Association of Chronotype and Shiftwork With COVID-19 Infection

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Objective: This study assesses whether chronotype is related to COVID-19 infection and whether there is an interaction with shift work. **Methods:** This study used a cross-sectional survey of 19,821 U.S. adults. **Results:** COVID-19 infection occurred in 40% of participants, 32.6% morning and 17.2% evening chronotypes. After adjusting for demographic and socioeconomic factors, shift/remote work, sleep duration, and comorbidities, morning chronotype was associated with a higher (adjusted odds ratio [aOR]: 1.15, 95% CI: 1.10–1.21) and evening chronotype with a lower (aOR: 0.82, 95% CI: 0.78–0.87) prevalence of COVID-19 infection in comparison to an intermediate chronotype. Working exclusively night shifts was not associated with higher prevalence of COVID-19. Morning chronotype and working some evening shifts was associated with the highest prevalence of previous COVID-19 infection (aOR: 1.87, 95% CI: 1.28–2.74). **Conclusion:** Morning chronotype and working a mixture of shifts increase risk of COVID-19 infection.

Keywords: COVID-19, shift work, chronotype, diurnal preference

LEARNING OUTCOMES

- Describe the association between chronotype and prevalence of COVID-19 infection
- Summarize the combined effect of chronotype and shift work on the prevalence of COVID-19 infection

A number of underlying medical conditions such as cardiovascular disease, diabetes, and obesity increase the risk for COVID-19 infection and severity.[1,2] Sleep conditions also are important risk factors associated with increased prevalence and worse outcomes for COVID-19 disease; emerging evidence demonstrates that obstructive sleep apnea[3–6] and more recently, insomnia and reduced sleep duration are linked to an increase in prevalence and worse COVID-19 disease outcomes.[7] Circadian rhythmicity is important in the regulation of immune system and inflammatory processes.[8,9] Chronotype is a trait that strongly reflects circadian timing as well as social and homeostatic factors.[10] Recently, evening chronotype has been associated with greater risk of poor health with increased rates of obesity, cardiovascular disease, and diabetes.[11,12] However, there have been few studies of whether a specific diurnal preference or chronotype is associated with a greater risk for COVID-19 disease. In a single-center study in France, social jet lag as a marker of evening chronotype was associated with a higher rate of COVID-19.[13] In contrast, the COVID-19 Outbreak Public Evaluation (COPE) Initiative reported that morning in comparison to evening chronotype was associated with a higher rate of COVID-19

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infection,[7] while in a study using UK Biobank participants, no association was observed between a specific chronotype and COVID-19.[14] Thus, the impact of chronotype on COVID-19 has not been determined.

During the height of the COVID-19 pandemic, sleep patterns changed. As a result of lockdowns and social restrictions, stress, meal timing, anxiety and depression, social isolation, and the migration to remote working, both increases and decreases in sleep duration as well as changes in sleep timing occurred.[15–17] The presence of these factors may allow the development of circadian misalignment, which increases risk of cardiovascular and metabolic disorders, and importantly infections. Circadian misalignment is a characteristic of shift workers who have been shown to have an increased risk of developing respiratory infections.[18,19] It has been suggested that shift workers are at greater risk for COVID-19.[20–22] This has been confirmed by several studies observing that night shift work is associated with higher rates of COVID-19 infection and hospitalization.[23–27]

Investigations examining whether the adverse effect of shift work on health is modified by chronotype suggest that shift workers with evening chronotype may have greater risk for diabetes and obesity.[12] However, there have been no assessments of whether risk of infection and in particular COVID-19 is similarly affected.

In this study, we examined whether both morning and evening chronotypes were more likely to have had a COVID-19 infection in comparison to those who were intermediate chronotypes. Additionally, we examined whether there is a synergistic association between chronotype and shift work, with COVID-19 infection. To accomplish this, we used data from the first four 2022 waves of COPE Initiative (http://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 August 18, 2022, the COPE Initiative administered four successive waves of public health surveillance surveys to adults living in the United States (U.S.). Dates of administration were: Wave 1 (March 10–30, 2022), Wave 2 (April 4–May 1, 2022), Wave 3 (May 4–June 2, 2022), and Wave 4 (July 28–August 18, 2022). Using demographic quota sampling to approximate population estimates for age, sex, race, and ethnicity based on the 2020 U.S. census, each wave consisted of more than 5000 unique participants recruited by Qualtrics, LLC (Provo, UT, and Seattle, WA). The Monash University Human Research Ethics Committee (study #24036) approved the study. The Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Supplemental Digital Content, http://links.lww.com/JOM/B558).

