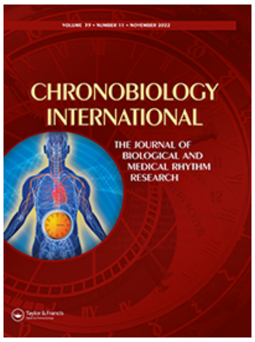

Chronobiology International

The Journal of Biological and Medical Rhythm Research

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icbi20

Shift workers are at increased risk of severe COVID-19 compared with day workers: Results from the international COVID sleep study (ICOSS) of 7141 workers

Bjørn Bjorvatn, Ilona Merikanto, Catia Reis, Maria Korman, Adrijana Koscec Bjelajac, Brigitte Holzinger, Luigi De Gennaro, Yun Kwok Wing, Charles M. Morin, Colin A. Espie, Christian Benedict, Anne-Marie Landtblom, Kentaro Matsui, Harald Hrubos-Strøm, Sérgio Mota-Rolim, Michael R. Nadorff, Giuseppe Plazzi, Rachel Ngan Yin Chan, Markku Partinen, Yves Dauvilliers, Frances Chung & Ingeborg Forthun

To cite this article: Bjørn Bjorvatn, Ilona Merikanto, Catia Reis, Maria Korman, Adrijana Koscec Bjelajac, Brigitte Holzinger, Luigi De Gennaro, Yun Kwok Wing, Charles M. Morin, Colin A. Espie, Christian Benedict, Anne-Marie Landtblom, Kentaro Matsui, Harald Hrubos-Strøm, Sérgio Mota-Rolim, Michael R. Nadorff, Giuseppe Plazzi, Rachel Ngan Yin Chan, Markku Partinen, Yves Dauvilliers, Frances Chung & Ingeborg Forthun (2022): Shift workers are at increased risk of severe COVID-19 compared with day workers: Results from the international COVID sleep study (ICOSS) of 7141 workers, Chronobiology International, DOI: 10.1080/07420528.2022.2148182

To link to this article: https://doi.org/10.1080/07420528.2022.2148182

CHRONOBIOLOGY INTERNATIONAL
https://doi.org/10.1080/07420528.2022.2148182

ORIGINAL ARTICLE

Shift workers are at increased risk of severe COVID-19 compared with day workers: Results from the international COVID sleep study (ICOSS) of 7141 workers

Bjørn Bjorvatn[a], Ilona Merikanto[b], Catia Reis[c], Maria Korman[d], Adrijana Koscec Bjelajac[e], Brigitte Holzinger[f], Luigi De Gennaro[g], Yun Kwok Wing[h], Charles M. Morin[i], Colin A. Espie[j], Christian Benedict[k], Anne-Marie Landtblom[l], Kentaro Matsui[m], Harald Hrubos-Strøm[n], Sérgio Mota-Rolim[o], Michael R. Nadorff[p], Giuseppe Plazzi[q], Rachel Ngan Yin Chan[h], Markku Partinen[r], Yves Dauvilliers[s], Frances Chung[t], and Ingeborg Forthun[a]

[a]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway and Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Bergen, Norway; [b]SleepWell Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland and Orton Orthopaedics Hospital, Helsinki, Finland; [c]Universidade Católica Portuguesa, Católica Research Centre for Psychological, Family and Social Wellbeing, Lisbon, Portugal and Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina de Lisboa, Lisboa, Portugal; [d]Department of Occupational Therapy, Faculty of Health Sciences, Ariel University, Ariel, Israel; [e]Institute for Medical Research and Occupational Health, Zagreb, Croatia; [f]Institute for Consciousness and Dream Research, Medical University of Vienna, Wien, Postgraduate, Sleep Coaching, Vienna, Austria; [g]Department of Psychology, Sapienza University of Rome, Roma, Lazio, Italy and IRCCS Fondazione Santa Lucia, Roma, Italy; [h]Li Chiu Kong Family Sleep Assessment Unit, Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China; [i]Centre de recherche CERVO/Brain Research Center, École de psychologie, Université Laval, Quebec, Quebec, Canada; [j]Sir Jules Thorn Sleep and Circadian Neuroscience Institute, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; [k]Department of Pharmaceutical Biosciences, Molecular Neuropharmacology, Uppsala University, Uppsala, Sweden; [l]Department of Medical Sciences, Neurology, Uppsala University, Uppsala, Sweden and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden; [m]Department of Clinical Laboratory, National Center Hospital, National Center of Neurology and Psychiatry, Kodaira, Japan; [n]Department of Otorhinolaryngology, Akershus University Hospital, Lørenskog, Norway and Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [o]Brain Institute, Physiology and Behavior Department and Onofre Lopes University Hospital, Federal University of Rio Grande do Norte, Natal, Brazil; [p]Department of Psychology, Mississippi State University, Mississippi, Mississippi, USA; [q]IRCCS Istituto Delle Scienze Neurologiche di Bologna, Bologna, Italy; and Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [r]Department of Clinical Neurosciences, University of Helsinki Clinicum Unit, Helsinki, Finland and Helsinki Sleep Clinic, Terveystalo Healthcare Services, Helsinki, Finland; [s]Sleep-Wake Disorders Center, Department of Neurology, Gui-de-Chauliac Hospital, Institute for Neurosciences of Montpellier INM, INSERM, University of Montpellier, Montpellier, France; [t]Department of Anesthesia and Pain Management, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, ON, Canada

