

RESEARCH ARTICLE

Disturbances in sleep, circadian rhythms and daytime functioning in relation to coronavirus infection and Long-COVID – A multinational ICOSS study

Ilona Merikanto^{1,2,3}  | Yves Dauvilliers⁴ | Frances Chung⁵ | Brigitte Holzinger^{6,7} | Luigi De Gennaro⁸  | Yun Kwok Wing⁹  | Maria Korman¹⁰ | Markku Partinen^{11,12} |
2nd ICOSS members

¹SleepWell Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland

²Department of Public Health and Welfare, Finnish Institute for Health and Welfare, Helsinki, Finland

³Orton Orthopaedics Hospital, Helsinki, Finland

⁴Sleep-Wake Disorders Unit, Department of Neurology, Gui-de-Chauliac Hospital, CHU Montpellier, INM, Univ Montpellier, INSERM, Montpellier, France

⁵Department of Anesthesiology and Pain Medicine, University Health Network, University of Toronto, Toronto, Canada

⁶Institute for Consciousness and Dream Research, Vienna, Austria

⁷ZK-Schlafcoaching, Medical University Vienna, Wien, Austria

⁸IRCCS Fondazione Santa Lucia, Rome, Italy

⁹Li Chiu Kong Family Sleep Assessment Unit, Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

¹⁰Department of Occupational Therapy, Faculty of Health Sciences, Ariel University, Ariel, Israel

¹¹Helsinki Sleep Clinic, Terveystalo Healthcare, Helsinki, Finland

¹²Department of Neurosciences, Clinicum, University of Helsinki, Helsinki, Finland

Correspondence

Ilona Merikanto, Sleep and stress in health and in transition from acute to chronic diseases Research Programs Unit, Faculty of Medicine, PL21, 00014 University of Helsinki, Helsinki, Finland.
Email: ilona.merikanto@helsinki.fi

Funding information

This study was funded by The Academy of Finland (project 322312). The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

Summary

This protocol paper describes the second survey produced by the International Covid Sleep Study (ICOSS) group with the aim to examine the associations between SARS-CoV-2 infection and sleep, sleepiness, and circadian problems as potential pre-disposing factors for more severe COVID-19 disease profile and for development of Long-COVID in the general population. The survey consists of 47 questions on sleep, daytime sleepiness, circadian rhythm, health, mental wellbeing, life habits, and socioeconomic situation before and during the pandemic, and conditional questions to those reporting having had coronavirus infection, being vaccinated, or suffering from particular sleep symptoms or sleep disorders. Surveys will be administered online between May and November 2021 in Austria, Brazil, Bulgaria, Canada, China, Croatia, Finland, France, Germany, Israel, Italy, Japan, Norway, Portugal, Sweden and USA. Data collected by the survey will give valuable information on the open questions regarding COVID-19 disease risk factors, symptomatology and evolution of Long-COVID, and on other long-term consequences related to the pandemic.

Further enquiries on ICOSS can be addressed both to Ilona Merikanto and to Markku Partinen by email: ilona.merikanto@helsinki.fi and markku.partinen@helsinki.fi

Ilona Merikanto, Yves Dauvilliers, Frances Chung, Brigitte Holzinger, Luigi De Gennaro, Yun Kwok Wing and Markku Partinen Member of the 2nd ICOSS core group.

See [Acknowledgements](#) for 2nd ICOSS members

KEYWORDS

chronotype, COVID-19, dreams, fatigue, pandemic, rapid eye movement behaviour disorder

1 | INTRODUCTION

The COVID-19 pandemic has had an enormous impact on societies and daily life worldwide since the global pandemic was announced by the World Health Organization (WHO) in March 2020. Researchers from different scientific fields allocated their focus on studying pandemic-related issues such as the pathogenicity of the novel coronavirus (severe acute respiratory syndrome [SARS]-CoV-2), development of vaccines and treatments towards the COVID-19 disease, and the impact of the pandemic on societies and on wellbeing. Interest in examining the impact of the COVID-19 pandemic was stirred up among sleep researchers as poor sleep and disturbed circadian rhythms do not only predispose to deteriorated health but are usually the first symptoms as our wellbeing is compromised. The International Covid Sleep Study (ICOSS) is an international collaboration that began in 2020 during the COVID-19 pandemic including experts in sleep research across four continents – Europe, Asia, North America and South America (<https://www2.helsinki.fi/en/projects/icoss>). The first survey (Partinen et al., 2021) was collected from 14 countries from May to August 2020 with the aim to investigate how COVID-19 pandemic has influenced on sleep, circadian rhythms and mental health in the general adult populations, especially from the perspective of confinement and changes in social and economic situation. We found that there was an increase of sleep problems in the global communities during the pandemic as compared with time before the pandemic. These changes were associated with deteriorated mental health and wellbeing (Brandão, Martikainen, & Merikanto, 2021; Chung, Waseem, & Pham, 2021; Fränkl, Scarpelli, & Nadorff, 2021; Merikanto, Kortesoja, & Benedict, 2021; Morin, Bjorvatn, & Chung, 2021). Based on these findings, social confinement, physiological, socioeconomic and psychological factors are related to the increase in sleep problems during the pandemic aggravating the risk for deteriorated health. Especially definite evening-types have developed more sleep problems during the pandemic and have had more mental health issues than other chronotypes (Merikanto et al., 2021). These findings are in line with previous studies indicating higher risk for sleep and mental health problems among evening-types already in adolescence as well as in adulthood (Chan, Zhang, & Tsang, 2020; Chen, Zhang, & Li, 2021; Merikanto et al., 2012; Merikanto & Partonen, 2020, 2021; Merikanto, Pesonen, & Kuula, 2017). On the other hand, certain sleep and circadian problems were partially eased during the pandemic. Many people have had more flexibility in their bedtimes and wake-up times resulting in a decrease in social jet lag and longer sleep duration as compared with time before the pandemic (Brandão et al., 2021; Korman, Tkachev, & Reis, 2020; Merikanto et al., 2021). However, the benefits of increased flexibility to sleep-wake behaviour seem

to be outweighed by the negative consequences of the pandemic on sleep and mental wellbeing (Brandão et al., 2021; Chung et al., 2021; Fränkl et al., 2021; Korman, Tkachev, & Reis, 2021; Merikanto et al., 2021; Morin et al., 2021).

