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Human sleep in COVID-19 pandemic times

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Summary

In the 2020–2022 biennium, humankind faced one of the worst public health crises of all time. The SARS-CoV-2 spread posed unprecedented challenges to modern societies, pervasively reshaping the everyday life of the world population. In this Thesis, we addressed how the multifaced lifestyle and societal changes due to the COVID-19 outbreak interacted with human sleep, describing a series of studies aimed at unraveling the brief- and long-term consequences of the pandemic period on sleep features of the Italian population.

The project consisted of a cross-sectional investigation engaging almost fourteen thousand participants during the first lockdown and three longitudinal assessments involving over two thousand respondents across different pandemic stages (the final weeks of lockdown, the second contagion wave period, and the emergency resolution two years later).

We examined the progression of sleep ad mental health, outlining possible demographic, psychological, and behavioral risk factors during different emergency phases. We addressed the transient changes in sleep duration and sleep schedules, the consequences of working adjustments, and how all these events interacted with the different circadian typologies. We also explored the repercussions of the increased digital screen time under social distancing, and the role of sleep on the subsequent risk for long COVID symptoms.

Finally, we contextualized the project results in the international framework, providing an updated and comprehensive overview of the scientific evidence in the field and discussing the learned lessons from the pandemic to better manage the complex and inextricable relationship between sleep and social/behavioral factors.

Preface

At the beginning of my PhD course, I enthusiastically approached the sleep field, planning a project about the sleep role on memory consolidation. In March 2020, the spread of COVID-19 forced all of us to suspend our research activity. However, when the Italian Prime Minister imposed the first nationwide lockdown, I immediately realized that such extraordinary situation constituted an incredible opportunity, giving rise to a colossal open-air laboratory to study human sleep.

This research project was conceived in the earliest days of home confinement, later becoming the first and most extensive investigation to understand the consequences of the COVID-19 pandemic on Italians' sleep. To date, the project has seen the participation of thousands of people across four survey waves during different pandemic phases, providing a valuable contribution to the scientific literature in understanding and managing the emergency period.

Those intuitions during the first days of lockdown triggered a prolific research line, turning out to be the best training ground for a young and ambitious student that approached the scientific research field for the first time. This project led me to publish 11 in-extenso articles in international peer-reviewed journals (9 as first author and 2 as result of international collaborations), 1 chapter in an international book, 7 abstracts as (inter-)national conference proceedings, and it allowed me to attend for three times the Italian Association of Sleep Medicine congress as invited-speaker.

With this Thesis, I would guide the reader on a 360º journey over the first two COVID-19 pandemic years, showing how all the characteristics of this historical period interacted with the people's sleep. We will start from the first weeks of lockdown and travel for its entire duration during the Spring 2020 (Part 1). Then, we will cross the second contagion wave during the subsequent Winter (Part 2), up to the end of the emergency two years after the lockdown (Part 3).

Chapter by chapter, the reader will witness the evolution of the COVID-19 emergency. Rather than a weakness, the lack of updating of some passages should be taken as a strength of the work, which offers an authentic stepwise representation of the pandemic's complexity by reflecting all the uncertainties and nuances that have characterized those turbulent periods.

At the same time, the reader would enjoy the professional growth of the writer, mirrored by the gradual refinement in formulating the most appropriate research questions, finely analyze data, and discuss the most disparate results.

Like in any journey, whether enjoyable or not, we should wait until the end to draw conclusions. In this view, the final chapter provides an updated discussion of the addressed topics, summing up the current knowledge and, even more importantly, addressing the lessons that the pandemic has taught us to better manage our sleep. Indeed, besides the obvious negative impact, the pandemic period gave birth to the broadest natural experiment in human history, representing a unique opportunity to deepen our knowledge about the role of the societal and environmental contexts on sleep behavior.

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I am grateful to the scientific committee of the Italian Association of Sleep Medicine, who invited me to participate in their symposia to present my results in the last three years.

I would also like to thank the staff and faculty of the Department of Biotechnological and Applied Clinical Sciences of the University of L'Aquila for their assistance and support.

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Publications

Articles in Peer-Reviewed Journals

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1. **Salfi F.**, & Ferrara M. (2023). Sleep patterns and sleep disturbances during the lockdown periods (Chapter 7). In: *COVID-19 and Sleep: A Global Outlook,* BaHammam A.S., Jahrami H., Pandi-Perumal S.R. (Ed.) Springer. https://doi.org/10.1007/978-981-99-0240-8_7.

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1. **Salfi F.**, Amicucci G., Cascioli J., Corigliano D., Viselli L., Tempesta D., & Ferrara M. (2020). The impact of home confinement due to COVID-19 pandemic on sleep quality and insomnia symptoms among the Italian population. 25th Congress of the European Sleep Research Society (ESRS), virtual congress. *Journal of Sleep Research*, 29(S1): 73–74. https://doi.org/10.1111/jsr.13181.

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7. **Salfi F.**, Amicucci G., Corigliano D., Viselli L., D'Atri A., Tempesta D., & Ferrara M. (2023). Poor sleep quality and insomnia severity before SARS-CoV-2 infection as risk factors for long COVID symptoms. eSleep Europe 2023, virtual congress. *Accepted*.

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1. **Salfi F.**, (2020). Il sonno ai tempi del Coronavirus: un'indagine trasversale e longitudinale sul sonno della popolazione italiana durante la pandemia di COVID-19. *Symposium ''I giovani e la ricerca''*, 30th National Congress of the Italian Association of Sleep Medicine (AIMS), virtual congress.

2. **Salfi F.**, (2022). Two years after lockdown: trajectories of sleep disturbances and mental health over the endless pandemic and the longitudinal relationship between insomnia and depression. *Symposium "I giovani e la ricerca"*, 32nd National Congress of the Italian Association of Sleep Medicine (AIMS), Rimini (Italy).

3. **Salfi F.**, (2022). Disturbi del sonno e salute mentale dopo due anni di pandemia e nel long Covid. *Symposium "Long Covid, sonno e memoria"*, 32nd National Congress of the Italian Association of Sleep Medicine (AIMS), Rimini (Italy).

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PART 2

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Part 1

The lockdown

This section refers to the chapter "Sleep patterns and sleep disturbances during the lockdown periods" in the book "COVID-19 and Sleep: A Global Outlook" (Salfi & Ferrara, 2023), reproduced with permission from *Springer Nature*.

The SARS-CoV-2 virus started to spread in China in the last months of 2019. This virus led to an acute respiratory syndrome associated with a potentially life-threatening pneumonia disease (COVID-19). In the subsequent months, the contagions increased worldwide, giving rise to a global pandemic (Platto et al., 2021). Governments around the world promptly reacted to this situation by applying unprecedented containment measures to counteract the increasing contagion, hospitalization, and death rates. The set of extreme restraining measures became known as *lockdown*, consisting of home confinement, social distancing, and the mandatory closure of schools and most work activities. The pervasive impact of these measures on the lifestyle of the general population was associated with generalized alterations in the main *zeitgebers*. Nationwide lockdown periods led to reduced sunlight exposure, social interactions, and physical activity (Altena et al., 2020). Meanwhile, the daily use of smartphones and computers dramatically increased to compensate for the limited face-to-face interactions, spend longer free time, and relieve boredom (Trott et al., 2022). In this scenario, millions of workers and students began to work from home (Brynjolfsson et al., 2020; Eurofound, 2020), while fears of contagion, economic and employment uncertainties, and worries about the well-being of loved ones burdened everyday life, leading to increased distress and anxiety levels (Rajkumar, 2020). It did not take long to realize that all the above-mentioned factors would have represented the perfect storm to impact the sleep health/habits of the world population.

In Part 1 of the Thesis, I provided a general overview of the multifaceted changes in human sleep under home confinement by reporting the results of the most extensive cross-sectional study (13,989 participants) performed during the Italian lockdown (Chapter 1, 2, and 3) and a longitudinal investigation held during the third and the seventh weeks of stay-at-home orders (Chapter 4 and 5).

In Chapter 1, we identified the main demographic and psychological risk factors of sleep disturbances, also evaluating the changes in sleep duration and sleep schedules under home confinement and how these factors interacted with the different circadian typologies. Finally, we addressed the repercussions of the lockdown-related working adjustments on sleep health/habits.

In Chapter 2, we evaluated the differential impact of the self-confinement period among two at-risk population groups such as late adolescents and older people.

Chapter 3 examined the lockdown effect on university students' sleep and psychological status by comparing a university sample under confinement and a student group evaluated in 2016.

In Chapter 4, we provided the results of the first longitudinal investigation aimed at understanding the cumulative impact of the extended lockdown period on sleep and mental health of the adult population, focusing on possible differences between men and women.

Finally, in Chapter 5, we addressed the effects of the increased use of digital devices over the confinement period on sleep disturbances/schedules of the Italian population.

Chapter 1

Demographic, psychological, chronobiological, and work-related predictors of sleep disturbances during the COVID-19 lockdown in Italy

1.1 Abstract

The first COVID-19 contagion wave caused unprecedented restraining measures worldwide. In Italy, a period of generalized lockdown involving home confinement of the entire population was imposed for almost two months (9 March–3 May 2020). The present is the most extensive Italian investigation aimed to identify the demographic, psychological, chronobiological, and work-related predictors of sleep disturbances throughout the pandemic emergency.