Survey Items

Participants self-reported demographic, anthropometric, and socioeconomic information including age, race, ethnicity, sex, height and weight, education level, employment status (including employment/job sector), 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: 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 or 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 receive treatment," and "Yes I have, and I am regularly taking medications or receiving treatment."

Each survey contained identical items related to COVID-19 infection status 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:

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?"

Chronotype was ascertained by asking participants the following question from the Horne & Östberg Morningness-Eveningness questionnaire:[28] "One hears about 'morning' and 'evening' types of people. Which one of these types do you consider yourself to be?" Possible responses were "Definitely a 'morning' type," "Rather more

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STROBE Statement: This analysis of the COPE initiative adhered to STROBE guidelines for reporting a cross-sectional study.

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of a 'morning' than an 'evening' type," "Rather more of an 'evening' than a 'morning' type," and "Definitely an 'evening' type."[29] Morningness was defined as definitely a "morning" type and eveningness conversely was defined as definitely an "evening" type. Rather more of an "evening" and rather more of a "morning" were classified as neither morning nor evening type (intermediate).

Sleep duration was assessed using a question from the Pittsburgh Sleep Quality Index.[30] Responses were rounded to the nearest hour; those <3 hours or >12 hours were excluded as improbable estimates ($N = 987$) as was done in a previous analysis of this cohort.[7]

For participants who endorsed self-employment, full- or part-time employment, the following question was asked to determine the presence of shift work: "Currently, what type of shifts do you work? (Select all that apply)" Possible responses were as follows:

1. "Day shift occurs any time between 6am and 7pm"
2. "Evening shift occurs any time between 3pm and midnight"
3. "Night shift is any shift in which the majority of the work hours occur between 10pm and 8am"

From these responses, five work shift categories were constructed: retired/not working, day shift only, day and/or some evening shifts, day and/or evening shifts and some night shifts, and night shift only. In addition, participants who were employed were asked to provide the percentage of their paid work hours that were completed remotely.

Statistical Analyses

Summary data for continuous or ordinal variables are reported as their respective means and standard deviations (SDs) and for categorical variables as their percentages. Consistent with previous analyses, we defined a positive history of COVID-19 infection as an affirmative response to having tested positive for COVID-19, new loss of taste or smell, or a clinical diagnosis of COVID-19. Number of COVID-19 vaccinations was utilized as an ordinal variable and also 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). Body mass index (BMI) 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 or higher), and income in U.S. dollars to approximate 200% of the 2022 U.S. poverty level for a family of 4 (<\$50,000 vs ≥ \$50,000).[31]

Comparisons of continuous or ordinal variables stratified by COVID-19 infection status were performed using Student's unpaired t test. Bivariate comparisons of categorical variables stratified by COVID-19 infection were completed using chi-squared test.[2] The associations between employment sector and shiftwork status were estimated using a multinomial logistic regression.

Multivariable modeling using logistic regression was utilized to determine whether circadian preference and shift work categories were associated with COVID-19 infection. In an initial analysis including all participants with complete data, an initial baseline model was constructed only entering chronotype as a categorical variable with morningness and eveningness compared to the referent of neither morningness nor eveningness. We then developed increasingly complex models by sequentially including demographic factors, comorbidities and vaccination status, socioeconomic factors, shift work category, and sleep duration. In a subsequent model, to separately determine the joint effects of diurnal preference and shift work on the prevalence of COVID-19 infection, analysis was limited only to participants who were full-time, part-time, or self-employed. Models sequentially included demographic factors, comorbidities and vaccination status, socioeconomic factors, employment sector, and sleep duration. An additional model was constructed with two-way interactions between diurnal preference and shift work categories. In addition, we performed sensitivity analyses with stricter (ie, using COVID-19 infection as a positive test only) and broader (ie, our original definition plus presumed positive, but not tested as an indicator of a past COVID-19 infection) definitions.