ABSTRACT

The present study had two main aims. First, to investigate whether shift/night workers had a higher prevalence and severity of COVID-19 compared with day workers. Second, to investigate whether people regularly working in face-to-face settings during the pandemic exhibited a higher prevalence and severity of COVID-19 compared with those having no need to be in close contact with others at work. Data consisted of 7141 workers from 15 countries and four continents who participated in the International COVID Sleep Study-II (ICOSS-II) between May and December 2021. The associations between work status and a positive COVID-19 test and several indications of disease severity were tested with chi-square tests and logistic regressions adjusted for relevant confounders. In addition, statistical analyses were conducted for the associations between face-to-face work and COVID-19 status. Results showed that shift/night work was not associated with an increased risk of COVID-19 compared to day work. Still, shift/night workers reported higher odds for moderate to life-threatening COVID-19 (adjusted odds ratio (aOR) = 2.71, 95%-confidence interval = 1.23–5.95) and need for hospital care (aOR = 5.66, 1.89–16.95). Face-to-face work was associated with an increased risk of COVID-19 (aOR = 1.55, 1.12–2.14) but not with higher disease severity. In conclusion, shift/night work was not associated with an increased risk of COVID-19, but when infected, shift/night workers reported more severe disease. Impaired sleep and circadian disruption commonly seen among shift/night workers may be mediating factors. Working face-to-face increased the risk of COVID-19, likely due to increased exposure to the virus. However, face-to-face work was not associated with increased disease severity.

ARTICLE HISTORY
Received 13 October 2022
Revised 4 November 2022
Accepted 10 November 2022

KEYWORDS
Coronavirus; SARS-CoV-2; night work; shift work; face-to-face work

CONTACT Bjørn Bjorvatn bjorn.bjorvatn@uib.no Department of Global Public Health and Primary Care, University of Bergen, Årstadveien 17, N-5009 Bergen, Norway
Supplemental data for this article can be accessed online at https://doi.org/10.1080/07420528.2022.2148182

Introduction

Shift work is associated with several negative health outcomes, including increased risk of infections (Kecklund and Axelsson 2016; Rizza et al. 2021; Salehinejad et al. 2022). Even though the underlying pathophysiological mechanisms behind this higher risk remain unclear, studies indicate that shift work may negatively impact the immune system, possibly as a result of interrelated sleep problems and circadian disruption (Besedovsky et al. 2019; Bjorvatn et al. 2020; Kecklund and Axelsson 2016; Liu et al. 2021). Sleep of adequate duration and quality is assumed to reduce the risk of infectious diseases and improve infection outcomes (Besedovsky et al. 2019; Lee and Glickman 2021; Robinson et al. 2021; Salehinejad et al. 2022). This notion is supported in a recent study using two large population cohorts, where an insomnia diagnosis causally predisposed for influenza, upper respiratory infections and severe COVID-19 (Jones et al. 2022). Studies suggest that prolonged sleep impairment (e.g., long-term short sleep duration and sleep disturbances) can lead to chronic, systemic low-grade inflammation and is associated with a multitude of diseases (Besedovsky et al. 2019; Irwin et al. 2016). Still, the association between shift work and infectious diseases is understudied but of special interest now during the COVID-19 pandemic.

Lim and colleagues reviewed the hypothesis that shift workers may be at increased risk of COVID-19 and discussed the role of the circadian rhythm and melatonin (Lim et al. 2020). However, very few studies have specifically addressed whether shift workers do, in fact, have a higher prevalence and severity of COVID-19. In a study with more than 18,000 participants from the UK Biobank cohort, people working at night had a higher prevalence of COVID-19 than others with an odds ratio of 1.85 (Fatima et al. 2021). One major limitation of that study was that data on work schedule was obtained several years before the pandemic started, thus making the association between shift work and risk of COVID-19 uncertain. In a smaller Italian study among 1180 health care workers, night work and obesity were associated with higher odds of COVID-19 (Rizza et al. 2021). The study included only 30 participants who reported having had COVID-19.

Based on these shortcomings in previous studies on shift work and COVID-19, the present study involving more than 7000 workers from 15 countries across four continents had two main aims. First, to investigate whether shift/night workers had a higher prevalence and severity of COVID-19 compared with day workers. Second, to investigate whether people regularly working in close proximity to other people (face-to-face) exhibited a higher prevalence and severity of COVID-19 than those having no need to be in close contact with others at work. Shift workers, e.g., health care workers, may work in closer proximity to other people than non-shift workers, and we therefore adjusted for face-to-face work when investigating the risk of COVID-19 among shift/night workers. We hypothesized a higher prevalence and severity of COVID-19 among shift/night workers and among those working in face-to-face settings.

Materials and methods

Study design and participants

The International COVID Sleep Study (ICOSS) is an international collaboration with sleep and circadian rhythm experts across four continents (Europe, Asia, North America, and South America). The collaboration was established in March 2020 during the beginning of the COVID-19 pandemic (Partinen et al. 2021). The present study is based on data from the second wave of the ICOSS (ICOSS-II) (Merikanto et al. 2022). Data were collected between May and December 2021 in 16 countries: Austria, Brazil, Bulgaria, Canada, China (Hong Kong), Croatia, Finland, France, Germany, Israel, Italy, Japan, Norway, Portugal, Sweden, and USA. A total of 15 813 people agreed to participate and completed an extensive questionnaire online. In the present study, data from USA (n = 933) were excluded due to these participants being younger (mean age 20 years). In addition, 85 participants who did not report country were excluded. Furthermore, since we were only interested in the working population, we excluded 3869 individuals who were not working at the time of completing the questionnaire (students, unemployed, retired, at home, temporary laid off) and 3785 who had missing data on working status. This resulted in a study sample of 7141 respondents.

The online survey was implemented through different online platforms across countries, most commonly by Qualtrics (https://www.qualtrics.com). The survey was promoted through e.g., newspapers, university communication systems, social media platforms (e.g., Facebook, Twitter, Instagram), sleep societies' websites and other professional societies and organizations. The complete survey took about 20–40 minutes to complete, depending on whether the participant reported having had COVID-19 or not.