A total of 13,989 Italians completed a web-based survey during the confinement period (25 March–3 May). We collected demographic and lockdown- related work changes information, and we evaluated sleep quality, insomnia, and depression symptoms, chronotype, perceived stress, and anxiety using validated questionnaires.

The majority of the respondents reported a negative impact of confinement on their sleep and a delayed sleep phase. We highlighted an alarming prevalence of sleep disturbances during the lockdown. Main predictors of sleep disturbances identified by regression models were: female gender, advanced age, being a healthcare worker, living in Southern Italy, confinement duration, and a higher level of depression, stress, and anxiety. The evening chronotype emerged as a vulnerability factor, while morning-type individuals showed a lower predisposition to sleep and psychological problems. Finally, working from home was associated with less severe sleep disturbances.

Besides confirming the role of specific demographic and psychological factors in developing sleep disorders during the COVID-19 pandemic, we propose that circadian typologies could react differently to a particular period of reduced *social jetlag*. Moreover, our results suggest that working from home could play a protective role against the development of sleep disturbances during the current pandemic emergency.

1.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Scientific Reports* (Salfi, Lauriola, et al., 2021) and reproduced with permission from *Springer Nature*.

The rapid spread of the new Coronavirus (SARS-CoV-2) outbreak led the global governments to adopt generalized lockdown and social distancing measures to limit the virus propagation. The Italian population was subjected to home confinement for almost two months (9 March–3 May 2020). The restraining measures involved unprecedented limitations of mobility rights and social interactions. This stressful situation profoundly compromised the general population's everyday life, resulting in pervasive psychological repercussions (Rajkumar, 2020; Vindegaard & Benros, 2020). In this extraordinary historical period, sleep represented one of the primary victims (Altena et al., 2020). Several cross-sectional and longitudinal studies confirmed this assumption, showing a high prevalence of sleep disturbances during the lockdown period (for a meta-analysis, see Jahrami et al., 2021).

In the current study, we present the most extensive Italian investigation (n = 13,989) aimed to provide a comprehensive snapshot of sleep health and habits during the entire home confinement period due to the COVID-19 outbreak. We used a web-based survey covering the two months of total lockdown to evaluate sleep quality, insomnia symptoms, chronotype, depression symptoms, perceived stress, and anxiety of the Italian population under restraining measures.

The present investigation was conceived to understand the sociodemographic, psychological, chronobiological, and work-related predictors of the sleep disturbances during the home confinement period. Several cross-sectional studies showed women (Casagrande et al., 2020; Cellini et al., 2021; Guadagni et al., 2020; X. Li et al., 2020; J. Wang et al., 2020) and healthcare workers (Muller et al., 2020; Pappa et al., 2020) as the categories suffering the most. Furthermore, literature also revealed a close relationship between psychological well-being and sleep disturbances during the pandemic period (Cellini et al., 2020; Guadagni et al., 2020; Jahrami et al., 2021; W. Wang et al., 2020). First of all, we expected to confirm these results within our larger sample.

Moreover, the present study aimed to provide new insights about some aspects not yet addressed, such as the role of the individual circadian preference (chronotype) and the lockdown-related work changes in the expression of sleep disturbances during the first COVID-19 outbreak wave.

The restraining measures impacted the sleep/wake rhythms. People delayed the bedtime and wake up time during the lockdown (Cellini et al., 2020, 2021; Korman et al., 2020; Leone et al., 2020), resulting in a reduction of *social jetlag* (Korman et al., 2020; Leone et al., 2020; Wright et al., 2020), which could be conceived as a proxy for a challenged circadian system and compromised sleep (Kantermann, 2020; Wittmann et al., 2006). Conventionally, three main chronotypes have been identified (Adan et al., 2012): the morning-type (MT), the neither-type (NT), and the evening-type (ET). The ET typically showed lower sleep quality (Fabbian et al., 2016; Merikanto et al., 2012; Rique et al., 2014), and this evidence was ascribed to the misalignment between the biological and social clock (i.e., the timing of social obligations), which is associated to the unhealthy manifestation of *social jetlag* (Adan et al., 2012; Wittmann et al., 2006).

Furthermore, higher levels of negative mood and anxiety characterize ET individuals (Au & Reece, 2017; Fabbian et al., 2016; Fares et al., 2015; Merikanto et al., 2013). The *social jetlag* and the sleep difficulties have been proposed to account for the ET's tendency to experience psychological symptoms (Kivelä et al., 2018; Levandovski et al., 2011; van den Berg et al., 2018). In this view, we could expect that during a period of large-scale reduction of the *social jetlag* such as the home confinement due to the COVID-19 outbreak, the gap between circadian typologies could be narrowed down because ET, in particular, may have benefitted from a period marked by a loosening of rigorous sleep/wake schedule due to weaker social and working obligations.

Finally, the lockdown impacted the working routine of the majority of the population, leading to the suspension of the working activity and the imposition of remote working. The widespread possibility of working from home in telematic mode with a great flexibility in the working schedule could be a further factor contributing to the general population's sleep quality. Therefore, we aimed at verifying the influence of changes in working activity caused by the restraining measures on sleep habits.

1.3 Materials and methods

1.3.1 *Participants and procedure*

A web-based survey has been disseminated through social media (Facebook, WhatsApp, Instagram, Twitter) from the third week to the end of the confinement period (25 March–3 May 2020), using a snowball sampling technique. A total of 13,989 Italian citizens (mean age ± standard deviation: SD, 34.8 ± 12.2 years, range, 18–86 years, 3223 males) participated in the present investigation. The survey started with demographic questions (age, gender, education, occupation, geographic location) and COVID-related information (infection or forced quarantine). Demographic information is reported in Table 1.1. Then, we asked to rate the perceived impact of the lockdown on sleep quality (positive, none, negative), and the occurred changes of bedtime (delayed, maintained, advanced), wake up time (delayed, unchanged, advanced), and nap habits (increased, unchanged, reduced). Subsequently, the survey comprised an evaluation of the working activity changes. We collected information on the suspension of the working activity (yes, no), the beginning of the remote working modality (yes, no), and the changes of the daily working time (increased, unchanged, reduced). Then, we evaluated sleep quality, insomnia severity symptoms, and chronotype, through a set of validated questionnaires (see next paragraph for a detailed description): the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989; Curcio et al., 2013), the Insomnia Severity Index (ISI; Bastien et al., 2001; Castronovo et al., 2016), the reduced version of the Morningness-Eveningness Questionnaire (MEQr; Natale, 1999). Finally, we assessed depression symptoms, perceived stress, and anxiety using (in order of presentation) the Beck Depression Inventory-second edition (BDI-II; Ghisi et al., 2006), the 10-item Perceived Stress Scale (PSS-10; Mondo et al., 2021), and the state-anxiety subscale of the State-Trait Anxiety Inventory (STAI-X1; Spielberger et al., 1970), respectively. Participation in the entire survey required approximately 25 min, and the compilation of the last three questionnaires (BDI-II, PSS-10, STAI-X1) was optional to avoid false/unreliable responses in the final part of the survey. A total of 9982 respondents (71.4%) compiled the BDI-II, 9282 also the PSS-10 (66.5%), and 9064 completed all the questionnaires (64.8%). The study was approved by the Institutional Review Board of the University of L'Aquila (protocol n. 43,066/2020) and carried out according to the principles established by the Declaration of Helsinki. Online informed consent to participate in the research was obtained from all the respondents.

Table 1.1. Demographic characteristics of the sample.

Variable	N (%)
Age	
18–30	7424 (53.0)
31–50	4755 (33.9)
Over 50	1810 (12.9)
Gender	
Men	3123 (22.3)
Women	10866 (77.6)
Geographical location	
Northern Italy[a]	5783 (41.3)
Central Italy[b]	3389 (24.2)
Southern Italy[c]	4817 (34.4)
Education	
Middle school	501 (3.6)
High school	5350 (38.2)
Graduated	6750 (48.2)
Over graduated	1388 (9.9)
Occupation	
Unemployed	1347 (9.6)
Student	4117 (29.4)
Worker	
Healthcare work	781 (5.6)
Other work	7744 (55.3)
COVID-19 infection	
No	13801 (98.6)
Yes	44 (0.3)
No response	144 (1.0)
Forced quarantine	
No	12890 (92.1)
Yes	1032 (7.4)
No response	67 (0.5)

Notes: [a]Northern Italy: Aosta Valley, Emilia Romagna, Friuli-Venezia Giulia, Liguria, Lombardy, Piedmont, Trentino-Alto Adige, and Veneto. [b]Central Italy: Lazio, Marche, Tuscany, and Umbria. [c]Southern Italy: Abruzzo, Apulia, Basilicata, Calabria, Campania, Molise, Sardinia, and Sicily.

1.3.2 *Questionnaires*

The PSQI is a 19-item questionnaire widely used to evaluate sleep quality (Buysse et al., 1989; Curcio et al., 2013), chosen to obtain a multidimensional description of sleep disturbances and sleep patterns (bedtime, get up time, and total sleep time). Each dimension covered by PSQI (sleep quality, sleep duration, sleep latency, habitual sleep efficiency, sleep disorders, the use of sleeping medications, daytime dysfunctions) is scored between 0 and 3, and higher scores (range, 0–21) point to more severe sleep difficulties. Scores higher than 5 represent a valid indicator of poor sleep quality (Buysse et al., 1989).