All analyses were conducted using IBM SPSS version 28 (Armonk, NY). A $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows the bivariate associations between COVID-19 infection status, diurnal preference, and comorbid medical, demographic, and social characteristics of the cohort. As shown in the Supplementary Digital Content, http://links.lww.com/JOM/B559, of the 19,821 participants, 7932 (40.0%) had at least one COVID-19 infection. Morning and evening diurnal preferences were observed in 31.9% and 19.4% of participants, respectively. Among COVID-19 positive in comparison to COVID-19 negative participants, there was a higher percentage of morning types (32.6 vs 31.4%) and a lower percentage of evening types (17.2 vs 20.9%, $P \leq 0.001$). Participants who were retired or unemployed were less likely to have had a COVID-19 infection (12.5 vs 30.8%, $P \leq 0.001$). COVID-19 positive in comparison to COVID-19 negative participants were younger (40.2 ± 15.8 vs 50.4 ± 18.0 y, $P \leq 0.001$), had a slightly shorter self-reported sleep duration (6.8 ± 1.6 vs 6.9 ± 1.7 hours, $P \leq 0.001$), had a slightly larger percent of time working remotely (36 ± 34 vs 32 ± 38%, $P \leq 0.001$), were slightly more overweight (BMI: 28.7 vs 28.3 kg/m^2, $P < 0.001$), had more comorbidities (1.7 ± 2.4 vs 0.8 ± 1.2, $P \leq 0.001$), and were less likely to have received a COVID-19 booster vaccination (27.6 vs 46.4%, $P \leq 0.001$). COVID-19-positive participants also were more likely to be Hispanic, not retired and have an income more than \$50,000 per year.

The unadjusted associations between COVID-19 infection and shiftwork status, and employment sector are shown in Table 2. In comparison to the health care sector, employees working in construction, financial, and protective services had higher rates of infection while those working in factory/manufacturing, retail, transportation, and other sectors had lower rates. In comparison to office/administration employees, arts/entertainment/media, cleaning/maintenance, factory/manufacturing, food industry, health care, protective services, retail, and transportation had a lower prevalence rate of day shift only positions. In contrast, those working in other sectors had higher rates of day shift only positions.

Table 3 displays the logistic regression models for the association between having had a COVID-19 infection and either a morning or evening diurnal preference in comparison to a reference group without a definite preference. In models including demographics, comorbidities, vaccination status, and socioeconomic factors, morning preference was related to a 20% greater likelihood of COVID-19 infection. In contrast, evening preference was 20% less likely to be linked to a COVID-19 infection. These associations were not materially affected by the type of work shift, percent time working remotely, or after adjustment for sleep duration.

In Table 4 are the bivariate associations between COVID-19 infection and diurnal preference, and comorbid medical, demographic, and social characteristics of the cohort limited only to members who were employed ($N = 11{,}114$, Supplemental Digital Content, Figure, http://links.lww.com/JOM/B559). In comparison to the entire cohort, participants were slightly younger, more likely to be male, and had a higher income. Participants who worked a mixture of shift types had a higher prevalence rate of infection in comparison to those who worked only day shifts or only night shifts ($P < 0.001$).

TABLE 1. Associations Between COVID-19 Infection Status, Diurnal Preference, Shift Work, and Comorbid Medical, Demographic, and Social Characteristics