Subjects voluntarily and anonymously took part in the survey. To access the questions, participants had to give their consent to participate, and they needed to be at least 18 years of age. Participants did not receive any monetary compensation. General data protection regulations were enforced to ensure privacy and confidentiality. This research was conducted according to the Declaration of Helsinki, and all countries obtained ethical approval or exemptions in keeping with national research governance and regulations. The study adhered to the ethical standards and methods outlined by Portaluppi et al. (2010).

Survey items analyzed in the present study

The participants responded to a question about their present work situation with the following eight response options: Student; Regular day work; Irregular day work/freelancer/artist/research; Shift work/night work; Unemployed; Retired; At home (no salary); and Temporary laid off. Only participants currently working were included in the analyses, leaving a variable with three categories: Regular day work; Irregular day work/freelancer/artist/research (named Non-regular day work); and Shift/night work. Furthermore, participants responded to a question about whether they had been working in face-to-face contact with other people during the pandemic with the following six response options: 1. Patient care (nurse, physician, other); 2. Other health or social care; 3. Personal services (barber, waiter, bartender, other); 4. Other jobs with contact with other people; 5. No need to be in close contact with other people; and 6. I have not been working or this question does not fit me well. For the present study, this variable was dichotomized (yes, including response options 1–4; no, response option 5).

The following socio-demographic data were collected: Age (18–99 years), gender (male; female; other), marital status (cohabiting (married/relationship); single (including single/divorced/separated/widowed)), race/ethnicity (Caucasian/white; Asian; African; Hispanic; other), highest attained education (primary/elementary/lower secondary school; secondary school/high school/vocational school; university/college/or above), children at home (living alone; living with children under age 18). Weight and height were self-reported, and body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Obesity was defined as BMI ≥30 kg/m^2. Habitual nocturnal sleep duration and sleep need were self-reported from drop-down menus, and sleep debt (≤2 hour versus >2 hour) was calculated based on the difference between sleep duration and sleep need. Furthermore, the participants indicated their COVID-19 vaccination status (no vaccination; one vaccination, two vaccinations).

COVID-19 status

All participants self-reported if they had tested positive for COVID-19 (no; yes). Participants with positive COVID-19 status were further asked about disease severity using the following five response options: No marked symptoms (no fatigue, fever, coughing or any other noticeable symptoms to indicate illness except possibly a loss of smell/taste); Mild symptoms (e.g., cough, fever, muscle pains etc. but no pneumonia) that disappeared quite soon; Moderate disease (receiving different medications as a treatment, non-severe pneumonia, but no received extra-oxygen); Severe disease (receiving extra-oxygen, severe pneumonia, IV lines attached); and Life-threatening disease (invasive ventilation or maximum available respiratory support, IV lines attached, sepsis, heart attack, stroke, embolism, acute respiratory distress syndrome). For the present study, this severity variable was dichotomized into 'no marked symptoms/mild symptoms' versus 'moderate/severe/life-threatening disease.' The highest level of care received during the acute phase of COVID-19 was indicated by the following six response options: At home/self-care/over-the-counter medications; At home/outpatient/telemedicine; Hospital ward: no oxygen therapy; Hospital ward: oxygen therapy; ICU admission: oxygen therapy/noninvasive ventilation; and ICU admission: intubated/invasive ventilation. This level of care variable was dichotomized into 'no hospitalization' (first two response options) versus 'hospitalization/ICU' (last four response options). Participants with positive COVID-19 status also reported how many weeks (from onset of symptoms) it took to return to the same level of daily functioning as before having the infection (drop-down menu: one week or less; two weeks; three weeks, and so on until more than 40 weeks/still persisting). This symptom duration variable was dichotomized into 'less than 8 weeks' versus '8 weeks or more.'

Statistics

Data were analyzed with Stata/SE version 17.0 (StataCorp, USA). We used chi-square tests to compare the risk of positive COVID-19 status, moderate to life-threatening disease, hospitalization, and symptom duration of ≥8 weeks across work status. Furthermore, we estimated odds ratio (OR) with 95% confidence interval (CI) for positive COVID-19 status, moderate to life-threatening disease, hospitalization, and symptom duration of ≥8 weeks using logistic regressions. While the analyses regarding the risk of positive COVID-19 status included all participants, the analyses for the other outcomes, only participants with positive COVID-19 status were considered. We applied three statistical models. In the crude model, only the exposure of interest was included. In model 1, we adjusted for age (age and age squared to account for a non-linear association), sex, marital status, highest attained education, ethnicity, and children living at home. In model 2, we additionally adjusted for obesity, vaccination status, and face-to-face work (face-to-face work was only adjusted for when including work status as the main exposure), as these factors may influence COVID-19 status. Analyses were weighted using the population age and sex distribution of each country (making the samples more representative of the population of each country). Supplementary Table 1 shows work status by country, and Supplementary Table 2 shows the age and sex distribution of the sample by country. In all statistical analyses, weighting and stratification were accounted for using the *svy* command in Stata. The significance level was set to $p \leq .05$.

Results

Table 1 presents the characteristics of the study sample. On average, shift/night workers (8.2% of the sample) were younger, had lower educational level, were more often involved in face-to-face work, and had more often received two vaccine doses compared to regular day workers (76.9% of the sample) and non-regular day workers (14.9% of the sample). Furthermore, 26.5% of the shift/night workers reported a sleep debt of >2 hour compared with 15.7% of the regular day workers and 13.3% of the non-regular day workers (Table 1).