The ISI was used to obtain a clinical evaluation of insomnia symptoms and their severity (Bastien et al., 2001; Castronovo et al., 2016). It is a screening instrument that comprises an evaluation of seven dimensions: difficulty falling asleep, difficulty staying asleep, waking too early, sleep satisfaction, sleep interference with daytime functioning, noticeability of sleep problems by others, and worry about sleep. Respondents rate each item using a 5-point Likert scale (0–4), yielding a total score ranging from 0 to 28. Validated cut-off scores can be used to identify clinical insomnia conditions (0–7: no insomnia; 8–14 subthreshold insomnia; 15–21: moderate insomnia; 22–28: severe insomnia) (Bastien et al., 2001).

The MEQr is a 5-item questionnaire comprising a self-report evaluation of ideal rising time and bedtime, personal efficiency peak time, morning freshness, and self-evaluation of chronotype (Natale, 1999). It represents a short version of the original 19-item mixed-format scale developed by Horne and Östberg (Horne & Östberg, 1976), which is the most widely used self-report instrument in chronopsychological research to identify circadian typologies (Adan et al., 2012). Discriminating power of the Italian version of MEQr to identify circadian typologies was confirmed using physiological measures (body temperature) and recorded motor activity as external criterion (Natale, 1999; Natale et al., 2006). Total score ranging from 4 to 25 is used to classify the chronotype (ET: 4–10; NT: 11–18; MT: 19–25).

The BDI-II is a 21-item self-report inventory designed to measure the severity of depression assessing affective, somatic, and cognitive symptoms according to diagnostic criteria listed in the Diagnostic and Statistical Manual for Mental

Disorders (American Psychiatric Association, 2000). Respondents rate the severity of each symptom using a 0 to 3 scale, and higher scores indicate more severe depression symptomatology (range, 0–63) (Ghisi et al., 2006; Sica & Ghisi, 2007). Validated cut-off scores can be used to classify depression conditions (0–13: no depression; 14–19 mild depression; 20–28: moderate depression; 29–63: severe depression).

The PSS-10 is a reduced version of the widely used PSS (S. Cohen et al., 1983). It is a 10-item questionnaire evaluating thoughts and feelings referred to stressful events. Respondents are asked how often they felt a certain way on a 0–4 Likert scale regarding six negatively stated and four positively stated (reverse score) items. Higher scores point to higher perceived stress (range, 0–40). The Italian version of PSS-10 showed greater psychometric properties than the original PSS (Mondo et al., 2021).

The STAI-X1 is a well-established instrument to measure state anxiety in research and clinical settings (Spielberger et al., 1970). It is a subscale of the State-Trait Anxiety Inventory, included in the Cognitive Behavioural Assessment battery 2.0 (Sanavio et al., 1998). STAI-X1 comprises 20 item items referred to feelings of apprehension, tension, nervousness, worry, and activation of the autonomic nervous system. Respondents rate the intensity of each symptom on a 4-point Likert scale; higher scores indicate more significant state anxiety (range, 20–80).

1.3.3 *Data analysis*

We performed frequencies analyses to show the proportion of the reported impact of the lockdown period on sleep (negative, none, positive), and the changes of bedtime (advanced, unchanged, delayed), wake up time (advanced, unchanged, delayed), and nap habits (increased, unchanged, reduced).

The analyses involving PSQI score were carried out excluding 814 participants due to compilation errors (i.e., respondents declared longer total sleep time compared with the reported total time in bed). According to the validated criteria of PSQI and ISI questionnaires, we calculated the prevalence of poor sleepers and clinical insomniacs to provide a descriptive overview of the entire sample.

Multiple regression analyses were carried out with PSQI and ISI scores as dependent variables. The regression models comprised the following continuous and categorical predictors: "*Age*" (continuous variable), "*Gender*" (man, woman), "*Education*" (middle school, high school, graduated, over-graduated), "*Occupation*" (healthcare work, other work, student, unemployed), "*Geographic location*" (Norther Italy, Central Italy, Southern Italy), the "*Experience of the forced quarantine*" (yes, no, no response), "*Duration of the confinement period*" (based on the day of participation to the survey), and the MEQr, BDI-II, PSS-10, and STAI-X1 questionnaire scores (continuous variables). We did not include the "*COVID-19 infection*" factor (yes, no, no response) due to the low number of infected subjects (only 44 participants).

We calculated the chronotype composition of our sample (MT, NT, ET) according to the MEQr cut-off scores. Then, we performed chi-square tests to evaluate the association of the three circadian typology groups with the perceived impact of the lockdown period on sleep, the reported changes of bedtime, wake up time, and nap habits, and the prevalence of poor sleepers and clinical insomnia conditions.

To evaluate differences in sleep quality, insomnia severity symptoms, depression, perceived stress, and anxiety, between MT, NT, and ET, we carried out ANCOVAs on the scores of the five questionnaires (PSQI, ISI, BDI-II, PSS-10, STAI-X1), with chronotype (MT, NT, ET) as three-level between-subjects factor. The current literature supports a strong relationship between age and chronotype (Adan et al., 2012; Carrier et al., 1997). Therefore, the analyses controlled for the effect of age (continuous variables) used as a covariate.

Finally, we applied a t-test analysis to compare the PSQI and ISI scores of the respondents who suspended or maintained the working activity. In order to evaluate the effect on sleep quality and insomnia symptoms due to the changes in the modality (remote working) and duration of the daily working activity, the PSQI and ISI scores were submitted to two-way ANOVAs, with "*Remote working*" (yes, no) and "*Daily working time*" (increased, unchanged, reduced) as two-level and three-level between-subjects factors, respectively.

In some cases, further exploratory analyses were performed, using the information of interest (i.e., bedtime, get up time, sleep duration) derived from the PSQI (see 1.4.3 and 1.4.4 sections).

All the analyses were two-tailed, and Bonferroni *post hoc* comparisons were performed in case of significant effects. A p-value < 0.05 was considered significant. When the data did not appear normally distributed or looked like heteroscedastic, "robust" or nonparametric techniques were used to check for bias in the inferential tests that could have led to misleading conclusions. Because these control analyses produced almost identical results to those obtained using the standard parametric tests, we concluded that violations of parametric assumptions were of negligible importance, and we reported only the parametric test results.

1.4 Results

1.4.1 *Lockdown-related consequences on sleep and prevalence of sleep disturbances*

Most respondents reported a negative impact of the restraining measures on their sleep, delayed bedtime and wake up time, and maintained unchanged nap habits. According to the PSQI and ISI criteria, over six out of ten of the participants were poor sleepers, and 15% of the respondents had symptoms of moderate/severe clinical insomnia (Table 1.2).

Table 1.2. Prevalence of lockdown-related consequences and sleep disturbance prevalence within the total sample.

Variable	N (%)
Perceived impact	
Negative	8455 (60.5)
None	3306 (23.6)
Positive	2228 (15.9)
Bedtime	
Advanced	1288 (9.2)
Unchanged	4483 (32.1)
Delayed	8218 (58.7)
Wake up time	
Advanced	1570 (11.2)
Unchanged	3563 (25.5)
Delayed	8856 (63.3)
Nap habits	
Increased	2477 (17.7)
Unchanged	9045 (64.7)
Reduced	2467 (17.6)
Sleep quality	
Good	5122 (38.9)
Poor	8053 (61.1)
Insomnia	
No	6597 (47.2)
Subthreshold	5297 (37.9)
Moderate	1840 (13.2)
Severe	255 (1.8)

Notes: Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section).

1.4.2 *Predictors of sleep disturbances*

Significant regression equations were found with PSQI and ISI scores as dependent variables (PSQI: $R^2 = 0.30$, $F_{17,8552} = 219.07$, $p < 0.001$; ISI: $R^2 = 0.35$, $F_{17,9046} = 285.07$, $p < 0.001$).

As shown in Table 1.3, older age, female gender, healthcare work, living in Southern Italy, and confinement duration were associated with highest PSQI and ISI scores. Moreover, lower education predicted poorer sleep quality. Lower scores of MEQr (pointing to evening chronotype), and a higher level of depression, perceived stress, and anxiety predicted poorer sleep quality and more severe insomnia symptoms.

Table 1.3. Results (β and p) of the multiple linear regressions on PSQI and ISI scores.

