015	6.9	57	13.2	1,072	7.1

Significant differences in means or proportions: †$P < .01$, *$P \leq .001$. SD = standard deviation.

Table 3—Odds ratio (adjusted) for reporting one or more COVID-19 infections based on symptoms or diagnosis of OSA, boosted vaccination status, and the interaction between the variables.

		OSA Diagnosis or Symptoms		Boosted Vaccination Status		OSA × Boosted Vaccination	
Model	N	aOR	95% CI	aOR	95% CI	aOR	95% CI
Baseline	15,057	2.95	2.65–3.28§	.42	.39–.46§	.85	.71–1.01#
+Demographics*	14,943	2.86	2.56–3.19§	.63	.58–.69§	.81	.68–.98¶
+Comorbidities†	14,697	1.62	1.43–1.84§	.61	.56–.67§	.41	.76–1.12
+Socioeconomic‡	14,069	1.58	1.39–1.79§	.58	.53–.64§	.94	.76–1.15

The baseline model includes only OSA, boosted vaccination status, and their interaction. Subsequent models are additive to their immediate predecessor and are adjusted as indicated below (see text for covariate definitions) with the fully adjusted model reflecting demographic, comorbid disease, and socioeconomic characteristics. *Age, sex, race. †Body mass index, number of the following conditions: diabetes, asthma, sickle cell disease, cardiovascular disease, hypertension, cancer, chronic kidney disease, liver disease, chronic obstructive pulmonary disease. ‡Education, income, employment. #P = .071; ¶P = .029; §P < .001. aOR = adjusted odds ratio, CI = confidence interval, OSA = obstructive sleep apnea.

of untreated vs treated). With respect to COVID-related hospitalization, there was a positive association only in those who were untreated (aOR: 1.54, 95% CI: 1.15–2.07). Both symptomatic and asymptomatic OSA were positively associated with COVID-19 infection, but this relationship was stronger in those who were symptomatic (aOR: 1.91 vs 1.46, $P < .05$ for comparison of symptomatic vs asymptomatic). When OSA was stratified by the presence of symptoms, neither symptomatic OSA nor asymptomatic OSA were associated with COVID-19 hospitalization.

Sensitivity analyses using alternative definitions of COVID-19 infection also confirmed an association with OSA and the effectiveness of having received a vaccine booster. However, the interaction between OSA and boosted vaccination status was not significant. There were similar findings when the definition of OSA did not include participants who had only OSA symptoms but did not report having a diagnosis of OSA.

DISCUSSION

Our analyses observed that the prevalence of OSA was substantially higher in persons who had been infected with COVID-19 or who had been hospitalized for COVID-19. These associations persisted even after adjustment for demographic and socioeconomic covariates and medical comorbidities. Although boosted vaccination status was found to have a protective association with COVID-19 infection, it did not attenuate the relationship between OSA and COVID-19 infection. However, it did appear to be associated with a decrease in OSA-related COVID-19 hospitalizations. Additional analyses suggest that these associations between OSA and COVID-19 infection or hospitalization were stronger in those who are untreated for OSA or who have OSA symptoms.

The principal finding in our study was that OSA is associated with COVID-19 infection and hospitalization after adjustment for multiple medical comorbidities including body mass index. Our results are consistent with many other studies demonstrating that OSA appears to be a risk factor for COVID-19 infection or hospitalization[5–8,10,12,14–18,33] as well as for influenza.[34] However, these prior studies utilized hospital records or other databases to identify COVID-19 cases with or without OSA and in some cases were susceptible to collider bias. In contrast, our data are derived from a large general population survey. Our findings are very similar to a report from a large worldwide

Table 4—Odds ratio (adjusted) for reporting one or more COVID-19-related hospitalizations based on symptoms or diagnosis of OSA, boosted vaccination status and the interaction between the variables.