A total of 1134 participants reported that they had tested positive for COVID-19 (15.9%). The prevalence of COVID-19 was 22.5% among shift/night workers as compared to 17.3% among non-regular day workers and 17.0% among regular day workers (Table 2). These differences in COVID-19 status were not significant (chi-square, p-value 0.087). Working face-to-face with other people during the pandemic was significantly associated with positive COVID-19 status ($p < .01$, Table 2).

Table 1. Characteristics of total study sample and by work status, not weighted and stratified.

	Total sample (n = 7141)	Regular day work (n = 5491; 76.9%)	Non-regular day work[1] (n = 1065; 14.9%)	Shift/night work (n = 585; 8.2%)	p-value[2]
Age, mean (sd), n = 7141	43.7 (12.4)	43.8 (12.1)	45.0 (13.6)	40.7 (12.6)	**<0.001**
Sex, n = 7139 (column %)					0.090
Male	2487 (34.8)	1927 (35.1)	380 (35.8)	180 (30.8)	
Female	4652 (65.2)	3564 (64.9)	683 (64.3)	405 (69.2)	
Marital status, n = 7134 (column %)					**<0.001**
Single	2487 (34.9)	1816 (33.1)	444 (41.7)	227 (38.9)	
Cohabiting	4647 (65.1)	3670 (66.9)	620 (58.3)	357 (61.1)	
Ethnicity, n = 7105 (column %)					**0.002**
Caucasian/White	4625 (65.1)	3572 (65.4)	666 (62.8)	387 (66.5)	
Asian	1965 (27.7)	1531 (28.0)	298 (28.1)	136 (23.4)	
African	59 (0.8)	39 (0.7)	15 (1.4)	5 (0.9)	
Hispanic	127 (1.8)	86 (1.6)	24 (2.3)	17 (2.9)	
Other	329 (4.6)	235 (4.3)	57 (5.4)	37 (6.4)	
Highest attained education, n = 6893 (column %)					**<0.001**
Primary/elementary/lower secondary school	195 (2.8)	136 (2.6)	33 (3.1)	26 (4.6)	
Secondary school/high school/vocational school	1890 (27.4)	1363 (25.9)	293 (27.8)	234 (41.1)	
University, College or above	4808 (69.8)	3772 (71.6)	727 (69.0)	309 (54.3)	
Children at home, n = 4842 (column %)					**0.002**
No	1698 (35.1)	1269 (33.9)	292 (40.8)	137 (36.1)	
Yes	3144 (64.9)	2477 (66.1)	424 (59.2)	243 (64.0)	
Sleep debt, n = 7095 (column %)					**<0.001**
≤2 hour	5945 (83.8)	4601 (84.3)	916 (86.7)	428 (73.5)	
>2 hour	1150 (16.2)	856 (15.7)	140 (13.3)	154 (26.5)	
Obesity (BMI ≥30), n = 7127 (column %)					0.168
No	6011 (84.3)	4603 (84.0)	917 (86.3)	491 (84.4)	
Yes	1116 (15.7)	879 (16.0)	146 (13.7)	91 (15.6)	
COVID-19 vaccination status, n = 7137 (column %)					**<0.001**
No vaccine	1510 (21.2)	1102 (20.1)	302 (28.4)	106 (18.2)	
1 dose	1187 (16.6)	915 (16.7)	186 (17.5)	86 (14.7)	
2 doses	4440 (62.2)	3472 (63.3)	576 (54.1)	392 (67.1)	
Face-to-face work, n = 7126 (column %)					<0.001
Patient care (nurse, physician, other)	997 (14.0)	676 (12.3)	95 (8.9)	226 (38.7)	
Other health or social care	848 (11.9)	668 (12.2)	101 (9.5)	79 (13.5)	
Personal services (barber, waiter, bartender)	261 (3.7)	143 (2.6)	78 (7.3)	40 (6.9)	
Other jobs with contacts to other people	2525 (35.4)	2057 (37.6)	307 (28.9)	161 (27.6)	
No need to be in close contact with others	1777 (24.9)	1412 (25.8)	329 (30.9)	36 (6.2)	
Not been working/this question is not relevant	718 (10.1)	522 (9.5)	154 (14.5)	42 (7.2)	

[1]Includes irregular day work/freelancer/artist/research
[2]p-value from chi-square test or ANOVA

Table 2. Prevalence of positive COVID-19 test by type of work among the participating workers from 15 different countries, weighted[1] results.

	Prevalence (%)	Chi-square test, p-value[2]
Current work status (n = 6566)		X^2=2.44, p = .087
Regular day work	854 (17.0)	
Non-regular day work[3]	177 (17.3)	
Shift/night work	116 (22.5)	
Face-to-face work (n = 5800)		**X^2=8.74, p = .003**
No close contact with others	244 (14.3)	
Yes, contact with others	775 (18.9)	

[1]Weighted according to age and sex distribution in each country
[2]p-value from design-adjusted Pearson chi-square test
[3]Includes irregular day work/freelancer/artist/research

Table 3. Prevalence of severe disease, need for hospital care, and long symptom duration among 1145 participants who have tested positive for COVID-19, weighted[1] results.

	Moderate to life-threatening disease (%)	Chi-square test, p-value[2]	Need for hospital care (%)	Chi-square test, p-value[2]	Symptoms ≥ 8 weeks (%)	Chi-square test, p-value[2]
Work status		X^2=0.68, p = .506		**X^2=4.84, p = .008**		X^2=0.49, p = .614
Regular day work	298 (35.3)		133 (15.7)		356 (44.4)	
Non-regular day work[3]	61 (34.3)		24 (13.9)		80 (46.7)	
Shift/night work	48 (43.0)		37 (33.3)		51 (51.3)	
Face-to-face work		X^2=0.48 P = .488		X^2=2.34, p = .126		X^2=0.085, p = .771
No	93 (38.2)		54 (22.4)		100 (44.4)	
Yes	267 (34.7)		121 (15.8)		335 (46.0)	

[1]Weighted according to age and sex distribution in each country
[2]p-value from design-adjusted Pearson chi-square test
[3]Includes irregular day work/freelancer/artist/research

Table 3 shows the prevalence of severe disease, need for hospital care, and long symptom duration in relation to work status and in relation to face-to-face work. Although shift/night workers had higher prevalence of moderate to life-threatening disease and symptoms lasting ≥8 weeks, only the difference in the need for hospital care was significant in the chi-square tests (Table 3). There was no statistically significant difference in reporting severe disease, need for hospital care, or long symptom duration by face-to-face work (Table 3).