Predictor	PSQI score		ISI score	
	β	p	β	p
Intercept		**< 0.001**		0.129
Age	0.136	**< 0.001**	0.048	**< 0.001**
Gender				
Woman		*Reference*		
Man	−0.182	**< 0.001**	−0.087	**< 0.001**
Education				
Middle school		*Reference*		
High school	−0.165	**0.003**	0.003	0.957
Graduated	−0.218	**< 0.001**	−0.063	0.224
Over graduated	−0.256	**< 0.001**	−0.082	0.151
Occupation				
Health work		*Reference*		
Other work	−0.134	**< 0.001**	−0.078	**0.038**
Student	−0.201	**< 0.001**	−0.142	**< 0.001**
Unemployed	−0.084	0.088	−0.038	0.404
Geographic location				
Northern Italy		*Reference*		
Central Italy	0.003	0.903	−0.015	0.487
Southern Italy	0.094	**< 0.001**	0.040	0.054
Home confinement duration	0.073	**< 0.001**	0.068	**< 0.001**
Forced quarantine				
Yes		*Reference*		
No	−0.053	0.142	−0.006	0.859
No response	0.126	0.386	0.230	0.097
MEQr score	−0.079	**< 0.001**	−0.070	**< 0.001**
BDI-II score	0.330	**< 0.001**	0.369	**< 0.001**
PSS-10 score	0.073	**< 0.001**	0.097	**< 0.001**
STAI-X1 score	0.148	**< 0.001**	0.157	**< 0.001**

Notes: Bold values are statistically significant. [a] Northern Italy: Aosta Valley, Emilia Romagna, Friuli-Venezia Giulia, Liguria, Lombardy, Piedmont, Trentino-Alto Adige, and Veneto. [b] Central Italy: Lazio, Marche, Tuscany, and Umbria. [c] Southern Italy: Abruzzo, Apulia, Basilicata, Calabria, Campania, Molise, Sardinia, and Sicily.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced; BDI-II, Beck Depression Inventory-second edition; PSS-10, Perceived Stress Scale-10 item; STAI-X1, State-anxiety subscale of the State-Trait Anxiety Inventory.

1.4.3 *Chronotype differences*

According to the MEQr criteria, our sample consisted of 3261 MT subjects (21.3%), 9181 NT (65.6%), and 1547 ET (11.1%). Chi-square tests (Table 1.4) showed significant associations of the chronotype group (MT, NT, ET) with the perceived impact of the restraining measures, with the reported changes in bedtime, wake up time, and nap frequency, and with the prevalence of poor sleepers and clinical insomnia conditions. Specifically, a higher proportion of ET subjects reported a negative impact of the restraining measures, delayed bedtime and wake up time, and changes in nap habits. Additionally, the ET group was marked by a higher prevalence of poor sleepers and clinical insomniacs. MT participants showed the opposite pattern of results.

Table 1.4. Frequency of the lockdown-related perceived impact on sleep, reported changes of bedtime, wake up time and nap habits, and prevalence of poor sleepers and clinical insomnia conditions within the three chronotype groups (MT, NT, ET). Chi-square test results are also reported (χ^2 and p).

Variable	MT	NT	ET	χ^2	p
		N (%)			
Perceived impact					
Negative	1645 (50.4)	5740 (62.5)	1067 (69.0)		
None	1017 (31.2)	2015 (21.9)	277 (17.9)	211.02	**< 0.001**
Positive	599 (18.4)	1426 (15.5)	203 (13.1)		
Bedtime					
Advanced	384 (11.8)	820 (8.9)	84 (5.4)		
Unchanged	1433 (43.9)	2752 (30.0)	298 (19.3)	480.29	**< 0.001**
Delayed	1444 (44.3)	5609 (61.1)	1165 (75.3)		
Wake up time					
Advanced	454 (13.9)	994 (10.8)	122 (7.9)		
Unchanged	1184 (36.3)	2146 (23.4)	233 (15.1)	419.39	**< 0.001**
Delayed	1623 (49.8)	6041 (65.8)	1192 (77.1)		
Nap habits					
Increased	563 (17.3)	1575 (17.2)	339 (21.9)		
Unchanged	2223 (68.2)	5926 (64.5)	896 (57.9)	59.84	**< 0.001**
Reduced	475 (14.6)	1680 (18.3)	312 (20.2)		
Sleep quality					
Poor	1599 (51.9)	5433 (62.6)	1021 (72.2)	190.25	**< 0.001**
Good	1481 (48.1)	3247 (37.4)	394 (27.8)		
Insomnia					
No	1901 (58.3)	4131 (45.0)	565 (36.5)		
Subthreshold	1041 (31.9)	3614 (39.4)	642 (41.5)	291.11	**< 0.001**
Moderate	288 (8.8)	1264 (13.8)	288 (18.6)		
Severe	31 (1.0)	172 (1.9)	52 (3.4)		

Notes: Bold values are statistically significant. Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section).
Abbreviations: MT, Morning-type; NT, Neither-type; ET, Evening-type.

As hypothesized, the MEQr scores and the age variable were highly correlated ($R = 0.28$; $p < 0.001$), confirming the assumption of using the age as covariate in the subsequent analyses. One-way ANCOVAs carried out on sleep and psychological questionnaires showed a significant effect of the "*Chronotype*" factor (MT, NT, ET) (PSQI: $F_{13171} = 152.70$, $p < 0.001$; ISI: $F_{13985} = 173.01$, $p < 0.001$;

BDI-II: $F_{9978} = 134.17$, $p < 0.001$; PSS-10: $F_{9278} = 95.01$, $p < 0.001$; STAI-X1: $F_{9060} = 45.58$, $p < 0.001$). The "*Age*" covariate yielded a significant effect in the analyses on PSQI, BDI-II, and PSS-10 scores (all $p < 0.001$), while it was not significant for ISI ($p = 0.35$) and STAI-X1 ($p = 0.58$). *Post hoc* comparisons (Figure 1.1) showed that the ET group had higher scores in all the dimensions compared to MT and NT (all $p < 0.001$). NT showed higher scores compared to MT group for all the variables (all $p < 0.001$).

Control analyses were performed adding the "*Gender*" factor as a further covariate in the ANCOVAs, confirming all the above-reported pattern of results. Finally, exploratory analyses highlighted a significant difference between the three chronotype groups for the reported sleep duration ($F_{13986} = 14.14$, $p < 0.001$). ET participants slept more (mean ± standard error: SE, 444 min ± 2 min) than NT (426 min ± 1 min) and MT groups (420 min ± 1 min; both $p < 0.001$).

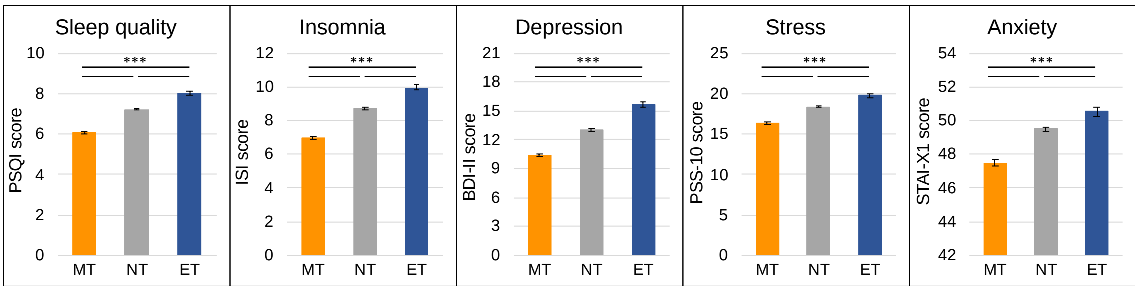

Figure 1.1. Sleep quality, insomnia, depression, perceived stress, and anxiety in the three chronotype groups (Morning-type, Neither-type, Evening-type).

Notes: Mean (and standard errors) of questionnaire scores are reported. Analyses were adjusted for age. Results of Bonferroni *post hoc* comparisons are indicated with asterisks (***$p < 0.001$).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; BDI-II, Beck Depression Inventory-second edition; PSS-10, Perceived Stress Scale-10 item; STAI-X1, State-anxiety subscale of the State-Trait Anxiety Inventory; MT, Morning-type; NT, Neither-type; ET, Evening-type.

1.4.4 *Working activity changes*

A total of 3314 workers (38.9% of the total workers' sample) suspended their working activity during the lockdown. T-tests on PSQI and ISI scores showed significant differences between the group of respondents that suspended and the group that preserved their working activity (PSQI: $t_{8084} = 2.56$, $p = 0.01$; ISI: $t_{8523} = 6.18$, $p < 0.001$). The suspension of the working activity was associated with lower sleep quality (mean ± SE, 7.15 ± 0.07 vs. 6.91 ± 0.05) and more severe insomnia symptoms (8.67 ± 0.10 vs. 7.91 ± 0.08).

Among the sample who continued to work (5211 subjects), a total of 3536 respondents worked from home, 2125 reported reduced working time, 1989 maintained unchanged the work duration, and 1097 subjects increased their daily working time.

Two-way ANOVAs on PSQI and ISI scores highlighted significant effects of "*Remote working*" (PSQI: $F_{1,4941} = 45.91$, $p < 0.001$; ISI: $F_{1,5205} = 17.60$, $p < 0.001$), and "*Daily working time*" factors (PSQI: $F_{2,4941} = 28.49$, $p < 0.001$; ISI: $F_{2,5205} = 25.21$, $p < 0.001$). The interactions between the two factors ("*Remote working*" and "*Daily working time*") were significant in both analyses (PSQI: $F_{2,4941} = 6.23$, $p = 0.002$; ISI: $F_{2,5205} = 4.13$, $p = 0.02$).

Post hoc comparisons (Figure 1.2) pointed to lower sleep quality and more severe insomnia symptoms for the participants who increased the daily working time within both remote working and regular working group (all $p < 0.01$). There were no differences in PSQI and ISI scores between the two groups (remote vs. regular work) when they reduced the working time (both $p = 1.00$). When the daily working time was the same or increased compared with the pre-outbreak period, the remote workers showed lower scores on PSQI (both $p < 0.001$) and ISI questionnaires ($p = 0.03$, $p = 0.01$; respectively). Notably, the remote workers who increased the daily working time reported the same sleep quality and insomnia symptoms of the regular workers who reduced (PSQI: p = 1.00; ISI: p = 0.25) or maintained unchanged the working duration (PSQI: p = 1.00; ISI: p = 0.85).