Since the pandemic has progressed, along with increasing infection numbers, the incidents of persisting COVID symptoms (Long-COVID; post-COVID-19 condition) have increased. Commonly reported long-lasting symptoms have been, for example, fatigue, dyspnoea, headache and anosmia (Sudre, Murray, & Varsavsky, 2021). Estimates on the incidence of one or more long-lasting symptoms among COVID patients range from ~13% to 80% (Lopez-Leon, Wegman-Ostrosky, & Perelman, 2021; Sudre et al., 2021; Taquet et al., 2021), with no clear consensus on the prevalence of Long-COVID. According to the recent clinical case definition for Long-COVID published by WHO on 6 October 2021, the three most common symptoms are fatigue, cognitive disorders (so-called brain fog) and shortness of breath. Definition by the WHO states that these symptoms should be persistent or occur as novel symptoms approximately 3 months after being infected by SARS-CoV-2 and last at least 2 months. This definition and description of the main symptoms is based on voting using the Delphi-method by the WHO post-COVID-19 working group (<https://apps.who.int/iris/bitstream/handle/10665/345824/WHO-2019-nCoV-Post-COVID-19-condition-Clinical-case-definition-2021.1-eng.pdf>). There is still a lack of evidence on how common these symptoms are in the general population of infected individuals reporting persistent or fluctuating symptoms after COVID-19. There is thus a need for more evidence-based refinement of what constitutes a Long-COVID phenotype or whether there are different Long-COVID phenotypes. There is also a novel interest in examining the potential predisposing factors for developing Long-COVID as these factors are largely unknown.

Besides the effects of pandemic, it is essential to examine the role of sleep and circadian rhythms in relation to the risk for coronavirus infection, disease severity and persistent symptoms. As sleep and circadian rhythmicity have a profound role in physiological functions and mental wellbeing (Baron & Reid, 2014; Bishir, Bhat, & Essa, 2020), such as immune system and neural functioning (Bishir et al., 2020; Imeri & Opp, 2009; Lange, Dimitrov, & Born, 2010; Richter, Kellner, Hillemecher, & Golubnitschaja, 2021), it is likely that disturbances in sleep and circadian rhythms play a significant role in the liability to COVID-19 disease of different severity and the risk for developing persisting symptoms. Previous research findings imply that neurological effects of the SARS-CoV-2 infection may also reciprocally increase the risk for sleep and mental health problems, such as nightmares, insomnia symptoms and depression severity (Boldrini, Canoll, & Klein, 2021; Rogers, Watson, & Badenoch, 2021).

1.1 | Objectives and hypotheses

In the first ICOSS survey, we could not examine the role of sleep in COVID-19 disease severity or infection risk as < 2.5% of our multinational sample of more than 25,000 participants reported having had COVID-19. Therefore, there was an incentive to examine the role of sleep and circadian rhythm in association with SARS-CoV-2 infection and its symptomatology in a novel international ICOSS survey. The primary objectives of the international harmonized ICOSS 2nd online survey are: (1) examine the pandemic effects of sleep, circadian profiles and sleep disorders in relation to SARS-CoV-2 infection risk, COVID-19 severity and Long-COVID as compared with non-infected; and (2) examine the role of pre-existing sleep and circadian problems as potential predisposing factors for more severe COVID-19 disease and Long-COVID in the general population. The secondary objective is to compare these potential associations between different countries.

Based on the current literature on SARS-CoV-2 infection suggesting potential disturbances in daytime functioning and sleep due to changes in cytokine levels and neurotransmission (Boldrini et al., 2021; Rogers et al., 2021; Zubair et al., 2020), we have established five main hypotheses:

1. COVID-19 with involvement of the nervous system infection is associated with an increased incidence of excessive daytime sleepiness with resemblance to post-viral fatigue syndrome (Komaroff & Bateman, 2021) in distinction of increased general fatigue, more often associated with, for example, psychological effects.
2. SARS-CoV-2 infection with involvement of nervous system infection can increase the risk for sleep disorders, such as rapid eye movement (REM) sleep behaviour disorder (RBD).
3. Pre-existing circadian misalignment, sleepiness, insomnia and other sleep problems, frequent dreaming and nightmares during the COVID-19 pandemic might be associated with severity of infection in terms of intensity and duration. Changes in circadian rhythms, sleep problems, dreaming and nightmares are likely related to both psychological and biological factors, such as pandemic restrictions and changes in social environment and economic situation, as indicated previously (Fränkl et al., 2021; Korman et al., 2020; Merikanto et al., 2021; Morin et al., 2021).
4. We also hypothesize that suicidal thoughts during the COVID-19 pandemic reflect anxiety and depression, and that they have been more frequent in people having traumatic experiences and extreme stress during the pandemic, and who have had infection as compared with non-infected people. This association is likely corroborated by a potential relationship between the increased rate of sleep problems, such as nightmares, and suicidal thoughts.
5. Besides the biological differences in factors predisposing to Long-COVID, psychological factors may determine the risk for Long-COVID symptoms, and whether they are persistent or fluctuating. It is possible that different kinds of Long-COVID phenotypes exist. Potential different Long-COVID phenotypes could possibly

include, for example, those with or without dysfunction of the autonomic nervous system as well as those having displayed different levels of disease severity.

2 | METHODS

The harmonized ICOSS 2nd survey with the emphasis on the role of sleep and circadian problems in coronavirus (SARS-CoV-2) infection severity and post-infection symptoms will be collected between May and November 2021 with 16 participating countries: Austria, Brazil, Bulgaria, Canada, China (Hong Kong), Croatia, Finland, France, Germany, Israel, Italy, Japan, Norway, Portugal, Sweden and USA. The second survey was developed by a core group of ICOSS members, and included novel questionnaires and items in line with the new study objectives in addition to some existing questionnaires and items from the first survey (Partinen et al., 2021).