Table 4 shows logistic regression analyses with COVID-19 status as the dependent variable and work status and face-to-face work as predictors. Regular day work and not working in close contact with others during the pandemic were references, respectively. Shift/night work was significantly associated with increased odds (OR = 1.42, CI = 1.03–1.94) for COVID-19 in the crude analysis, but not in the adjusted analyses (Table 4). Non-regular day work was associated with reduced odds (OR = 0.66, 0.45–0.97) for COVID-19 in the fully adjusted model. Working face-to-face during the pandemic was associated with increased odds for COVID-19 in both crude and the fully adjusted (OR = 1.55, 1.12–2.14) model.

Table 5 shows logistic regression analyses with severe disease, need for hospital care, and long symptom duration as dependent variables. Shift/night work was associated with increased odds of moderate to life-threatening disease (OR = 2.71, 1.23–5.95) and increased odds of hospitalization (OR = 5.66, 1.89–16.95) in the fully adjusted logistic regression analyses. Face-to-face work was not associated with

Table 4. Odds of positive COVID-19 test by work status and contact with others, weighted and stratified.

	Crude OR (95% CI)	Adjusted OR (95% CI)[1]	Adjusted OR (95% CI)[2]
Work status			
Regular day work	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Non-regular day work[3]	1.02 (0.80–1.31)	0.90 (0.64–1.26)	**0.66 (0.45–0.97)**
Shift/night work	**1.42 (1.03–1.94)**	1.19 (0.76–1.86)	1.23 (0.78–1.96)
Face-to-face work			
No	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Yes	**1.40 (1.12–1.75)**	1.35 (0.98–1.86)	**1.55 (1.12–2.14)**

[1]Adjusted for age and age squared, sex, highest attained education, marital status, children living at home, ethnicity
[2]Adjusted for age and age squared, sex, highest attained education, marital status, children living at home, ethnicity, obesity, vaccination status and face-to-face contact (only in model on work status)
[3]Includes irregular day work/freelancer/artist/research

Table 5. Odds of moderate-life threatening disease, need for hospital care, and long duration of symptoms by work status and contact with others among COVID-19-positive participants, weighted and stratified results.

	Moderate to life-threatening disease		
	Crude OR (95% CI)	Adjusted[1] OR (95% CI)	Adjusted[2] OR (95% CI)
Work status			
Regular day work	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Non-regular day work[3]	0.96 (0.60–1.52)	0.71 (0.35–1.46)	1.05 (0.47–2.34)
Shift/night work	1.38 (0.76–2.52)	**2.67 (1.17–6.09)**	**2.71 (1.23–5.95)**
Face-to-face work			
No	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Yes	0.86 (0.56–1.32)	0.95 (0.53–1.70)	0.92 (0.51–1.66)
		Need for hospital care	
	Crude OR (95% CI)	Adjusted[1] OR (95% CI)	Adjusted[2] OR (95% CI)
Work status			
Regular day work	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Non-regular day work[3]	0.86 (0.43–1.74)	1.27 (0.56–2.92)	1.71 (0.57–5.15)
Shift/night work	**2.67 (1.34–5.35)**	**3.62 (1.23–10.67)**	**5.66 (1.89–16.95)**
Face-to-face work			
No	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Yes	0.65 (0.37–1.13)	0.67 (0.32–1.42)	0.75 (0.35–1.57)
		Long symptom duration (≥8 weeks)	
	Crude OR (95% CI)	Adjusted[1] OR (95% CI)	Adjusted[2] OR (95% CI)
Work status			
Regular day work	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Non-regular day work[3]	1.09 (0.69–1.73)	1.01 (0.54–1.89)	1.34 (0.67–2.67)
Shift/night work	1.32 (0.75–2.32)	1.15 (0.50–2.63)	1.08 (0.43–2.69)
Face-to-face work			
No	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Yes	1.06 (0.70–1.61)	1.53 (0.89–2.65)	1.61 (0.93–2.77)

[1]Adjusted for age and age squared, sex, highest attained education, marital status, children living at home, ethnicity.
[2]Adjusted for age and age squared, sex, highest attained education, marital status, children living at home, ethnicity, obesity, vaccination status and face-to-face contact (only in model on work status).
[3]Includes irregular day work/freelancer/artist/research

moderate to life-threatening disease, hospitalization or long symptom duration, neither in crude nor adjusted regression analyses (Table 5).

Discussion

When adjusted for relevant confounders, shift/night workers did not have an increased risk of COVID-19 as compared to regular day workers. However, shift/night workers reported significantly more severe disease and need for hospital care than regular day workers in adjusted models. Shift/night workers did not seem to suffer from prolonged symptom duration, as we found no significant difference compared to regular day workers in reporting a recovery period of eight or more weeks. Non-regular day work was not associated with an increased risk of COVID-19 or disease severity, but in fact was associated with a reduced risk of COVID-19 in the fully adjusted model. Furthermore, face-to-face work was associated with increased risk of COVID-19 but not with severe disease, need for hospital care, and long symptom duration. These findings suggest that our hypotheses were partially confirmed.