Exploratory analyses showed that the remote working group went to bed and got up later (bedtime: hh:mm ± SE, 00:01 ± 1 min; get up time: 08:17 ± 1 min) and slept more (419 min ± 1 min) compared to the respondents who continued to reach the workplace (bedtime: 23:33 ± 2 min, t_{5209} = 11.93, p < 0.001; get up time: 07:28 ± 2 min, t_{5209} = 19.20, p < 0.001; sleep duration: 392 min ± 2 min, t_{5209} = 11.38, p < 0.001).

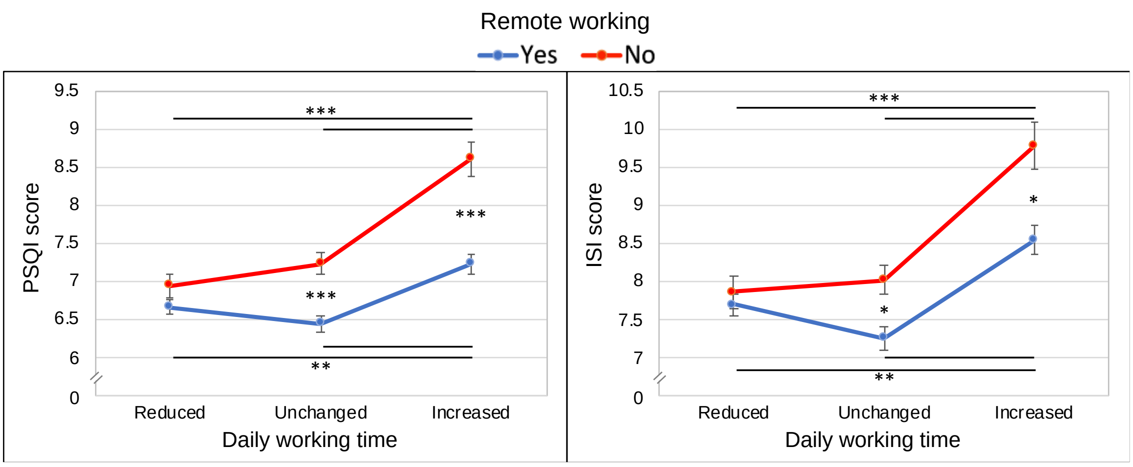

Figure 1.2. Interaction between "*Remote working*" (yes, no) and "*Daily working time*" (reduced, unchanged, increased) factors, for sleep quality (PSQI) and insomnia severity symptoms scores (ISI).

Note: The figures report mean (and standard errors) of the PSQI and ISI questionnaire scores. Results of Bonferroni *post hoc* comparisons are reported with asterisks (*p < 0.05; **p < 0.01 ***p < 0.001).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index.

1.5 Discussion

Our study provided a comprehensive description of sleep health during the lockdown in Italy. Most respondents (approximately 60%) declared a negative impact of the restraining measure and delayed bedtime and wake up time. We highlighted an alarming prevalence of poor sleepers and clinical insomniacs within our large sample: six out of ten participants were poor sleepers, and more than half of the sample presented from subthreshold to severe insomnia symptoms.

On the other hand, it is noteworthy that a proportion of the respondents (approximately 16%) declared a positive impact of the lockdown measures on their sleep, supporting the assumption that a loosening of rigorous sleep/wake schedule due to weaker social and working obligations could have a beneficial effect on part of the population (Kocevska et al., 2020).

In line with the current literature (Cellini et al., 2020; Guadagni et al., 2020; Jahrami et al., 2021; W. Wang et al., 2020) we demonstrated a strong relationship between sleep variables and depression, stress, and anxiety. We confirmed the results of other cross-sectional investigations on healthcare workers (Muller et al., 2020; Pappa et al., 2020) and women (Casagrande et al., 2020; Cellini et al., 2021; Guadagni et al., 2020; X. Li et al., 2020; J. Wang et al., 2020), which appeared as the categories experiencing the most severe sleep problems during lockdown worldwide. Furthermore, advanced age predicted more severe sleep disturbances. An interpretation of the healthcare workers' results is related to the well-known increased stressful workload, accompanied by higher contagion risk. Consistently, several studies demonstrated a high prevalence of post-traumatic stress disorder (PTSD) symptoms and mental health problems among the healthcare operators during the COVID-19 pandemic (Pappa et al., 2020; Rossi, Socci, Pacitti, et al., 2020). On the other hand, we suggest caution in the interpretation of the results on women and elderly population since these two factors were typically associated with the poorest sleep quality (Madrid-Valero et al., 2017; Mander et al., 2017) and the higher predisposition to insomnia conditions even in the pre-outbreak period (Kamel & Gammack, 2006; B. Zhang & Wing, 2006). Consistently, our recent longitudinal study (Salfi et al., 2020) showed that the time course of sleep disturbance was different between men and

women, and the male gender appeared as the most vulnerable to the prolongation of the restraining measures.
We highlighted more severe sleep disturbances in Southern Italy, and this result is inconsistent with the available literature on sleep and COVID-19 in the Italian population (Casagrande et al., 2020), which identified a higher prevalence of sleep problems in Northern Italy. However, differences in the period under consideration might explain the different results. The previous investigation (Casagrande et al., 2020) was referred to the first weeks of the outbreak, when the geographic propagation of the contagion in Italy was extremely unbalanced towards Northern regions (Istituto Superiore di Sanità, 2020). Our study covered the entire confinement period instead, providing a more reliable overview of the effect of the pandemic propagation in Southern Italy. Moreover, we hypothesize that our results could also reflect the economic consequences of the pandemic since Southern Italy was the territorial area most economically affected by the COVID-19 crisis (SVIMEZ, 2020).
Finally, the confinement duration was a predictive factor of sleep disturbances, corroborating the hypothesis of a cumulative detrimental effect of the protracted lockdown period. However, scarce evidence had been provided worldwide, with only a few studies addressing this question through longitudinal investigations across the confinement period (Salfi, Amicucci, et al., 2021; Salfi et al., 2020; C. Wang, Pan, Wan, Tan, Xu, McIntyre, et al., 2020).

1.5.1 *Chronotypes under lockdown*

According to the initial hypothesis, ET respondents reported the most prevalent delay of the sleep phase. These results are consistent with another Italian cross-sectional study carried out during the lockdown (Marelli et al., 2021). However, the ET participants reported suffering more from the confinement situation than the other circadian typologies. Coherently, this group showed the lowest sleep quality and the highest level of insomnia, depression, perceived stress, and anxiety. Meanwhile, MT showed the opposite pattern of results, declaring a lower negative impact of the restraining measures and a higher prevalence of preserved sleep schedule. This finding was exemplified by the highest sleep quality, less marked insomnia and depression symptoms, and the lowest perceived stress and anxiety levels.

The present results pointed to a particular vulnerability of the ET group, although the lockdown was a favorable period to reduce the mismatch between internal and social clocks. Of note, the present results are consistent with those obtained during the pandemic period in an adolescent clinical population (Çetin et al., 2020).

Our findings suggest that the well-known higher predisposition to sleep disturbances of the ET people (Fabbian et al., 2016; Merikanto et al., 2012; Rique et al., 2014) should not be considered only as a consequence of the accumulated sleep debt due to social and working obligations. In fact, during an unprecedented condition that unlocked time for sleep (Kantermann, 2020), the ET respondents paradoxically reported a slightly longer sleep time although they typically slept less than other circadian typologies in the workdays of pre-pandemic period (Adan et al., 2012), however preserving the more severe sleep problems. This evidence suggests that the evening-individuals' sleep disturbances may instead originate from the misalignment of the delayed sleep pattern to the biological night (Baron & Reid, 2014), which became more pronounced during the lockdown.

On the other hand, morning chronotype emerged as a protective factor, both on the sleep and psychological sides. Recent studies demonstrated that the three chronotype groups differ for resilience level (Antúnez et al., 2015; Jeon & Lee, 2019; Lee et al., 2016) and perceived stress (Romo-Nava et al., 2016). The morning chronotype seems to be more able to cope with challenging situations, while ET individuals are more predisposed to develop PTSD (Hasler et al., 2013; Yun et al., 2015). Our findings confirm this assumption, even in a context of reduced *social jetlag*, such as during the lockdown.

Finally, several studies showed that circadian typologies are associated with specific personality traits and social behavior (Jankowski et al., 2014; Tsaousis, 2010), which could interact with the period of restraining measures (AL-Omiri et al., 2021), contributing to explaining our pattern of results.

1.5.2 *Working during pandemic*

As expected, a substantial percentage of participants suspended the working activity during the lockdown (38.9%), leading to a lower sleep quality and more severe insomnia symptoms. We believe that these findings can be ascribable to the economic repercussions of the work interruption, although this dimension was not assessed in the present study. However, the possibility of maintaining a regular working activity during the confinement could have had a direct positive impact on preserving sleep health. The absence of a daily activity routine could emphasize the sense of boredom, leading to a slowing of the felt pace of the time flow (Zakay, 2014). Consistently, a recent study demonstrated a relationship between the increase of sleep difficulties and the feeling of time dilatation during the lockdown period (Cellini et al., 2020). Coherently, in our study, the unemployed participants were the only group that did not differ from the healthcare workers for sleep disturbances.