2.1 | Survey questionnaire

The 2nd ICOSS survey consists of general questions being asked from everyone participating in the survey. In addition, multiple conditional questions would be shown in the web-survey only to those reporting having had coronavirus infection, being vaccinated, or suffering from particular sleep symptoms or disorders. Estimations of sleep, circadian rhythm, health and mental wellbeing are asked separately regarding the time before the pandemic and during the pandemic, as well as conditionally in relation to time before and after the coronavirus infection. The survey is composed of questions from existing and validated questionnaires, as well as questions that are developed for the purpose of this study. In total, the survey consists of 47 questions, and it is divided into different sections:

1. Basic participant information: for example, country, gender and age.
2. Information on the situation during the COVID-19 pandemic: questions on whether the participant has been infected with coronavirus, been tested positive with the virus in polymerase chain reaction test, timeline of the infection, infection severity and symptoms, and coronavirus vaccination information.
3. Diagnosed conditions: health conditions diagnosed by a physician, and whether diagnosed before or during the pandemic or after having coronavirus infection.
4. Health symptoms during the pandemic: symptoms the participant has had during the pandemic, how long they have lasted, and whether they needed health care attendance, for example, been treated in hospital or in intensive care unit.
5. Sleep before and during the pandemic: individual sleep items developed for the purpose of this survey and taken from the Basic Nordic Sleep Questionnaire (BNSQ; Partinen & Gislason, 1995). Questions assess nightly sleep duration, sleep quality, daytime sleepiness, fatigue, dream frequency and content on COVID-19

- or pandemic measures, nightmares, lucid dreams, sleep talking/singing/laughing/shouting, excessive sleepiness in the morning, and sleep naps. Most items on the occurrence of sleep symptoms are rated on a five-point scale.
6. Diurnal preference and sleep-wake behaviour: circadian type is asked with a single modified item from the 19-item Morningness-Eveningness Questionnaire (Horne & Östberg, 1976). This modified item self-assesses circadian type into either definite morning-type, moderate morning-type, neither morning- nor evening-type (day-type), moderate evening-type and definite evening-type, depending on the time of the day on which the participant is most alert or sleepy. Additionally, easiness of getting up from the bed in the morning, how long it takes the participant to be fully functional in the morning, and how long it usually takes the participant to fall asleep once going to bed are asked for assessing sleep latency on working days and free days separately. The ultra-short Munich Chronotype Questionnaire (micro-MCTQ) is used for assessing midpoint of sleep on school/working days and free days separately, and social jet lag (Ghotbi, Pilz, & Winnebeck, 2020).
 7. REM sleep behaviour: items about acting out of dreams and symptoms of constipation are asked to assess RBD, as RBD consists of acting out of violent and vivid dreams (Postuma, Arnulf, & Hogl, 2012), and is often associated with gastrointestinal symptoms, especially constipation (Postuma, Iranzo, & Hu, 2019). Questions on sense of smell are asked in separate survey sections and can be assessed in relation to RBD, which commonly associates with olfactory deficits (Ross, Petrovitch, & Abbott, 2008).
 8. Sleep need: amount of total sleep needed daily to feel refreshed. Sleep deprivation may be computed as: (sleep need) – (average total sleeping time per 24 hr).
 9. Insomnia symptoms during the past 2 weeks: Insomnia Severity Index (ISI; Bastien, Vallières, & Morin, 2001) and use of sleeping pills. ISI assessment is previously described in the 1st ICOS protocol (Partinen et al., 2021).
 10. Daytime sleepiness: Epworth Sleepiness Scale (ESS; Johns, 1991) and Fatigue Severity Scale (FSS; Krupp, 1989). The ESS assesses excessive daytime sleepiness with eight items asking how likely a person is to fall asleep at certain situations with a scale of 0 (never) to 3 (high chance; Johns, 1991). The FSS assesses severity of fatigue symptoms especially regarding performance and motor functions with nine items (Krupp, 1989). FSS items are asked with seven-point Likert scale ranging from 1 ("strongly disagree") to 7 ("strongly agree"), and a cut-point of ≥ 4 from the total FSS score is usually used to indicate fatigue (Krupp, Coyle, & Doscher, 1995).
 11. Sleep apnea: four-item STOP questionnaire to assess obstructive sleep apnea (OSA) symptoms (Chung, Yegneswaran, & Liao, 2008). STOP questionnaire items are answered with Yes/No, and answering yes to at least two out of four items indicates a high risk of OSA.
 12. Change in weight: height (in cm, except in USA in inches), current weight (in kg, except in USA in pounds), and weight before the pandemic for assessing body mass index before and during the pandemic.
 13. Socioeconomic situation during the pandemic: questions on, for example, living area and situation, marital status, number of children, education profession, working status and economic situation.
 14. Mental wellbeing and quality of life during the pandemic: ultra-brief Screening Scale for Anxiety and Depression (PHQ-4; Kroenke, Spitzer, Williams, & Löwe, 2009), items asking about change in depression and anxiety symptoms during the pandemic versus time before the pandemic, World Health Organization Five Well-Being Index (WHO-5; Topp, Østergaard, Søndergaard, & Bech, 2015) and its change, two items on post-traumatic stress disorder symptoms (Lang, Wilkins, & Roy-Byrne, 2012), two items on suicidal thought, and single items on stress (Elo, Leppänen, & Jahkola, 2003), quality of life and quality of health. The assessments of PHQ-4 and WHO-5 are previously described in the 1st ICOS protocol (Partinen et al., 2021). Suicidal thoughts are asked with two items on how often the participant has been thinking about suicide in the past year or in the year before the pandemic. The first item of these is taken from the Suicide Behaviors Questionnaire-Revised (SBQ-R; Osman et al., 2001). The participant is instructed to seek help in case of suicidal thoughts, and information on where this help could be found nationally is provided in the survey. Quality of life and health are asked separately with a linear visual analogue scale from 0 to 100, with 0 indicating the worst possible and 100 the best possible quality of life/health one could imagine.
 15. Life habits: single question each on smoking, alcohol consumption and physical activity. Smoking or snuffing tobacco products is asked with answer options from 1 (Never or less than once per month) to 5 (Every day or almost daily). Alcohol consumption per week refers to WHO standardized alcohol units. Weekly light, moderate and vigorous intensity exercise habits are rated with intensity on a scale from 1 (Not at all) to 5 (4 hr or more per week).
 16. Functioning and health conditions during the pandemic: WHO Disability Assessment Schedule 2.0 (WHODAS 2.0), sense of smell, and the possible influence of COVID-19 on sense of smell. WHODAS 2.0 consists of 12 items asking about difficulties to function due to health conditions during the past 30 days scaled from 1 (None) to 5 (Extreme or cannot do), with a higher full score indicating more functional limitations (Üstün, Kostanjsek, Chatterji, & Rehm, 2010). WHODAS 2.0 also includes questions on orthostatic intolerance and post-exertional malaise.