		COVID-19 Negative (n = 11,889)		COVID-19 Positive (n = 7,932)		Overall (N = 19,821)	
	n	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Age (y)[a]	19,812	50.4	18.0	40.2	15.8	46.3	17.9
Body mass index (kg/m^2)[a]	19,578	28.3	7.8	28.7	10.3	28.5	8.9
No. comorbidities[a]	19,821	0.8	1.2	1.7	2.4	1.2	1.9
Remote work (%)[a]	11,057	32	38	36	34	34	36
Sleep duration self-report (h)[ab]	14,409	6.9	1.6	6.6	1.8	6.8	1.7
		n	*%*	*n*	*%*	*n*	*%*
Sex	19,665						
Male		5,752	48.6	3,871	49.4	9,681	48.9
Female		6,080	51.4	3,962	50.6	10,042	51.0
Race/ethnicity[a]	19,821						
White		7,832	65.9	4,691	59.1	12,523	63.2
Black		1,248	10.5	841	10.6	2,089	10.5
Hispanic		1,493	12.6	1,720	21.7	3,213	16.2
Other		1,316	11.1	680	8.6	1,996	10.1
Employment[a]	19,821						
Retired		3,659	30.8	988	12.5	4,647	23.4
Not retired		8,230	69.2	6,944	87.5	15,174	76.6
Education	19,821						
High school or less		3,187	26.8	2,137	26.9	5,324	26.9
Some college		8,702	73.2	5,795	73.1	14,497	73.1
Income (yearly)[a]	18,990						
<\$50,000		5,421	48.0	3,219	41.9	8,640	45.5
≥\$50,000		5,882	52.0	4,468	58.1	10,350	54.5
Diurnal preference [a]	19,821						
Definitely morning type		3,739	31.4	2,588	32.6	6,327	31.9
Definitely evening type		2,481	20.9	1,367	17.2	3,848	19.4
Not definitely morning or evening type		5,669	47.7	3,977	50.1	9,646	48.7
Work shift category[a]							
Retired/not working	19,818	6,210	52.2	2,550	32.2	8,760	44.2
Day shift only		4,170	35.1	3,430	43.3	7,600	38.3
Day and/or some evening shifts		976	8.2	1,334	16.8	2,310	11.7
Day/evening and some night shifts		290	2.4	393	5.0	683	3.4
Night shifts only		242	2.0	223	2.8	465	2.3
Vaccination number[a]	19,926						
0		2,659	22.3	1,795	22.5	4,454	22.4
1		692	5.8	1,272	15.9	1,964	9.9
2		3,047	25.5	2,712	34.0	5,759	28.9
3		4,385	36.7	1,855	23.2	6,240	31.3
4		1,162	9.7	347	4.3	1,509	7.6
Vaccination boosted[a]	19,926						
No (≤2 vaccinations)		6,398	53.6	5,779	72.4	12,177	61.1
Yes (>2 vaccinations)		5,547	46.4	2,202	27.6	7,749	38.9

[a]$P \leq 0.001$, significant differences in means or proportions.
[b]Participants with self-reported sleep duration <3 or >12 hours were excluded as improbable.

Table 5 shows the fully adjusted logistic regression model, which adjusted for percent remote work and sleep duration documenting the association between COVID-19 infection and diurnal preference, work shift category, and the interactions between diurnal preference and work shift category. In comparison to neither definite morning nor evening preference, there was a 18% greater likelihood of infection in those with morning preference and a 16% lower likelihood in those with an evening preference. Both were comparable to the adjusted odds ratios (aORs) observed for the overall cohort. Addition of employment sector did not substantially alter these findings. In comparison to working only a day shift, a greater risk of COVID-19 infection was observed in those working a mixture of day and evening shifts (aOR: 1.25, 95% CI: 1.10–1.41); working a mixture of day, evening, and night shifts approached significance (aOR: 1.18, 95% CI: 0.97–1.44). Working only night shifts was not associated with a higher prevalence of COVID-19 infection. The overall interaction between diurnal preference and work shift category was significant (Wald χ^2=13.864, P = 0.031). Individual interaction terms indicated that there was a higher likelihood of infection in participants who had a morning preference and working a combination of day and evening shifts (aOR: 1.87, 95% CI: 1.28–2.74); the association with those with a morning preference and working a mixture of day, evening, and night shifts approached significance (aOR: 1.72, 95% CI: 0.98–3.02).

Sensitivity analyses indicated that our findings were similar using slightly stricter or more liberal definitions of COVID-19. However, a definition that required a positive test only lost statistical significance.

DISCUSSION

In this study, morning and evening chronotypes were found to be differentially associated with COVID-19 infection; morning types

TABLE 2. Associations of COVID-19 Infection and Shiftwork Status With Employment Sector