On the other hand, within the group of respondents that continued to work, remote working seemed to be a protective factor. During this historical period, working from home was strictly associated with a reduced likelihood of contagion, and thus to a lower perception of risk. Moreover, the higher flexibility of the working schedule could encourage a better organization of the sleep/wake rhythms, favoring longer sleep duration. Consistently, the remote workers slept almost half an hour more than those who continued to reach the workplace.

The changes in daily working time emerged as an essential predictor of sleep disturbances, and the increased work hours were associated with significant sleep problems. This result is consistent with other studies showing an adverse effect of the increased work routine on sleep quality and quantity (Biddle & Hamermesh, 1990; Virtanen et al., 2009). Interestingly, when working time was reduced, there was no benefit of remote working. On the other hand, when the working schedule was maintained or increased, participants who worked remotely showed better sleep quality and fewer insomnia symptoms. However, when the remote workers increased their daily working time, they reached the sleep disturbance level of the regular workers who maintained/reduced the working hours. Therefore, working remotely during the current pandemic should be encouraged as a protective factor, focusing on avoiding extra working time. When the regular working day is not punctuated by fixed starting and ending time point, a common con- sequence could be the increase of daily working duration, with negative consequences on sleep.

1.6 Conclusions

To the best of our knowledge, the present is the most extensive Italian investigation aimed at understanding the pandemic-related consequences on the general population's sleep. However, it should be acknowledged that we used a non-probabilistic sampling technique, with a higher representativity of the female gender and the young population, and the information was collected via self-report questionnaires. Moreover, no data referred to the pre-pandemic period are available, and the cross-sectional nature of the present study precludes causal conclusions regarding the relationship between the examined dimensions.

The results confirmed the hypothesis that the lockdown due to the COVID-19 outbreak had significant repercussions on the sleep quality of the general population (Altena et al., 2020).

The restraining measures had a cumulative cost, and our results confirm the need to avoid over precautionary approaches, keeping the home confinement period as short as possible to limit its long-term negative consequences for sleep and mental health (Brooks et al., 2020).

Our results are consistent with the current literature suggesting a higher predisposition of the female gender to develop sleep problems. In addition, the healthcare workers emerged again as an at-risk category. Moreover, our results showed that the differences in individual daily activity pattern preferences could represent a crucial predictor of sleep and psychological health during the pandemic period. We demonstrated a particular vulnerability of the ET people, while the morning chronotype seems to be a protective factor during the current challenging period.

In light of this evidence, the vulnerable categories should be placed at the center of preventive interventions to avoid the exacerbation of sleep disturbances and mental health problems in the long run. Chronobiological interventions, such as melatonin, light exposure, and social rhythm regulation, could be effective strategies for ET people to hinder the onset or exacerbation of depression symptoms during the period of restraining measures (Adan et al., 2012).

In conclusion, we propose some guidelines for working during the COVID-19 pandemic. Individuals who suspended the working activity should maintain a regular daily activity to counteract the development and exacerbation of sleep disturbances. Remote working should be encouraged, as long as the overall daily activity duration does not increase, establishing fixed starting and ending times of the workday. This aspect should be regulated since remote working and teleworking could become increasingly widespread modalities regardless of the pandemic's conclusion (European commission, 2020). In this view, the results of the present investigation could be generalizable to non-emergency periods. Furthermore, people who work in telematic modality should avoid exposure to backlit screens of electronic devices before falling asleep since the increased evening exposure was suggested as a causal factor in developing sleep disturbances during lockdown (Salfi, Amicucci, et al., 2021).

An adequate sleep quality/quantity is essential to deal with stressful events (Leggett et al., 2016) and preserve mental health (Pigeon et al., 2017), emotional regulation (Tempesta et al., 2018, 2020), as well as the proper functioning of the immune system (Bryant et al., 2004). Consequently, the present results have a broad-spectrum of implications. Our study's findings could be essential in the present period, where the second contagion wave has become a reality, hundreds of thousands of people are subjected to restraining measures worldwide, and the impact of current emergency on sleep and mental health of general population persists (Salfi, D'Atri, et al., 2021). All the insights provided in this study should be considered from the institutions to design public campaigns aimed to promote sleep health and general well-being during the current unprecedented situation.

Chapter 2

The differential impact of COVID-19 lockdown on sleep quality, insomnia, depression, stress, and anxiety among late adolescents and elderly in Italy

2.1 Abstract

The restraining measures due to the COVID-19 outbreak deeply affected the general population's sleep health and psychological status. The current literature proposes young and older people as two particularly at-risk groups. However, the differential impact of the lockdown period in these specific age categories needs to be disentangled.

Through a web-based survey adopting validated questionnaires, we evaluated and compared sleep quality/habits, insomnia, perceived stress, depression, and anxiety symptoms of Italian late adolescents (n = 670; mean age ± SD, 19.38 ± 0.74; range, 18–20 years) and elderly (n = 253; 68.18 ± 2.79; range, 65–75 years).

Young respondents reported more severe insomnia symptoms, worse subjective sleep quality, longer sleep latency, higher daytime dysfunction, and a more prevalent disruption of sleep habits (bedtime, get up time, nap) than the elderly. On the other hand, older participants showed shorter sleep duration, lower habitual sleep efficiency, and greater use of sleep medications. Finally, the younger population displayed higher levels of depression and perceived stress.

Our findings indicate that the lockdown period had more pervasive repercussions on sleep and the mental health of late adolescents. The implementation of supportive strategies is encouraged for this vulnerable population group.

2.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Brain Sciences* (Amicucci et al., 2021).

During the lockdown, the elderly could be considered as one of the most at-risk population groups. As far as sleep is concerned, older people normally exhibit several alterations of sleep patterns due to the physiological aging process (Gulia & Kumar, 2018; Mander et al., 2017). Moreover, the elderly's sleep problems can be exacerbated by an increasing prevalence of multimorbidity, polypharmacy, and psychosocial factors (Miner & Kryger, 2017). Several studies showed that older adults report poor sleep quality, with insomnia as the most common sleep disorder (Kamel & Gammack, 2006; Patel et al., 2018). Notably, the prevalence of sleep disturbances is higher in the elderly than in the young population (J. Li et al., 2018; Patel et al., 2018).

The pandemic-related factors, including home confinement, social isolation, and the fear of contracting the virus, could directly impact the sleep of older adults (Pires et al., 2021). However, the relationship between sleep and COVID-19 outbreak in the elderly is still unclear. Recent studies indicated that older age represented a protective factor for sleep health (Gualano et al., 2020; Pinto et al., 2020). During home confinement, the younger population reported lower sleep quality (S. Yuan et al., 2020), increased occurrence of sleep problems (Barros et al., 2020; Beck et al., 2021), and worsening of existing sleep problems (Barros et al., 2020) compared to older people. Conversely, other investigations identified advanced age as a risk factor for sleep disturbances (J. Wang et al., 2020)[16], being associated with a decline of sleep quality (de Pue et al., 2021), especially in older individuals with depressive and anxiety symptoms (Cigiloglu et al., 2021). A recent study also showed that older age represented a significant predictor of a higher association between sleep problems and psychological distress (Alimoradi et al., 2021). Moreover, social isolation could exacerbate feelings of loneliness which, in turn, could compromise sleep and psychological health among the older population (Grossman et al., 2021; Rout, 2020).

The fear of contagion could be considered a further factor that can negatively affect general well-being due to the high morbidity and mortality rates in the elderly (Onder et al., 2020). However, several studies showed that the older population reported less psychological distress during the COVID-19 outbreak (for a review, Lebrasseur et al., 2021), exhibiting higher levels of resilience than the younger counterpart (Rossi et al., 2021). Although these results may be counterintuitive, it has been shown that late adolescents are more prone to suffer the repercussions of the lockdown on their mental health, representing the less resilient population group than previous generations (Carson et al., 2020). Young people exhibited even lower resilience during the pandemic when compared with normative data (Killgore et al., 2020). Consistently, they seemed to represent an age group strongly affected by the current emergency. Several studies indicated that the younger population showed higher levels of stress, anxiety, and depression (Rossi, Socci, Talevi, et al., 2020; Ueda et al., 2020), also ascribable to the deeply disrupted education and social life (Nwachukwu et al., 2020).

In the present study, we evaluated sleep quality/habits, insomnia, depression, perceived stress, and anxiety symptoms of two particularly at-risk age population groups, that is, late adolescents (18–20 years) and elderly (65–75 years) during the lockdown of Spring 2020 in Italy. We hypothesized to highlight differences in sleep quality/habits, insomnia, and mental health between late adolescents and elderly. However, the above-reported articulated literature does not allow hypothesizing the direction and the extent of the effects of the lockdown on these specific age groups. Therefore, we exploratively compared these two Italian samples to identify specific age-related vulnerabilities for sleep disturbances and psychological problems during the home confinement due to the COVID-19 outbreak. Determining the most vulnerable population categories is essential for designing and implementing specific interventions to mitigate the potential repercussions on sleep and mental health.