		OSA Diagnosis or Symptoms		Boosted Vaccination Status		OSA × Boosted Vaccination	
Model	n	aOR	95% CI	aOR	95% CI	aOR	95% CI
Baseline	15,057	2.92§	2.34–3.65	.48§	.36–.63	.59¶	.36–.63
+Demographics*	14,943	2.76§	2.20–3.45	.58§	.43–.77	.59¶	.38–.93
+Comorbidities†	14,697	1.64§	1.24–2.16	.53§	.39–.72	.52#	.32–.82
+Socioeconomic‡	14,069	1.55#	1.17–2.05	.53§	.39–.72	.53#	.33–.85

The baseline model includes only OSA, boosted vaccination status, and their interaction. Subsequent models are additive to their immediate predecessor and are adjusted as indicated below (see text for covariate definitions) with the fully adjusted model reflecting demographic, comorbid disease, and socioeconomic characteristics. *Age, sex, race. †Body mass index, number of the following conditions: diabetes, asthma, sickle cell disease, cardiovascular disease, hypertension, cancer, chronic kidney disease, liver disease, chronic obstructive pulmonary disease. ‡Education, income, employment. ¶$P \leq .05$; #$P < .01$; §$P < .001$. aOR = adjusted odds ratio, CI = confidence interval, OSA = obstructive sleep apnea.

Table 5—Adjusted relative odds of COVID-19 infection or COVID-related hospitalization as a function of OSA symptoms or treatment.

	OSA Treated (n = 996)		OSA Untreated (n = 1,651)	
Model	**aOR**	**95% CI**	**aOR**	**95% CI**
COVID infection‡	1.33†	1.08–1.64	1.67§	1.44–1.84
COVID hospitalization	1.19	.75–1.89	1.54§	1.15–2.07
Analysis n = 14,069				
	OSA Asymptomatic (n = 2,031)		**OSA Symptomatic (n = 691)**	
COVID infection¶	1.46§	1.26–1.69	1.91§	1.53–2.38
COVID hospitalization	1.06	.77–1.46	1.36	.89–2.06
Analysis n = 14,069				

All models adjusted as follows (see text for definitions): age; vaccination status; sex; race; body mass index; number of the following conditions: diabetes, asthma, sickle cell disease, cardiovascular disease, hypertension, cancer, chronic kidney disease, liver disease, chronic obstructive pulmonary disease; education; income; employment. †P < .05; §P < .001 vs COVID infection or COVID hospitalization. ‡P < .001 OSA treated vs OSA untreated. ¶P < .05 OSA asymptomatic vs OSA symptomatic. aOR = adjusted odds ratio, CI = confidence interval, OSA = obstructive sleep apnea.

cross-sectional survey that utilized the STOP questionnaire to classify participants as high or low risk for OSA.[7] The latter study found a 25.5% prevalence of high risk for OSA in COVID-19-positive vs 9.0% in COVID-19-negative participants. In contrast, we identified COVID-19 infection based on self-report of a positive test, clinical diagnosis, or symptoms and noted a 29.6% prevalence of OSA in COVID-19-positive vs 13.0% in COVID-19-negative participants. Prevalence rates for COVID-19 hospitalization also were comparable. Therefore, our findings provide strong additional support for the concept that OSA increases the risk for COVID-19 infection and hospitalization.

The explanation for why OSA is a potential risk factor for COVID-19 infection or hospitalization is unclear.[35,36] There is substantial evidence that OSA is an inflammatory condition.[37] Intermittent hypoxemia promotes the release of inflammatory cytokines such as interleukin-6, c-reactive protein, and tumor necrosis factor-α.[38] It is possible that introduction of the SARS-CoV-2 virus into a pre-existing inflammatory milieu could increase the likelihood of more severe COVID-19 outcomes. Such a scenario has been suggested as one possible explanation of why there is an increased risk of severe COVID-19 in diabetics in whom chronic inflammation is frequently present.[39] There also is some evidence OSA is associated with cellular immune dysfunction.[40] Additionally, sleep deprivation can occur with OSA, and the former may lead to a chronic low-grade inflammatory state.[41] All or some of these could lead to enhanced susceptibility to COVID-19 infection. Alternatively, the elevated risk conferred by OSA may be related to its co-occurrence with obesity or heart disease. In contradistinction to the aforementioned potential mechanisms, other studies suggest that hypoxemia explains the association of OSA with COVID-19.[24,42]

Our finding that boosted vaccination status was protective against COVID-19 infection and hospitalization is consistent with previous surveillance reports of vaccine effectiveness.[43] We also observed that boosted vaccination status attenuated the increased risk conferred by OSA associated with hospitalization but not for infection. This supports current doctrine that COVID-19 vaccination boosters are critically important for preventing severe infection, hospitalization, and death.