			COVID-19 Infection Status[a]				Shiftwork Status[b]					
	Overall		COVID-19 Negative		COVID-19 Positive		Days Only		Mixture		Nights Only[c]	
Employment Sector	n	%	n	%	n	%	n	%	n	%	n	%
Arts, entertainment, media	411	3.7	184	1.7	227	2.0	231	2.1*	159	1.4	21	0.2
Cleaning/maintenance	227	2.0	104	0.9	123	1.1	148	1.3*	67	0.6	11	0.1
Construction*	912	8.2	369	3.3	543	4.9	644	5.8	246	2.2	20	0.2
Education	850	7.7	448	4.0	402	3.6	712	6.4	129	1.2	10	0.1
Factory/manufacturing*	583	5.3	339	3.1	244	2.2	415	3.7*	116	1.0*	46	0.4
Financial*	952	8.6	381	3.4	571	5.1	698	6.3	229	2.1	21	0.2
Food industry	743	6.7	403	3.6	340	3.1	370	3.3*	331	3.0	38	0.3
Health care	1,021	9.2	512	4.6	509	4.6	636	5.7*	288	2.6*	90	0.8
Office/administration	1,075	9.7	524	4.7	551	5.0	874	7.9	182	1.6	21	0.2
Other*	2,602	23.5	1,518	13.7	1,084	9.8	1,929	17.4*	570	5.2	99	0.9
Personal care	137	1.2	67	0.6	70	0.6	77	0.7	57	0.5	3	0.0
Protective services*	248	2.2	72	0.6	176	1.6	112	1.0*	115	1.0	21	0.2
Retail*	928	8.4	537	4.8	391	3.5	517	4.7*	378	3.4	34	0.3
Transportation**	401	3.6	226	2.0	175	1.6	238	2.2*	129	1.2**	34	0.3
Totals	11,090	100.0	5,684	51.3	5,406	48.7	7,601	68.7	2,996	27.1	469	4.2

[a]Reference category: health care.
[b]Reference category: office/administration.
[c]Reference category: nights only.
*$P < 0.01$, **$P < 0.05$.

were more likely and evening types were significantly less likely to be infected. Additionally, in comparison to working only day shifts, working a combination of different shift types, as opposed to day shifts, only was associated with a higher prevalence of COVID-19 infection. This finding of higher infection rate was primarily observed in individuals with a morning chronotype who worked a combination of different shifts.

Morning chronotypes were more susceptible to COVID-19 infection than evening chronotypes; this finding is consistent with earlier preliminary results from the same cohort.[7] This observation stands in contrast to a large body of evidence demonstrating that the prevalence of cardiovascular disease risk factors and metabolic disorders is higher in evening chronotypes.[11,12] Furthermore, our results are distinct from the limited studies that also have assessed the association between chronotype and COVID-19. In a single-center study, social jet lag as a marker of evening chronotype was found to be associated with a higher rate of COVID-19.[13] In contrast, no association between chronotype and COVID-19 infection was observed in two separate analyses of the UK Biobank[14,26] as well as in an analysis of long COVID from the Nurses' Health Study.[32] Additionally, to our knowledge, there have been no previous studies of an association between chronotype and infection risk from other pathogens.

Despite the paucity of clinical investigations related to chronotype and infection risk, there are mechanisms that could explain our finding of an association between morning chronotype and COVID-19 infection. A reduction in sleep duration has been linked to increased susceptibility to infection.[19] However, our observation remained robust after controlling for sleep duration in our modeling. Alternatively, various components of the immune system exhibit circadian rhythmicity.[33] Secretion of inflammatory cytokines, trafficking myeloid and lymphocyte subsets, and maturation of leukocytes exhibit a circadian rhythm with the

TABLE 3. Odds Ratio (Adjusted) for Reporting One or More COVID-19 Infections Based on Circadian Preference ($N = 19{,}821$)

	Morningness		Eveningness	
Model	aOR	95% CI	aOR	95% CI
Baseline	1.07	1.03–1.12*	0.86	0.81–0.90*
+Demographics[a]	1.21	1.15–1.26*	0.76	0.73–0.81*
+Comorbidities and vaccination status[b]	1.23	1.16–1.31*	0.77	0.72–0.83*
+Socioeconomic[c]	1.20	1.13–1.28*	0.80	0.74–0.86*
+Shift work	1.21	1.14–1.29*	0.79	0.73–0.85*
+Self-reported sleep duration and % remote work	1.23	1.15–1.31*	0.78	0.73–0.85*

aOR, adjusted odds ratio; CI, confidence interval.
The baseline model includes only definitely morning or definitely evening preference. 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, socioeconomic characteristics, and the occurrence of shift work.
[a]Age, sex, and race.
[b]BMI, vaccination status (boosted vs not boosted), # of the following conditions: diabetes, asthma, sickle cell disease, cardiovascular disease, hypertension, cancer, chronic kidney disease, liver disease, and chronic obstructive pulmonary disease.
[c]education, income, and employment.
*$P < 0.001$.