The full survey is in [Supplementary Material](#).

2.2 | Target sample

The target sample consists of the general population of adults 18 years old, with no upper age limit regardless of whether they have had coronavirus infection or not. The aim is to recruit several

thousand participants from different continents and countries with various backgrounds to get representable samples from each country on participants who have not been infected with coronavirus, who have been infected at various levels of disease severity with either non-persisting or persisting disease symptoms and were/were not vaccinated. Recruitment methods for participants include, for example: (1) public national, local and social media outlets, such as on newspapers, TV, radio, webinars, Twitter, Facebook pages and groups, health blogs; (2) marketing via newsletters and webpages of different research institutes, universities, hospitals, sleep societies, health organizations, student organizations and work environments. Recruitment of participants to the survey will be ongoing during the period when the survey is open for answering in each country.

2.3 | Method of survey

The survey is completed via University/Departmental licensed on-line platforms such as Qualtrics and RedCap. Survey has optional encouraging text between the different sections to motivate completion of the survey. Most of the participating countries use the University of Helsinki-provided Qualtrics platform formulated for the survey format first in English and then translated to each native language to ensure harmonized study procedure between the countries. Using Qualtrics' built-in programming architecture, we embedded one script to enhance user experience and another one to simplify offline data management and analysis (Box 1). The survey is answered anonymously between May 2021 and November 2021. Each participating country was responsible for obtaining ethical approval from their local Ethics Committee when relevant depending on their respective country-specific ethical guideline. In many countries, the survey protocol did not require statement from the local Ethical Committee as national ethical requirements were met for waiver of ethical approval.

2.4 | Consent, privacy and burden on participants

Completion of the online survey is expected to take about 20 min in healthy subjects, and about 40 min in subjects who have had coronavirus infection. All questionnaire data are pseudo-anonymized. Participation to the survey is voluntary, and consent to use the given data for research purposes is asked from the participant at the beginning of the online survey; this response could be changed at any time during the survey. The participants do not receive any monetary compensation or benefit directly from the survey.

2.5 | Data assessment

We will evaluate the prevalence of different symptoms considered as COVID-19 or Long-COVID symptoms, and whether COVID-19 severity or Long-COVID phenotype differs regarding confounding

BOX 1 Java script used in Qualtrics

Using Qualtrics' built-in programming architecture, we embedded one script to enhance user experience, and another one to simplify offline data management and analysis. First JavaScript is used to present time-related questions in a simple and intuitive manner using novel interactive interface. Asking time questions in a global survey is challenging as some countries use a 24-hr clock while other countries use a 12-hr clock, and some use both. In ICOS2, questions about habitual sleep-wake times should be responded to by moving a sliding bar along a 24-hr colour-coded time scale (Figure 1). The scale colours gradually change from dark blue (evening, starting at 18:00 hours) to black (night), to orange (morning), to yellow (daytime) – in allusion to changes in natural daylight. To the left of the slider, the chosen time is presented in a 24-hr format. Note that the current solution eliminates the need to input hours and minutes separately. Pilot experiments (M. Korman, and V. Tkachev, unpublished data) showed that the new interface reduced input errors due to confusion between time formats and by ~15% in comparison to typing.

The second Javascript performs on-the-fly calculations of the core variables of daily behaviours for each individual in accordance with the methods of Roenneberg et al. (2019). Briefly, the following variables are being added to the original answers in the database. (1) Mean sleep duration across the week (SDweek) calculated as weighted average of the sleep duration on workdays (SDW, assuming 5 workdays) and work-free days (SDF), $[SDweek = (5 \times SDW + 2 \times SDF)/7]$. (2) Chronotype (MSFsc), quantifying individual sleep timing as an indicator for phase of entrainment. MSFsc is calculated a mid-point of sleep on free days (MSF) and corrected for sleep deficit accumulated on workdays. The mid-point of sleep is also calculated for workdays (MSW). (3) Social jet-lag is calculated as the difference between MSF and MSW.

premorbid conditions, daytime functioning and sleep, circadian and psychological profiles in relation to time before and during the pandemic. We will also consider the influence of vaccine status on these different profiles as compared with time before the pandemic as well as during the pandemic before the vaccination.

2.6 | Sharing information and confidentiality

Similarly as with the first ICOS2 study, the objective of the second ICOS2 study is to publish findings as a joint effort between the



FIGURE 1 24-hr colour-coded time scale for habitual sleep-wake times

principal investigators from each participating country. Although data from each country are owned by the ICOSS principal investigators of that country, for research purposes the data from different countries can be pooled together and accessed freely by other researchers involved in the ICOSS collaboration. In order to avoid overlapping studies of the same topic and unnecessary analyses, members of the consortium will work jointly and in a coordinated, but open way. Study plans are to be accepted by the ICOSS second survey core group. All information gathered during the course of the study will be stored safely at the participating research institutes. Data are shared between the ICOSS collaborators using secure data-sharing solutions offered by the participating research institutions.