Participants with OSA symptoms were more likely than those without symptoms to have had a COVID-19 infection, although this finding was not observed for COVID-19 hospitalization. There is some evidence to support the concept that OSA with excessive daytime sleepiness represents a distinct phenotype of OSA with greater susceptibility to adverse consequences such as cardiovascular disease.[44] Our results suggest that this phenotype may be important in risk for developing COVID-19 infection as well.

In our study, persons with OSA who were reported receiving treatment had lower risk for both COVID-19 infection and hospitalization. Although we did not collect data on the type of OSA treatment participants were receiving, positive airway pressure is the most prescribed form of therapy, and there is no reason to believe this study sample differed. Recent studies also indicate that treatment of OSA with positive airway pressure reduces or is not associated with COVID-19 infection, respiratory failure, or death.[45,46] Thus, our results provide additional evidence to support the hypothesis that treatment of OSA may reduce the risk of COVID-19 infection or hospitalization. Positive airway pressure therapy appears to at least partially correct altered inflammatory responses in OSA[47] and has also been used to treat hypoxemia in COVID-19, which may explain the improved outcomes on positive airway pressure.

Several demographic and socioeconomic factors in this study were related to a higher prevalence of COVID-19. Although older age is a risk for developing more severe COVID-19 outcomes,[2,3] we observed that infection occurred more frequently in younger persons and those who were working. This is consistent with data from a large community-based study who also found higher infection rates at lower ages later in the pandemic.[48] Most likely this reflects greater interpersonal interaction and hence greater exposure to the SARS-CoV-2 virus resulting from employment and less adherence to viral transmission mitigation strategies among young individuals.

Our results indicating that COVID-19 was more common among non-Whites and those with lower income are consistent with previous reports and highlight the racial and socioeconomic disparities of the pandemic.[49,50]

The most important limitation to this study is that both identification of COVID-19 infection and OSA were by self-report, which may have resulted in misclassification of the exposure and/or outcome. However, we do not have reason to believe that the direction of any misclassification would have systematically differed and altered our conclusions. Sensitivity analyses indicate that changes in definitions of both OSA and COVID-19 infection resulted in similar findings. By including in our classification of OSA those with symptoms of OSA, we reduced the impact of undiagnosed OSA in our analyses. Conversely, it also is possible that by including participants with OSA symptoms, we may have overidentified OSA in the cohort. However, we acknowledge that we did not use a validated assessment of sleepiness, and this may have led to some misclassification of participants. We also recognize that the number of participants reporting a COVID-19 hospitalization was relatively small, and the lack of information regarding treatment for OSA (eg, adherence, type of treatment) tempers our finding that OSA treatment is associated with lower infection and hospitalization rates. Finally, our analyses were cross-sectional. Although we believe that most participants had OSA prior to their COVID-19 infection, OSA has been reported to develop after COVID-19.[51] Nevertheless, we believe that these limitations are counterbalanced by the strength of this study in which >15,000 participants were surveyed in a general population.

In conclusion, OSA is associated with an increased prevalence of both COVID-19 infection and hospitalization. Boosted vaccination status did not attenuate the increase in risk of COVID-19 infection associated with OSA but did reduce the association with hospitalization. In addition, these findings are most apparent in those who are symptomatic and untreated. Further research is necessary to understand the mechanisms underlying the increased in COVID-19 infection and hospitalization conferred by OSA.

ABBREVIATIONS

aOR, adjusted odds ratio
CI, confidence interval
OSA, obstructive sleep apnea

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