TABLE 4. Associations Between COVID-19 Infection Status, Diurnal Preference, Shift Work, and Comorbid Medical, Demographic, and Social Characteristics in Employed Participants

		COVID-19 Negative (n = 5,678)		COVID-19 Positive (n = 5,379)		Overall (N = 11,114)	
	n	***Mean***	***SD***	***Mean***	***SD***	***Mean***	***SD***
Age (yr)*	11,028	43.7	14.9	37.3	12.6	40.6	14.2
Body mass index (kg/m^2)**	10,826	27.8	7.8	28.2	10.9	28.0	9.4
No. comorbidities*	11,036	0.6	1.3	1.9	2.6	1.3	2.2
Remote work (%)	11,036	32	38	36	34	34	36
Sleep duration self-report (h)*[a]	10,375	6.8	1.5	6.6	1.8	6.7	1.7
		n	*%*	*n*	*%*	*n*	*%*
Sex*	10,950						
Male		2,829	50.1	2,932	55.3	5,761	52.6
Female		2,820	49.9	2,369	44.7	5,189	47.4
Race/ethnicity*	11,036						
White		3,476	61.2	3,082	57.5	6,555	59.4
Black		663	11.7	579	10.8	1,247	11.3
Hispanic		849	15.0	1,256	23.4	2,105	19.1
Other		687	12.1	447	8.3	1,134	10.3
Education	11,036						
High school or less		1,254	22.1	1,177	21.9	2,431	22.0
Some college		4,418	77.9	4,187	78.1	8,605	78.0
Income (yearly)*	10,751						
<\$50,000		2,226	40.5	1,729	32.9	3,955	36.8
≥\$50,000		3,264	59.5	3,532	67.1	6,796	63.2
Diurnal preference*	11,036						
Definitely morning type		1,856	32.7	1,960	36.5	3,816	34.6
Definitely evening type		1,156	20.4	780	14.5	1,936	17.5
Not definitely morning or evening type		2,660	46.9	2,624	48.9	5,284	47.9
Work shift category*	11,036						
Day shift only		4,168	73.5	3,421	63.8	7,589	68.8
Day and/or some evening shifts		974	17.2	1,330	24.8	2,304	20.9
Day/evening and some night shifts		288	5.1	392	7.3	680	6.2
Night shifts only		242	4.3	221	4.1	463	4.2
Vaccination number**	11,036						
0		1,317	55.8	1,045	44.2	2,362	21.4
1		417	29.6	990	70.4	1,407	12.7
2		1,663	45.8	1,968	54.2	3,631	32.9
3		1,961	61.4	1,231	38.6	3,192	28.9
4		314	70.7	130	29.3	444	4.0
Vaccination boosted**	11,036						
No (≤2 vaccinations)		3,397	45.9	4,003	54.1	7,400	67.1
Yes (>2 vaccinations)		2,275	62.6	1,361	37.4	3,636	32.9

[a]Participants with self-reported sleep duration <3 or >12 hours were excluded as improbable.
*$P < 0.05$, **$P \leq 0.001$, significant differences in means or proportions.

aggregate response favoring a proinflammatory response while asleep.[33] Some,[34,35] but not all,[36,37] have found that time of day influences the antibody response to COVID-19 vaccination. Therefore, it is possible that immunity to COVID-19 is less robust in morning chronotypes resulting in greater susceptibility to infection.

In this study, the association between working night shift and COVID-19 infection was the same as working day shift. However, working a mixture of shifts, particularly ones that included evening shifts, was associated with a higher likelihood of COVID-19 infection. These findings stand in contrast to some previous observations that have noted a positive association between rotating and consistent/permanent night shift work and COVID-19 infection.[24,25,27] However, not all studies have found a significant relationship among those who only worked consistent/permanent night shift.[23,26] Working night shifts and early morning shifts are associated with circadian misalignment as well as shorter sleep duration. Both may increase the propensity for COVID-19 infection as well as other respiratory contagions. However, night shift workers tend to have less interpersonal contact than day shift workers.[38] This may mitigate the adverse impact of circadian misalignment on increased risk of COVID-19 infection. Our results suggest that the impact of circadian misalignment and sleep loss, and consequent predisposition toward being infected with COVID-19 is greater among persons who irregularly perform shift work rather than in those who work permanent/consistent day or night shifts.