3 | DISCUSSION

To the best of our knowledge, there is no other large-scale multinational sleep study targeting the general population regarding the role of sleep and circadian rhythms along with a variety of psychological, biological, social and economic aspects considered in relation to COVID-19 disease infection risk, severity or Long-COVID. Systematic reviews and cohort studies on the frequency and variety of persistent COVID-19 symptoms indicate that sleep problems and disorders, such as sleep difficulties and insomnia, can be high among

COVID-19 patients (Lopez-Leon et al., 2021; Nalbandian, Sehgal, & Gupta, 2021). It is, however, unknown whether different sleep, circadian rhythm, daytime functioning and psychological factors have a role in COVID disease risk and prognosis, and the long-term consequences of the infection, or if there are reciprocal relationships between COVID disease prognosis and development of Long-COVID and sleep disorders.

It is plausible that the neurotropic nature of the SARS-CoV-2 infection includes similar peripheral nerve pathways to the central nervous system as Middle East respiratory syndrome (MERS-CoV) and SARS-CoV-1 (Zubair et al., 2020), which also affect sleep, dreaming and daytime functioning (Boldrini et al., 2021; Lam, Wing, & Yu, 2009; Rogers et al., 2021; Zubair et al., 2020). Furthermore, the suggested shared pathways between sleep, dreaming, daytime functioning and SARS-CoV-2 infection leading to Long-COVID can have potential neurodegenerative propensity related to, for example, RBD, parkinsonism and dementia (Brundin, Nath, & Beckham, 2020; Taquet et al., 2021). In a recent polysomnography study, REM sleep without atonia was more prevalent among COVID-19 patients than is usual in general population samples (Heidbreder, Sonnweber, & Stefani, 2021). Furthermore, olfactory impairment is common among patients with RBD (Ross et al., 2008) similarly as among COVID-19 patients (Xydakis, Albers, & Holbrook, 2021).

Historical viral outbreaks affecting neurological functioning before the current COVID-19 pandemic include the Russian flu pandemic in the late 19th century, the Spanish flu pandemic in 1918–1919, and encephalitis lethargica between 1915 and 1926 (Stefano, 2021). Other significant viral infections with cognitive effects are, for example, diphtheria, myalgic encephalomyelitis (post-viral fatigue syndrome; Stefano, 2021), as well as MERS-CoV and SARS-CoV-1 discussed earlier (Boldrini et al., 2021; Lam et al., 2009; Rogers et al., 2021; Zubair et al., 2020). For instance, post-viral fatigue syndrome, which has been shown to follow after many different viral infections (Komaroff & Bateman, 2021), shares similarities to cognitive dysfunction symptoms and fatigue described in Long-COVID (Stefano, 2021). It has also been suggested that Long-COVID is another manifestation of post-viral fatigue syndrome with a new name (Komaroff & Bateman, 2021). Therefore, conducting large-scale collaborative research with a harmonized protocol such as presented here is essential in filling the gap in knowledge in order to delineate the long-term negative consequences related to COVID-19 pandemic.

The strengths of the 2nd ICOSS survey and additional value related to the 1st ICOSS include that information is collected both regarding the time before the pandemic and during the pandemic, as well as conditionally in relation to time before and after the coronavirus infection. Survey will give information on a variety of behavioural, health, wellbeing, social and economic factors, and pandemic-related situations and measures that will enable broad examination of multiple study questions. The multinational general population samples allow comparison between different countries that have faced different pandemic measures, and differ by culture, environmental and biological factors, demographics and socioeconomic structures. Limitation of the survey is that there is a potential for recall bias when answering

about time before the pandemic. Also, compromises between excluding or including items of interest versus keeping the survey length feasible enough for participants to fill out in a reasonable time frame had to be made when planning the final survey.

The 2nd ICOSS survey was planned to gather information on health and wellbeing, especially from the perspective of sleep and circadian rhythm, in relation to the pandemic event. Although the survey was designed during the COVID-19 pandemic, it can be modified and used for examining similar research questions also during other potential future pandemic events. For these other purposes, potential users must contact owners of copyright before use. The aim is that the use will be free of cost for research purposes.

ACKNOWLEDGEMENTS

Principal investigators and main collaborators in the second ICOSS study other than the authors of this paper are (in alphabetical order): Christian Benedict from the Uppsala University (Sweden), Adrijana Bjelajac from the University of Zagreb (Croatia), Bjørn Bjorvatn from the University of Bergen (Norway), Ngan Yin Chan from the Chinese University of Hong Kong (China), Harald Hrubos-Strøm from the Akershus University Hospital (Norway), Yuichi Inoue from the Tokyo Medical University (Japan), Roumen Kirov from the Bulgarian Academy of Sciences Institute of Neurobiology (Bulgaria), Anne-Marie Landtblom from the Uppsala University (Sweden), Damien Léger from the Université de Paris (France), Kentaro Matsui from the Tokyo Women's Medical University (Japan), Charles M. Morin from the Université Laval (Canada), Sergio Mota-Rolim from the Federal University of Rio Grande do Norte (Brazil), Michael RNadorff from the Mississippi State University (USA), Thomas Penzel from the Charite Universitätsmedizin Berlin (Germany), Giuseppe Plazzi from the University of Modena and Reggio Emilia (Italy), Catia Reis from the Catholic University in Lisbon (Portugal) and Juliana Yordanova from the Bulgarian Academy of Sciences Institute of Neurobiology (Bulgaria). The authors would also like to acknowledge all the PhD students involved in the ICOSS study who have helped in the country-specific survey data collection, especially PhD student Laura Kortesoja from the University of Helsinki, supervised by Dr Merikanto, who has had a major role in setting up the Qualtrics survey used in many of the participating ICOSS countries. Other PhD students involved in ICOSS 2 data collection include Alessandra De Santis from the University of Rome supervised by Dr De Gennaro, Courtney Bolstad from the Mississippi State University supervised by Dr Nadorff, Tainá Freitas de Macêdo and Ana Suely Cunha from the Federal University of Rio Grande do Norte supervised by Dr Mota-Rolim, Franziska Nierwetberg from the Medical University Vienna supervised by Dr Holzinger, Dor Agami and Elizabeth Schwartzberg from Ariel University supervised by Dr Korman, and Silvia Koumanova and Laura Lyamova from the Bulgarian Academy of Sciences Institute of Neurobiology supervised by Dr Yordanova. Also to be acknowledged are collaborators Dr Anna Kristoffersson and Associate Prof. Shala Berntsson from Uppsala University (Sweden), Dr Yaping Liu from the Chinese University of Hong Kong