The finding that shift/night workers did not have a significant increased risk of COVID-19 contrasts with findings from two other studies (Fatima et al. 2021; Rizza et al. 2021). In data from the UK Biobank cohort, people working at night reported a significant 1.85 higher odds for COVID-19 compared to people not working at night (Fatima et al. 2021). Similarly, an Italian study among health care workers reported that night work was associated with higher odds of COVID-19 (Rizza et al. 2021). These contrasting findings may be related to differences in methodologies and time frames of data acquistion. SARS-CoV-2 is considered very contagious, and our data suggest that the risk of becoming infected does not differ much between regular day workers and shift/night workers. However, when infected, shift/night workers are more likely to suffer from severe disease. This may be related to the impact that sleep deficiency and circadian disruption have on the immune system (Besedovsky et al. 2019; Lee and Glickman 2021). Shift/night workers need to sleep and work at a circadian phase that is not according to their biological clock (Bjorvatn and Pallesen 2009; Kecklund and Axelsson 2016). As shown in Table 1, more shift/night workers reported a sleep debt of >2 hour as compared to both regular and non-regular day workers. This may possibly explain why we found an increased disease burden for these workers.

Sufficient sleep of good quality is assumed to reduce the risk of infections, improve infection outcome and vaccination responses (Besedovsky et al. 2019; Lee and Glickman 2021; Robinson et al. 2021). This notion is supported by a study showing that the susceptibility for rhinovirus infection (the common cold) is increased in people sleeping less than 6 hours (Prather et al. 2015). Furthermore, prolonged sleep deficiency (e.g., chronic short sleep duration and sleep disturbances) can lead to chronic, systemic low-grade inflammation (Besedovsky et al. 2019; Irwin et al. 2016). A Swedish study showed that acute sleep deprivation leads to functional and structural changes in blood neutrophils (Christoffersson et al. 2014). Interestingly, an influenza vaccination study compared habitual sleep with restricted sleep (time in bed was restricted to 4 hours per night for 4 days before and 2 days after the vaccination) and found that influenza-virus-specific antibody titers after vaccination were doubled in participants with habitual sleep compared to restricted sleep (Spiegel et al. 2002). Furthermore, short sleep duration, sleep disturbances and circadian misalignment, all commonly seen among shift/night workers, have been reported to be associated with increased levels of pro-inflammatory biomarkers such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor (TNF) (Besedovsky et al. 2019; Irwin et al. 2016).

Studies investigating the association between shift/night work and immunity are still few and show conflicting results. In a cross-sectional study among airline employees, Puttonen et al. (2011) reported that rotating shift work was associated with increased systemic inflammation. In a longitudinal study among nurses, IL-1beta and TNF-alpha were significantly lower in shift workers compared to day workers at baseline, but not at 12 months follow-up. Moreover, no effect of shift work on immunological biomarkers was present at follow-up when data were adjusted for baseline values and job seniority (Copertaro et al. 2011). One study compared day workers with rotating shift workers and the latter showed higher levels of leucocytes (Sookoian et al. 2007). Furthermore, another study among nurses showed that natural killer (NK) cell activity was reduced following night work compared to day work (Nagai et al. 2011). However, one study with night shift workers and non-shift workers reported no association in relation to work status on a range of cytokines. Still, night work was associated with an increased number of monocytes and lymphocytes (Loef et al. 2019). In a Norwegian study among nurses, short sleep duration (<6 hours) was associated with lower IL-1beta levels and higher TNF-alpha levels, but no association between self-reported sleep quality and immunological biomarkers was seen (Bjorvatn et al. 2020). More research is clearly needed to elucidate how shift and night work affect health and the immune system.

In the fully adjusted regression analysis, we found a reduced risk of COVID-19 among non-regular day workers compared to regular day workers. This may at first glance be surprising, as non-regular day workers may possibly suffer from sleep deficiency, and thereby having increased risk of COVID-19. However, this group of workers was heterogenous, and included irregular day work, freelancer, artist, and research. This kind of work may have allowed the workers to follow their own preferred circadian rhythm more often than regular day workers, and this may reduce sleep problems, sleep loss and circadian misalignment. Our data corroborated this interpretation when we examined who had a sleep debt of >2 hours. Fewer non-regular day workers reported such a sleep debt compared with regular day workers. Furthermore, non-regular day workers may have worked fewer hours per day/week than the other work groups, possibly influencing the results.

Working face-to-face with other people during the pandemic increased the risk of COVID-19. The coronavirus is considered to be very contagious and working in close proximity to others increases the risk of exposure to the virus, and thereby to be infected (Buitrago-Garcia et al. 2022). Interestingly, face-to-face work did not increase the severity of the disease. Thus, even though people working face-to-face with other people have an increased risk of the disease, they do not seem to be at increased risk of becoming severely ill. One possible explanation is that sleep and the circadian rhythm may not be compromised by face-to-face work, in contrast to what is typical in shift/night work.

Strengths and limitations

One major strength was the diversity of our sample, with participants coming from 15 different countries spanning four continents. This diversity helps increase the generalizability of our findings compared to those recruiting participants from just one country, which increases the impact of each location's local COVID-19 response. Further, more than 1100 participants reported to have tested positive for COVID-19, rendering our study population available for multiple statistical comparisons and adjustment for relevant confounders (including obesity, vaccination status and face-to-face work when studying the risk among shift/night workers). However, a limitation was that for some of the analyses the comparison groups were small (e.g., not many participants were hospitalized due to COVID-19), making these interpretations more uncertain. Another strength was that all data were weighted according to the sex and age distribution in each country to make the samples more representative. Still, there were differences between countries in the sample distribution of sex and age, and also in relation to work status, and this needs to be considered when interpreting the results. One major limitation was that the participants reported current work status, and this may have changed from when they tested positive for COVID-19. However, we do not consider it very likely that this influenced the main findings. Another potential bias is that shift workers may be more likely to have been tested for COVID-19 because of frequent obligatory tests (e.g., health care workers). This can contribute to a higher observed risk of COVID-19 in this group, and may contribute to an unfair comparison when estimating relative risks (Griffith et al. 2020). Furthermore, studies show that morning vaccination enhances antibody response more than afternoon vaccination (de Bree et al. 2020; Long et al. 2016). Whether this influenced the present results is unclear, as we have no data on the time of vaccination in the different work groups. Other limitations include potential recall bias, convenience samples, and lack of more detailed information regarding work schedules. For instance, we have no information about workload (e.g., hours of work per day/week) in any of the groups or the number of night shifts worked.