2.3 Materials and methods

2.3.1 *Participants and procedure*

According to the present study's objective, two subsamples of participants were selected from the whole sample of participants described in 1.3.1 section. The administered questionnaires are detailed in 1.3.2 section. The first subsample comprised 253 elderly subjects aged 65 to 75 years (mean age ± SD, 68.18 ± 2.79 years, 104 males), while the other subsample consisted of 670 late adolescents (18–20 years, 19.38 ± 0.74 years, 182 males). The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the University of L'Aquila (protocol n. 43,066/2020). Online informed consent was obtained from all subjects involved in the study.

2.3.2 *Statistical analysis*

The statistical analyses were performed using SPSS v.22 (IBM Corp., Armonk, NY, USA). Of the older respondents, 67.6% and 64.0% completed the BDI-II and the PSS-10, respectively, while 63.6% completed all the questionnaires. On the other hand, among young respondents, 69.6% and 63.0% compiled BDI-II and PSS-10, respectively, and 61.0% of them also completed the STAI-X1.

The questionnaire scores (PSQI, ISI, MEQr, BDI-II, PSS-10, STAI-X1) of the two subsamples (Elderly, Young) were compared using the Kruskal-Wallis test due to violation of the normality/heteroscedasticity assumptions. The same analysis was applied to bedtime, get up time, and each sub-component of the PSQI to further understand putative differences in sleep quality/habits between the two groups (Elderly, Young).

We excluded 16 older and 62 young respondents from the analysis on PSQI total score and one of its sub-components (habitual sleep efficiency) due to compilation errors, as respondents reported longer sleep duration than time in bed.

Moreover, we carried out frequency analyses to investigate the proportion within the two groups (Elderly, Young) of the reported impact of the lockdown period on sleep (negative, none, positive) and the changes of bedtime (advanced, unchanged, delayed), wake up time (advanced, unchanged, delayed), and nap habits (increased, unchanged, reduced). Likewise, the same analysis was applied to the PSQI and ISI scores identifying the proportion of poor sleepers and clinical insomniacs through the validated cut-off scores (see 1.3.2 section). Then, we performed Chi-square tests to evaluate the association between the group membership (Elderly, Young) and the above-mentioned self-report variables.

All the analyses were two-tailed, and the level of significance was set at $p < 0.05$. All p-values were corrected for multiple comparisons with false discovery rate (Benjamini & Hochberg, 1995). Eta squared (ε^2) and Cramer's V were computed to provide effect size estimates for Kruskal-Wallis and Chi-square tests, respectively.

2.4 Results

2.4.1 *Sleep variables*

The two groups did not significantly differ in overall sleep quality (Figure 2.1), as shown by the analysis on PSQI total scores (mean ± SD; Elderly: 7.13 ± 3.95; Young: 6.79 ± 3.33; $\chi^2 = 0.68$, $p = 0.41$, $\varepsilon^2 < 0.001$). However, the comparisons on PSQI sub-components highlighted several significant differences (Table 2.1). The elderly showed shorter sleep duration, lower habitual sleep efficiency, and greater use of sleep medications than young participants. On the other hand, they reported better subjective sleep quality, shorter sleep latency, and lower daytime dysfunction than late adolescents. Moreover, older respondents reported an earlier bedtime and get up time.

The analysis of ISI scores highlighted a significant difference between the two groups (χ^2 = 24.43, p < 0.001, ε^2 = 0.03). Elderly participants showed lower insomnia symptoms (6.84 ± 5.34) than young respondents (8.69 ± 5.33).

Furthermore, the analysis on MEQr scores displayed a significant difference between the two groups (χ^2 = 150.37, p < 0.001, ε^2 = 0.16). Elderly respondents showed a greater inclination to morning chronotype (17.19 ± 3.61) than young subjects (13.74 ± 3.47).

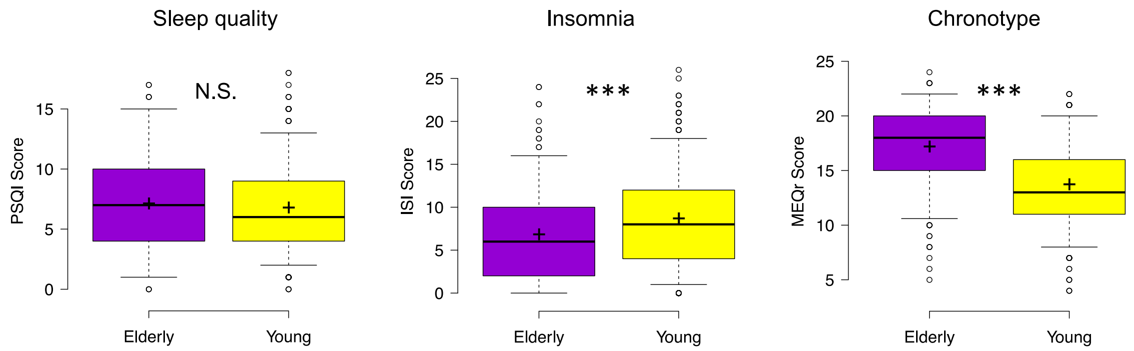

Figure 2.1. Sleep quality (PSQI), severity of insomnia symptoms (ISI), and inclination to morningness-eveningness (MEQr) for elderly and young respondents during the COVID-19 lockdown.

Notes: Center lines show the medians; box limits indicate the 25th and 75th percentiles; whiskers extend to 5th and 95th percentiles, outliers are represented by dots; crosses represent sample means. Significant differences of Kruskal-Wallis test between elderly (violet) and young (yellow) participants are indicated with asterisks (***p < 0.001).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness–Eveningness Questionnaire-reduced version.

Table 2.1. Mean and standard deviations of the two groups (Elderly, Young), and the corresponding statistical comparisons (Kruskal-Wallis: χ^2, p, ε^2), for bedtime, get up time, and the PSQI sub-components.

Variable	Elderly (65–75 age) Mean ± SD	Young (18–20 age) Mean ± SD	χ^2	p	ε^2
Bedtime	23:46 ± 1:12	1:12 ± 1:41	138.25	**< 0.001**	0.15
Get up time	07:55 ± 1:26	9:36 ± 1:41	208.23	**< 0.001**	0.23
PSQI sub-component					
Subjective sleep quality	1.16 ± 0.77	1.39 ± 0.79	15.75	**< 0.001**	0.02
Sleep latency	1.11 ± 1.01	1.57 ± 1.00	36.76	**< 0.001**	0.04
Sleep duration	1.08 ± 0.92	0.50 ± 0.75	93.32	**< 0.001**	0.10
Habitual sleep efficiency	1.11 ± 1.14	0.55 ± 0.89	49.26	**< 0.001**	0.06
Sleep disturbances	1.40 ± 0.65	1.34 ± 0.58	1.37	0.28	0.001
Sleep medications	0.51 ± 1.05	0.23 ± 0.69	14.55	**< 0.001**	0.02
Daytime dysfunction	0.58 ± 0.65	1.15 ± 0.81	93.86	**< 0.001**	0.10

Notes: Bold values are statistically significant. All p-values were corrected for multiple comparisons with false discovery rate.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; SD, Standard deviation.

Finally, we observed significant associations between the two groups and the perceived impact of the restraining measures, the reported changes in bedtime, wake up time, and nap habits, and the prevalence of clinical insomnia conditions (Table 2.2). Prevalence data showed that more than six out of ten late adolescents reported a negative impact of the lockdown period, while a lower rate of older respondents reported a negative impact of the restraining measures.
Moreover, a higher proportion of elderly participants showed unchanged sleep patterns (bedtime, wake up time, and nap habits) than young subjects. Remarkably, three out of four young respondents declared a delayed sleep phase. Finally, older people were characterized by a lower rate of clinical insomnia conditions compared to young people. Chi-square tests did not show a significant association between the two groups and the prevalence of poor and good sleepers.

In the light of the higher proportion of women in the young sample and the well-documented gender differences of sleep problems during the lockdown period (Salfi et al., 2020), we performed control analyses that excluded a possible gender bias in our pattern of results (data not shown).

Table 2.2. Prevalence of the lockdown-related perceived impact on sleep, reported changes of bedtime, get up time, and nap habits, and proportion of poor/good sleepers and clinical insomnia conditions within the two groups (Elderly, Young). Chi-square test results are also reported (χ^2, *p*, *Cramer's V*).

Variable	Elderly (65–75 age)	Young (18–20 age)	χ^2	*p*	Cramer's *V*
	N (%)				
Perceived impact					
Negative	109 (43.1)	431 (64.3)			
None	110 (43.5)	120 (17.9)	64.42	**< 0.001**	0.26
Positive	34 (13.4)	119 (17.8)			
Bedtime					
Advanced	19 (7.5)	36 (5.4)			
Unchanged	142 (56.1)	134 (20.0)	123.48	**< 0.001**	0.37
Delayed	92 (36.4)	500 (74.6)			
Wake up time					
Advanced	27 (10.7)	57 (8.5)			
Unchanged	125 (49.4)	116 (17.3)	106.66	**< 0.001**	0.34
Delayed	101 (39.9)	497 (74.2)			
Nap habit					
Increased	33 (13.0)	124 (18.5)			
Unchanged	196 (77.5)	355 (53.0)	50.19	**< 0.001**	0.23
Reduced	24 (9.5)	191 (28.5)			
Sleep quality					
Poor	151 (63.7)	365 (60.0)	0.97	0.32	0.03
Good	86 (36.3)	243 (40.0)			
Insomnia					
Severe	4 (1.6)	10 (1.5)			
Moderate	22 (8.7)	96 (14.3)	13.35	**0.004**	0.12
Subthreshold	74 (29.2)	245 (36.6)			
No	153 (60.5)	319 (47.6)			

Notes: Bold values are statistically significant. Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section).