(China), Dr Diva Ferreira from Centro Hospitalar do Médio Ave (Portugal), Dr Selma Cvijetic Avdagic from the Institute for Medical Research and Occupational Health (Croatia), Dr Eva Andela Delale from the Institute for Anthropological Research (Croatia), Dr Jelena Macan from the Institute for Medical Research and Occupational Health (Croatia), Dr Biserka Ross from the Institute for Medical Research and Occupational Health (Croatia), Dr Domagoj Vidovic from the Univeristy Psychiatric Hospital Vrapce (Croatia), and Vasil Kolev Lyamova from the Bulgarian Academy of Sciences Institute of Neurobiology (Bulgaria), who have helped with the data collection in their respective countries.

CONFLICT OF INTEREST

There are no competing financial interests.

AUTHOR CONTRIBUTIONS

The 2nd survey and the survey protocol were designed by the ICOSS 2nd core group: Ilona Merikanto, Yves Dauvilliers, Frances Chung, Brigitte Holzinger, Luigi De Gennaro, Yun Kwok Wing and Markku Partinen. All the 2nd ICOSS members had the opportunity to give their critical comments on the survey and the protocol. Harmonized Qualtrics online survey was designed by Ilona Merikanto, and java script within Qualtrics designed by Maria Korman. The principal investigators of each participating country coordinated the data collection for the second survey. The original draft of the manuscript was written by Ilona Merikanto and all authors gave their critical comments on the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Data are solely shared between the ICOSS collaborators using secure data-sharing solutions offered by the participating research institutions. The survey is given as a supplement, and can be used for research purposes by request made to the ICOSS 2nd core group and cited properly.

ORCID

Ilona Merikanto  <https://orcid.org/0000-0002-1222-6678>

Luigi De Gennaro  <https://orcid.org/0000-0003-3613-6631>

Yun Kwok Wing  <https://orcid.org/0000-0002-5745-5474>

REFERENCES

- Baron, K.G., & Reid, K.J. (2014). Circadian misalignment and health. *International Review of Psychiatry*, 26, 139–154. <https://doi.org/10.3109/09540261.2014.911149>
- Bastien, C.H., Vallières, A., & Morin, C.M. (2001). Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Medicine*, 2, 297–307. [https://doi.org/10.1016/S1389-9457\(00\)00065-4](https://doi.org/10.1016/S1389-9457(00)00065-4)
- Bishir, M., Bhat, A., Essa, M.M., Ekpo, O., Ihunwo, A.O., Veeraraghavan, V.P., ... Ojcius, D.M. (2020). Sleep deprivation and neurological disorders. *BioMed Research International*, 2020, 1–19. <https://doi.org/10.1155/2020/5764017>
- Boldrini, M., Canoll, P.D., & Klein, R.S. (2021). How COVID-19 affects the brain. *JAMA Psychiatry*, 78, 682–683. <https://doi.org/10.1001/jamapsychiatry.2021.0500>