We observed a significant interaction between chronotype and shift work in which morning diurnal preference together with working a mixture of shifts was associated with the highest aOR of having had a COVID-19 infection. This implies that irregularity in sleep schedule was a major factor in susceptibility to COVID-19 infection in those with morning diurnal preference. Irregularity in sleep-wake patterns has been associated with higher levels of cardiovascular disease biomarkers[39] as well as a greater risk of cardiovascular disease.[40] Using UK Biobank data, sleep irregularity also has been demonstrated to increase risk of COVID-19 infection and its severity.[41] Potential explanatory mechanisms include the impact of sleep irregularity on reducing sleep duration as well as consequences of higher levels of circadian

TABLE 5. Odds Ratio (Adjusted) in Fully Adjusted Model[a] With Interactions for Reporting One or More COVID-19 Infections Based on Circadian Preference and Shift Work (N = 9,877)

	aOR	95% CI
Diurnal preference		
Neither morning nor evening preference	Referent	
Definite morning preference	1.23	1.16–1.32
Definite evening preference	0.79	0.73–0.85
Work shift category		
Day shift only	Referent	
Day and/or some evening shifts	1.25	1.10–1.41
Day/evening and some night shifts	1.18	0.97–1.44
Night shifts only	0.95	0.75–1.20
Diurnal preference x work shift interactions		
Neither morning nor evening preference x day shift only	Referent	
Morning preference x day and/or some evening shifts	1.87	1.28–2.74
Morning preference x day/evening and some night shifts	1.72	0.98–3.02
Morning preference x night shifts only	0.93	0.47–1.84
Evening preference x day and/or some evening shifts	0.89	0.59–1.33
Evening preference x day/evening and some night shifts	0.68	0.39–1.24
Evening preference x night shifts only	0.79	0.41–1.52

aOR, adjusted odds ratio; CI, confidence interval.

[a]Fully adjusted model includes age, sex, race, BMI, vaccination status (boosted vs not boosted), # of the following conditions: diabetes, asthma, sickle cell disease, cardiovascular disease, hypertension, cancer, chronic kidney disease, liver disease, and chronic obstructive pulmonary disease, and the following factors: education, income, employment, sleep duration, percent time working remotely, and employment sector.

misalignment. Both of these factors can contribute to greater amounts of both acute and chronic inflammation resulting in higher risk of COVID-19 infection.

Several other observations from our study are noteworthy. Remote workers in our study had a slightly higher COVID-19 infection rate, which is counterintuitive to the concept of less interpersonal contact should reduce infection risk.[42] However, this was not confirmed in a recent study where remote work was found to have a higher risk of COVID-19.[43] Possible explanations were that remote work led to a false sense of security and less use of personal protective measures such as mask wearing and handwashing as well as the opportunity to engage in other high-risk activities such as dining out with others.[43] We also noted that higher income was associated with greater COVID-19 infection risk. Although many studies have identified lower income as a risk factor for COVID-19 infection, others have noted the converse or no impact.[44] Income is associated with many factors, including type and place of employment, living conditions, educational attainment, race, and/or ethnicity. In our study, these factors favored a slightly greater COVID-19 rate in those with a higher income. Additionally, we observed that there was substantial variation in COVID-19 infection and shiftwork status among various employment sectors. Because of the heterogeneity between and within employment sectors and shiftwork status with respect to interpersonal contact, these differences were expected. We do not believe any of these factors altered our findings related to circadian preference in that they were included in our fully adjusted models.

Our study should be interpreted in the context of several limitations. First, all of the data were self-reported including ascertainment of both diurnal preference (using a single self-report item) and COVID-19 infection. However, sensitivity analyses using different definitions of COVID-19 infection were qualitatively similar to the findings reported herein. In addition, broadly similar to a previous report, we found that morning chronotypes were more prevalent than evening chronotypes, suggesting that our ascertainment of chronotype was acceptable.[45] Second, our analyses were cross-sectional and causal inference cannot be assumed. Third, although we attempted to adjust for a number of factors known to increase risk of COVID-19 infection, residual confounding is possible.

In conclusion, morning diurnal preference is associated with an increase and evening diurnal preference is associated with a decrease in COVID-19 infection. Neither working day nor night shifts were linked to an increase in prevalence of COVID-19 infection. However, COVID-19 infection was more likely in those working a mixture of shifts, with the greatest risk conferred on those with a morning chronotype. These findings may be informative for developing measures for greater COVID-19 surveillance of shift workers with a morning chronotype, particularly as first responders in health care and other settings are often engaged in shift work.

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