In conclusion, shift/night work was not associated with increased risk of COVID-19, but when infected, shift/night workers reported more severe disease. Working face-to-face increased the risk of COVID-19, but had no association with disease severity.

Acknowledgements

This study did not receive any specific funding. We acknowledge Thomas Penzel (Germany), Juliana Yordanova (Bulgaria) and Yuichi Inoue (Japan) for being instrumental in providing data to this study.

Disclosure statement

Dr. Bjorvatn reports that he has served as consultant for F. Hoffmann-La Roche Ltd and Cura of Sweden, and received honoraria for lectures from Sanofi-Aventis and AGB-Pharma AB. Dr. Chung reports grants from Ontario Ministry of Health Innovation Grant, grants from ResMed Foundation and University Health Network Foundation, and consultation fees from Takeda Pharma, outside the submitted work. Dr. Espie reports grants from the Wellcome Trust and NIHR (HTA) and is a co-founder and a shareholder in Big Health, outside of the submitted work. Dr. Holzinger reports grants from the City of Vienna, Cultural Department of the City of Vienna. Dr. De Gennaro reports consulting fees from Idorsia. Dr Landtblom reports personal fees from Takeda, Jazz Pharmaceuticals and UCB, as well as a research grant from Aoporphan drugs. Dr. Matsui reports personal fees from Eisai, Meiji Seika Pharma, Mochida, MSD, Otsuka Pharmaceutical, and Yoshitomi Pharmaceutical, outside the submitted work; Dr. Plazzi reports reseach grant from Italian Institute of Health and participated in advisor board with Bioprojet, Jazz Pharmaceuticals, Takeda, Idorsia, Orexia; Dr. Morin reports research grants from the Canadian Institutes for Health Research, Eisai, Idorsia, and Lallemand Health; consulting fees from Eisai, Idorsia, Pear Therapeutics and Sunovion; and royalties from Mapi Research Trust, all outside the submitted work. Dr. Partinen reports personal fees and other from Bioprojet, other from Jazz Pharmaceuticals, personal fees from UCB Pharma, personal fees from GSK, personal fees from Takeda, personal fees and other from MSD, personal fees from Orion, and personal fees and other from Umecrine. Dr. Wing reports personal fees for delivering a lecture-Eisai Co. Ltd and personal fees from Sponsorship from Lundbeck HK Ltd, outside the submitted work. The other authors have no disclosure of interest.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Bjørn Bjorvatn http://orcid.org/0000-0001-7051-745X
Charles M. Morin http://orcid.org/0000-0002-8649-8895
Michael R. Nadorff http://orcid.org/0000-0002-8107-7514
Rachel Ngan Yin Chan http://orcid.org/0000-0002-3009-3565

Data availability statement

The data that support the findings of this study are available from the corresponding author, BB, upon reasonable request.

References

Besedovsky L, Lange T, Haack M. 2019. The sleep-immune crosstalk in health and disease. Physiol Rev. 99:1325–80. doi:10.1152/physrev.00010.2018

Bjorvatn B, Axelsson J, Pallesen S, Waage S, Vedaa O, Blytt KM, Buchvold HV, Moen BE, Thun E. 2020. The association between shift work and immunological biomarkers in nurses. Front Public Health. 8:415. doi:10.3389/fpubh.2020.00415

Bjorvatn B, Pallesen S. 2009. A practical approach to circadian rhythm sleep disorders. Sleep Med Rev. 13:47–60. doi:10.1016/j.smrv.2008.04.009

Buitrago-Garcia D, Ipekci AM, Heron L, Imeri H, Araujo-Chaveron L, Arevalo-Rodriguez I, Ciapponi A, Cevik M, Hauser A, Alam MI, et al. 2022. Occurrence and transmission potential of asymptomatic and presymptomatic

SARS-CoV-2 infections: Update of a living systematic review and meta-analysis. PLoS Med. 19:e1003987. doi:10.1371/journal.pmed.1003987

Christoffersson G, Vagesjo E, Pettersson US, Massena S, Nilsson EK, Broman JE, Schioth HB, Benedict C, Phillipson M. 2014. Acute sleep deprivation in healthy young men: Impact on population diversity and function of circulating neutrophils. Brain Behav Immun. 41:162–72. doi:10.1016/j.bbi.2014.05.010

Copertaro A, Bracci M, Gesuita R, Carle F, Amati M, Baldassari M, Mocchegiani E, Santarelli L. 2011. Influence of shift-work on selected immune variables in nurses. Ind Health. 49:597–604. doi:10.2486/indhealth.MS1210

de Bree LCJ, Mourits VP, Koeken VA, Moorlag SJ, Janssen R, Folkman L, Barreca D, Krausgruber T, Fife-Gernedl V, Novakovic B, et al. 2020. Circadian rhythm influences induction of trained immunity by BCG vaccination. J Clin Invest. 130:5603–17. doi:10.1172/JCI133934