- Brandão, L.E.M., Martikainen, T., Merikanto, I., Holzinger, B., Morin, C.M., Espie, C.A., ... Cedernaes, J. (2021). Social jetlag changes during the COVID-19 pandemic as a predictor of insomnia – A multi-national survey study. *NSS*, 13, 1711–1722. <https://doi.org/10.2147/NSS.S327365>
- Brundin, P., Nath, A., & Beckham, J.D. (2020). Is COVID-19 a perfect storm for Parkinson's disease? *Trends in Neurosciences*, 43, 931–933. <https://doi.org/10.1016/j.tins.2020.10.009>
- Chan, N.Y., Zhang, J., Tsang, C.C., Li, A.M., Chan, J.W.Y., Wing, Y.K., & Li, S.X. (2020). The associations of insomnia symptoms and chronotype with daytime sleepiness, mood symptoms and suicide risk in adolescents. *Sleep Medicine*, 74, 124–131. <https://doi.org/10.1016/j.sleep.2020.05.035>
- Chen, S.-J., Zhang, J.-H., Li, S.X., Tsang, C.C., Chan, K.C.C., Au, C.T., ... Chan, N.Y. (2021). The trajectories and associations of eveningness and insomnia with daytime sleepiness, depression and suicidal ideation in adolescents: A 3-year longitudinal study. *Journal of Affective Disorders*, 294, 533–542. <https://doi.org/10.1016/j.jad.2021.07.033>
- Chung, F., Waseem, R., Pham, C., Penzel, T., Han, F., Bjorvatn, B., ... Fernandes, A. (2021). The association between high risk of sleep apnea, comorbidities, and risk of COVID-19: a population-based international harmonized study. *Sleep Breath*, 25, 849–860. <https://doi.org/10.1007/s11325-021-02373-5>
- Chung, F., Yegneswaran, B., Liao, P., Chung, S.A., Vairavanathan, S., & Islam, S., ... Shapiro, C.M. (2008). STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *The Journal of the American Society of Anesthesiologists*, 108, 812–821.
- Elo, A.-L., Leppänen, A., & Jähkola, A. (2003). Validity of a single-item measure of stress symptoms. *Scandinavian Journal of Work, Environment & Health*, 444–451. <https://doi.org/10.5271/sjweh.752>
- Fränkl, E., Scarpelli, S., Nadorff, M.R., Bjorvatn, B., Bolstad, C.J., Chan, N.Y., ... Holzinger, B. (2021). How our dreams changed during the COVID-19 pandemic: effects and correlates of dream recall frequency - a multinational study on 19,355 adults. *NSS*, 13, 1573–1591. <https://doi.org/10.2147/NSS.S324142>
- Ghotbi, N., Pilz, L.K., Winnebeck, E.C., Vetter, C., Zerbini, G., Lenssen, D., ... Roenneberg, T. (2020). The μ MCTQ: An ultra-short version of the munich ChronoType questionnaire. *Journal of Biological Rhythms*, 35, 98–110. <https://doi.org/10.1177/0748730419886986>
- Heidbreder, A., Sonnweber, T., Stefani, A., Ibrahim, A., Cesari, M., Bergmann, M., ... Högl, B. (2021). Video-polysomnographic findings after acute COVID-19: REM sleep without atonia as sign of CNS pathology? *Sleep Medicine*, 80, 92–95. <https://doi.org/10.1016/j.sleep.2021.01.051>
- Horne, J.A., & Östberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology*, 4(2), 97–110.
- Imeri, L., & Opp, M.R. (2009). How (and why) the immune system makes us sleep. *Nature Reviews Neuroscience*, 10, 199–210. <https://doi.org/10.1038/nrn2576>
- Johns, M.W. (1991). A new method for measuring daytime sleepiness: The epworth sleepiness scale. *Sleep*, 14, 540–545. <https://doi.org/10.1093/sleep/14.6.540>
- Komaroff, A.L., & Bateman, L. (2021). Will COVID-19 lead to myalgic encephalomyelitis/chronic fatigue syndrome? *Frontiers in Medicine*, 7, 606824. <https://doi.org/10.3389/fmed.2020.606824>
- Korman, M., Tkachev, V., Reis, C., Komada, Y., Kitamura, S., Gubin, D., ... Roenneberg, T. (2020). COVID-19-mandated social restrictions unveil the impact of social time pressure on sleep and body clock. *Scientific Reports*, 10, 22225. <https://doi.org/10.1038/s41598-020-79299-7>
- Korman, M., Tkachev, V., Reis, C., Komada, Y., Kitamura, S., Gubin, D., ... Roenneberg, T. (2021). Outdoor daylight exposure and longer sleep promote wellbeing under COVID-19 mandated restrictions. *Journal of Sleep Research*, e13471. <https://doi.org/10.1111/jsr.13471> [Epub ahead of print].
- Kroenke, K., Spitzer, R.L., Williams, J.B., & Löwe, B. (2009). An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics*, 50, 613–621. [https://doi.org/10.1016/S0033-3182\(09\)70864-3](https://doi.org/10.1016/S0033-3182(09)70864-3)
- Krupp, L.B. (1989). The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology*, 46, 1121. <https://doi.org/10.1001/archneur.1989.00520460115022>
- Krupp, L.B., Coyle, P., Doscher, C., Miller, A., Cross, A.H., Jandorf, L., ... Grimson, R. (1995). Fatigue therapy in multiple sclerosis: results of a double-blind, randomized, parallel trial of amantadine, pemoline, and placebo. *Neurology*, 45, 1956–1961. <https://doi.org/10.1212/WNL.45.11.1956>
- Lam, M.-H.-B., Wing, Y.-K., Yu, M.-W.-M., Leung, C.M., Ma, R.C., & Kong, A.P., ... Lam, S.P. (2009). Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up. *Archives of Internal Medicine*, 169, 2142–2147. <https://doi.org/10.1001/archinternmed.2009.384>
- Lang, A.J., Wilkins, K., Roy-Byrne, P.P., Golinelli, D., Chavira, D., Sherbourne, C., ... Stein, M.B. (2012). Abbreviated PTSD Checklist (PCL) as a guide to clinical response. *General Hospital Psychiatry*, 34, 332–338. <https://doi.org/10.1016/j.genhosppsych.2012.02.003>
- Lange, T., Dimitrov, S., & Born, J. (2010). Effects of sleep and circadian rhythm on the human immune system: Sleep, rhythms, and immune functions. *Annals of the New York Academy of Sciences*, 1193, 48–59. <https://doi.org/10.1111/j.1749-6632.2009.05300.x>
- Lopez-Leon, S., Wegman-Ostrosky, T., Perelman, C., Sepulveda, R., Rebolledo, P.A., Cuapio, A., & Villapol, S. (2021). More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Scientific Reports*, 11, 16144. <https://doi.org/10.1038/s41598-021-95565-8>
- Merikanto, I., Kortesoja, L., Benedict, C., Chung, F., Cedernaes, J., Espie, C.A., ... Bjorvatn, B. (2021). Evening-types show highest increase of sleep and mental health problems during the COVID-19 pandemic—multinational study on 19 267 adults. *Sleep*, zsab216. <https://doi.org/10.1093/sleep/zsab216>
- Merikanto, I., Kronholm, E., Peltonen, M., Laatikainen, T., Lahti, T., & Partonen, T. (2012). Relation of chronotype to sleep complaints in the general Finnish population. *Chronobiology International*, 29, 311–317.
- Merikanto, I., & Partonen, T. (2020). Increase in eveningness and insufficient sleep among adults in population-based cross-sections from 2007 to 2017. *Sleep Medicine*, 75, 368–379. <https://doi.org/10.1016/j.sleep.2020.07.046>
- Merikanto, I., & Partonen, T. (2021). Eveningness increases risks for depressive and anxiety symptoms and hospital treatments mediated by insufficient sleep in a population-based study of 18,039 adults. *Depression and Anxiety*, 38(10), 1066–1077. <https://doi.org/10.1002/da.23189>
- Merikanto, I., Pesonen, A.-K., Kuula, L., Lahti, J., Heinonen, K., Kajantie, E., & Räikkönen, K. (2017). Eveningness as a risk for behavioral problems in late adolescence. *Chronobiology International*, 34, 225–234. <https://doi.org/10.1080/07420528.2016.1267739>
- Morin, C.M., Bjorvatn, B., Chung, F., Holzinger, B., Partinen, M., Penzel, T., ... Espie, C.A. (2021). Insomnia, anxiety, and depression during the COVID-19 pandemic: an international collaborative study. *Sleep Medicine*, 87, 38–45. <https://doi.org/10.1016/j.sleep.2021.07.035>
- Nalbandian, A., Sehgal, K., Gupta, A., Madhavan, M.V., McGroder, C., Stevens, J.S., ... Wan, E.Y. (2021). Post-acute COVID-19 syndrome. *Nature Medicine*, 27, 601–615. <https://doi.org/10.1038/s41591-021-01283-z>
- Osman, A., Bagge, C.L., Gutierrez, P.M., Konick, L.C., Kopper, B.A., & Barrios, F.X. (2001). The Suicidal Behaviors Questionnaire-Revised (SBQ-R): Validation with clinical and nonclinical samples. *Assessment*, 8, 443–454. <https://doi.org/10.1177/107319110100800409>

- Partinen, M., Bjorvatn, B., Holzinger, B., Chung, F., Penzel, T., Espie, C.A., & Morin, C.M. (2021). Sleep and circadian problems during the coronavirus disease 2019 (COVID-19) pandemic: the International COVID-19 Sleep Study (ICOSS). *Journal of Sleep Research*, 30(1), e13206. <https://doi.org/10.1111/jsr.13206>
- Partinen, M., & Gislason, T. (1995). Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *Journal of Sleep Research*, 4, 150–155. <https://doi.org/10.1111/j.1365-2869.1995.tb00205.x>
- Postuma, R.B., Arnulf, I., Hogl, B., Iranzo, A., Miyamoto, T., Dauvilliers, Y., ... Montplaisir, J.Y. (2012). A single-question screen for rapid eye movement sleep behavior disorder: a multicenter validation study. *Movement Disorders*, 27, 913–916. <https://doi.org/10.1002/mds.25037>
- Postuma, R.B., Iranzo, A., Hu, M., Högl, B., Boeve, B.F., & Manni, R., ... Pelletier, A. (2019). Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder: A multicentre study. *Brain*, 142, 744–759.
- Richter, K., Kellner, S., Hillemecher, T., & Golubnitschaja, O. (2021). Sleep quality and COVID-19 outcomes: the evidence-based lessons in the framework of predictive, preventive and personalised (3P) medicine. *EPMA Journal*, 12, 221–241. <https://doi.org/10.1007/s13167-021-00245-2>
- Roenneberg, T., Pilz, L. K., Zerbini, G., & Winnebeck, E. C. (2019). Chronotype and social jetlag: a (self-) critical review. *Biology (Basel)*, 8(3), 54. <https://doi.org/10.3390/biology8030054>
- Rogers, J.P., Watson, C.J., Badenoch, J., Cross, B., Butler, M., Song, J., ... Rooney, A.G. (2021). Neurology and neuropsychiatry of COVID-19: a systematic review and meta-analysis of the early literature reveals frequent CNS manifestations and key emerging narratives. *Journal of Neurology, Neurosurgery & Psychiatry*, 92(9), 932–941.
- Ross, G.W., Petrovitch, H., Abbott, R.D., Tanner, C.M., Popper, J., Masaki, K., ... White, L.R. (2008). Association of olfactory dysfunction with risk for future Parkinson's disease. *Annals of Neurology*, 63, 167–173. <https://doi.org/10.1002/ana.21291>
- Stefano, G.B. (2021). Historical Insight into Infections and Disorders Associated with Neurological and Psychiatric Sequelae Similar to Long COVID. *Medical Science Monitor*, 27, e931447. <https://doi.org/10.12659/MSM.931447>
- Sudre, C.H., Murray, B., Varsavsky, T., Graham, M.S., Penfold, R.S., Bowyer, R.C., ... Steves, C.J. (2021). Attributes and predictors of long COVID. *Nature Medicine*, 27, 626–631. <https://doi.org/10.1038/s41591-021-01292-y>
- Taquet, M., Dercon, Q., Luciano, S., Geddes, J.R., Husain, M., & Harrison, P.J. (2021). Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19. *PLoS Medicine*, 18, e1003773. <https://doi.org/10.1371/journal.pmed.1003773>
- Topp, C.W., Østergaard, S.D., Søndergaard, S., & Bech, P. (2015). The WHO-5 Well-Being Index: A systematic review of the literature. *Psychotherapy and Psychosomatics*, 84, 167–176. <https://doi.org/10.1159/000376585>
- Üstün, T.B., Kostanjsek, N., Chatterji, S., & Rehm, J. (2010). Measuring health and disability: Manual for WHO disability assessment schedule WHODAS 2.0. World Health Organization.
- Xydakis, M.S., Albers, M.W., Holbrook, E.H., Lyon, D.M., Shih, R.Y., Frasnelli, J.A., ... Perlman, S. (2021). Post-viral effects of COVID-19 in the olfactory system and their implications. *The Lancet Neurology*, 20(9), 753–761. [https://doi.org/10.1016/S1474-4422\(21\)00182-4](https://doi.org/10.1016/S1474-4422(21)00182-4)
- Zubair, A.S., McAlpine, L.S., Gardin, T., Farhadian, S., Kuruvilla, D.E., & Spudich, S. (2020). Neuropathogenesis and neurologic manifestations of the coronaviruses in the age of coronavirus disease 2019: a review. *JAMA Neurology*, 77, 1018–1027. <https://doi.org/10.1001/jamaneurol.2020.2065>

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Merikanto, I., Dauvilliers, Y., Chung, F., Holzinger, B., De Gennaro, L., Wing, Y. K., Korman, M., & Partinen, M. (2022). Disturbances in sleep, circadian rhythms and daytime functioning in relation to coronavirus infection and Long-COVID – A multinational ICOSS study. *Journal of Sleep Research*, 31, e13542. <https://doi.org/10.1111/jsr.13542>