Fatima Y, Bucks RS, Mamun AA, Skinner I, Rosenzweig I, Leschziner G, Skinner TC. 2021. Shift work is associated with increased risk of COVID-19: Findings from the UK Biobank cohort. J Sleep Res. 30:e13326. doi:10.1111/jsr.13326

Griffith GJ, Morris TT, Tudball MJ, Herbert A, Mancano G, Pike L, Sharp GC, Sterne J, Palmer TM, Davey Smith G, et al. 2020. Collider bias undermines our understanding of COVID-19 disease risk and severity. Nat Commun. 11:5749. doi:10.1038/s41467-020-19478-2

Irwin MR, Olmstead R, Carroll JE. 2016. Sleep disturbance, sleep duration, and inflammation: A systematic review and meta-analysis of cohort studies and experimental sleep deprivation. Biol Psychiatry. 80:40–52. doi:10.1016/j.biopsych.2015.05.014

Jones SE, Maisha FI, Strausz SJ, Cade BE, Tervi AM, Helaakoski V, Broberg ME, Lammi V, FinnGen LJM, Redline S, et al. 2022. The public health impact of poor sleep on severe COVID-19, influenza and upper respiratory infections. medRxiv. doi:10.1101/2022.02.16.22271055

Kecklund G, Axelsson J. 2016. Health consequences of shift work and insufficient sleep. BMJ. 355:i5210. doi:10.1136/bmj.i5210

Lee RU, Glickman GL. 2021. Sleep, circadian health and melatonin for mitigating COVID-19 and optimizing vaccine efficacy. Front Neurosci. 15:711605. doi:10.3389/fnins.2021.711605

Lim RK, Wambier CG, Goren A. 2020. Are night shift workers at an increased risk for COVID-19? Med Hypotheses. 144:110147. doi:10.1016/j.mehy.2020.110147

Liu PY, Irwin MR, Krueger JM, Gaddameedhi S, Van Dongen HPA. 2021. Night shift schedule alters endogenous regulation of circulating cytokines. Neurobiol Sleep Circadian Rhythms. 10:100063. doi:10.1016/j.nbscr.2021.100063

Loef B, Nanlohy NM, Jacobi RHJ, van de Ven C, Mariman R, van der Beek AJ, Proper KI, van Baarle D. 2019. Immunological effects of shift work in healthcare workers. Sci Rep. 9:18220. doi:10.1038/s41598-019-54816-5

Long JE, Drayson MT, Taylor AE, Toellner KM, Lord JM, Phillips AC. 2016. Morning vaccination enhances antibody response over afternoon vaccination: A cluster-randomised trial. Vaccine. 34:2679–85. doi:10.1016/j.vaccine.2016.04.032

Merikanto I, Dauvilliers Y, Chung F, Holzinger B, De Gennaro L, Wing YK, Korman M, Partinen M,NI, Benedict C, Bjelajac A. 2022. Disturbances in sleep, circadian rhythms and daytime functioning in relation to coronavirus infection and Long-COVID - A multinational ICOSS study. J Sleep Res. 31:e13542. doi:10.1111/jsr.13542

Nagai M, Morikawa Y, Kitaoka K, Nakamura K, Sakurai M, Nishijo M, Hamazaki Y, Maruzeni S, Nakagawa H. 2011. Effects of fatigue on immune function in nurses performing shift work. J Occup Health. 53:312–19. doi:10.1539/joh.10-0072-OA

Partinen M, Bjorvatn B, Holzinger B, Chung F, Penzel T, Espie CA, Morin CM. 2021. Sleep and circadian problems during the coronavirus disease 2019 (COVID-19) pandemic: The International COVID-19 Sleep Study (ICOSS). J Sleep Res. 30:e13206. doi:10.1111/jsr.13206

Portaluppi F, Smolensky MH, Touitou Y. 2010. Ethics and methods for biological rhythm research on animals and human beings. Chronobiol Int. 27:1911–29. doi:10.3109/07420528.2010.516381

Prather AA, Janicki-Deverts D, Hall MH, Cohen S. 2015. Behaviorally assessed sleep and susceptibility to the common cold. Sleep. 38:1353–59. doi:10.5665/sleep.4968

Puttonen S, Viitasalo K, Harma M. 2011. Effect of shiftwork on systemic markers of inflammation. Chronobiol Int. 28:528–35. doi:10.3109/07420528.2011.580869

Rizza S, Coppeta L, Grelli S, Ferrazza G, Chiocchi M, Vanni G, Bonomo OC, Bellia A, Andreoni M, Magrini A, et al. 2021. High body mass index and night shift work are associated with COVID-19 in health care workers. J Endocrinol Invest. 44:1097–101. doi:10.1007/s40618-020-01397-0

Robinson CH, Albury C, McCartney D, Fletcher B, Roberts N, Jury I, Lee J. 2021. The relationship between duration and quality of sleep and upper respiratory tract infections: A systematic review. Fam Pract. 38:802–10. doi:10.1093/fampra/cmab033

Salehinejad MA, Azarkolah A, Ghanavati E, Nitsche MA. 2022. Circadian disturbances, sleep difficulties and the COVID-19 pandemic. Sleep Med. 91:246–52. doi:10.1016/j.sleep.2021.07.011

Sookoian S, Gemma C, Fernandez Gianotti T, Burgueno A, Alvarez A, Gonzalez CD, Pirola CJ. 2007. Effects of rotating shift work on biomarkers of metabolic syndrome and inflammation. J Intern Med. 261:285–92. doi:10.1111/j.1365-2796.2007.01766.x

Spiegel K, Sheridan JF, Van Cauter E. 2002. Effect of sleep deprivation on response to immunization. JAMA. 288:1471–72. doi:10.1001/jama.288.12.1471-a