2.4.2 *Psychological variables*

There was a significant difference between the two groups in severity of depression symptoms ($\chi^2 = 54.13$, $p < 0.001$, $\varepsilon^2 = 0.08$), and perceived stress ($\chi^2 = 72.99$, $p < 0.001$, $\varepsilon^2 = 0.12$), while anxiety measure did not differ between elderly and young respondents ($\chi^2 = 1.03$, $p = 0.33$, $\varepsilon^2 = 0.002$). As showed in Figure 2.2, notwithstanding that the two groups did not differ in STAI-X1 scores (mean ± SD; Elderly: 48.20 ± 9.74; Young: 49.0 ± 9.59), older participants showed less severe depression symptoms (BDI-II: 9.01 ± 8.21) and lower stress levels (PSS-10: 13.88 ± 7.10) than late adolescents (BDI-II: 14.45 ± 9.90; PSS-10: 19.95 ± 7.31). Control analyses including gender factor in the models confirmed the differences between the two groups on depression and perceived stress.

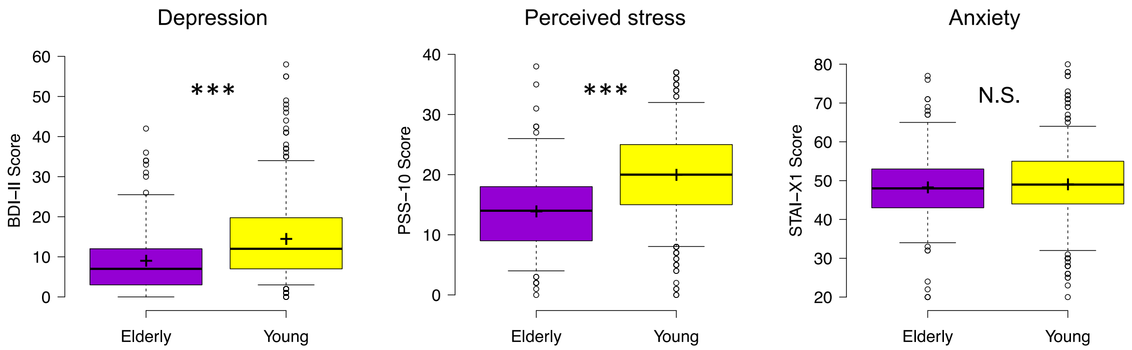

Figure 2.2. Depression symptoms (BDI-II), perceived stress (PSS-10), and anxiety (STAI-X1) for elderly and young respondents during the COVID-19 lockdown.

Notes: Center lines show the medians; box limits indicate the 25th and 75th percentiles; whiskers extend to 5th and 95th percentiles, outliers are represented by dots; crosses represent sample means. Significant differences of Kruskal-Wallis test between elderly (violet) and young (yellow) participants are indicated with asterisks (***$p < 0.001$).

Abbreviations: BDI-II, Beck Depression Inventory-second edition, PSS-10, Perceived Stress Scale-10; STAI-X1, State-anxiety subscale of the State-Trait Anxiety Inventory.

2.5 Discussion

According to the study's hypothesis, we highlighted several differences in sleep and psychological health between late adolescents and older people during the lockdown of Spring 2020 in Italy.

Two-thirds of young participants (64.3%) perceived a negative impact of the restraining measures on their sleep, a greater prevalence than older adults (43.1%). Furthermore, three out of four young respondents showed a delayed sleep phase (bedtime, get up time). On the other hand, elderly subjects prevalently showed unchanged sleep patterns.

Maintaining the sleep schedule has been suggested as a protective factor to deal with sleep problems during home confinement (Altena et al., 2020). In line with this assumption, older people presented lower severity of insomnia than young participants. Conversely, more than half of the late adolescents reported insomnia symptoms from subthreshold to severe extent.

Paradoxically, although the differences in insomnia levels between the two groups, we did not identify significant differences in overall sleep quality. This evidence could be ascribable to the different sleep dimensions covered by the PSQI, whose sum gives rise to the sleep quality measure. Older participants showed shorter sleep duration, lower habitual sleep efficiency, and greater use of sleep medications, in line with the well-documented sleep changes occurring across the lifespan (J. Li et al., 2018; Patel et al., 2018). We hypothesize that these variables could hardly be affected by the home confinement period in the short term, balancing the outcomes of the other PSQI sub-components. On the other hand, late adolescents showed a worse subjective sleep quality, longer sleep latency, and higher daytime dysfunction, putatively reflecting the more severe insomnia symptoms of this population.

Moreover, a high percentage of late adolescents declared a reduction of naps. Young people's well-known biological tendency to late sleep timing is typically misaligned with the social clock (academic pressure and social activities) (Randler et al., 2009; Touitou et al., 2016), configuring the so-called *social jetlag* phenomenon (Wittmann et al., 2006). This situation results in an overall reduction of sleep duration and an accumulated sleep debt during the weekdays among adolescents, leading them to develop compensatory nap habits (Carvalho-Mendes et al., 2020). As the lockdown period represented an unprecedented condition that unlocked time for sleep for most of the population, we hypothesize that the greater reduction of nap habits of late adolescents reflected the reduction of the *social jetlag* phenomenon documented among the young population during the period of restraining measures due to COVID-19 outbreak (Wright et al., 2020).

Although the elderly population exhibits the highest risk of morbidity and mortality during the current pandemic (Onder et al., 2020), late adolescents seemed to suffer more from the restrictive measures on the psychological side. In line with the current literature on mental health during the pandemic (Lebrasseur et al., 2021), older respondents reported less severe depression symptoms and lower stress levels. However, we did not observe a significant difference in anxiety between the two groups.

Our results are supported by previous research (MacLeod et al., 2016), which showed that older people exhibit a higher level of resilience in difficult times than young people, as they experienced greater stressful events during their lifetime, developing better emotional regulation and coping strategies (S. B. Scott et al., 2013; Uchino et al., 2006). Consistent with this interpretation, a recent study on the Italian population showed that resilience mediated the relationship between pandemic-related stressful events and depression, anxiety, and perceived stress, while age moderated the mediating effect of resilience (Rossi et al., 2021). Moreover, in line with our findings, another study highlighted that young people presented higher levels of depression, perceived stress, and insomnia than the older counterpart (Rossi, Socci, Talevi, et al., 2020).

Furthermore, according to the pre-COVID literature (Adan et al., 2012), the elderly population reported earlier bedtime and get up time, and a tendency to morning chronotype. This evidence could constitute a protective factor of older people, as morningness was associated with higher resilience (Antúnez et al., 2015; Jeon & Lee, 2019; Lee et al., 2016), lower perceived stress (Romo-Nava et al., 2016), and a lower tendency to develop PTSD (Hasler et al., 2013; Yun et al., 2015). In this regard, we recently proposed the evening chronotype as a vulnerability factor during the lockdown period (Salfi, D'Atri, et al., 2021; Salfi, Lauriola, et al., 2021).

Moreover, the current pandemic emergency impacted younger's education, contributing to impair mental health of university students (Elmer et al., 2020; Sundarasen et al., 2020). Late adolescents were particularly affected by isolation resulting from social distancing (Lips, 2021; Nwachukwu et al., 2020), considering the prominent role of peers and social connections at this stage of life. We hypothesize that these factors could play a role in explaining the greater psychological distress of the young population during the COVID-19 lockdown.

Finally, limited social interactions led to a pervasive increase in the use of digital devices in the hours before falling asleep (Salfi, Amicucci, et al., 2021), a deeply rooted habit in our society already before the isolation period among young people. Increased screen exposure has been associated with reduced sleep quality, exacerbation of insomnia symptoms, reduced sleep duration, and longer sleep onset latency during home confinement (Salfi, Amicucci, et al., 2021). Sleep problems could, in turn, negatively affect the psychological well-being of the young population (Orchard et al., 2020). Of note, excessive screen time was associated with a concomitant higher rate of anxiety and depression symptoms during the lockdown period, especially among young people (Smith et al., 2020).

To our knowledge, this is the first study on the Italian population aimed at comparing sleep problems and psychological well-being between late adolescents and the older population. However, we must report some limitations. The first one consists of the non-probabilistic sampling technique adopted, as the recruitment of the sample was performed via social networks. This recruitment strategy could limit the generalization of our results to the older population. Moreover, our samples comprised a higher prevalence of women, in particular in the young group. Nevertheless, control analyses confuted a putative gender bias due to the unbalanced gender composition of the two samples. Finally, under-eighteen years old people were not recruited. Future investigations are necessary to clarify the impact of the COVID-19 pandemic on sleep and psychological well-being in this younger population group, considering the strong relationship between sleep and mental health and their influence in the transition toward adulthood (Bruce et al., 2017).

In conclusion, considering the well-known bidirectional relationship between sleep problems and psychological well-being (Alvaro et al., 2013), interventions to improve sleep health should be implemented among the young population. Paying attention to sleep hygiene, keeping a stable sleep schedule, and avoiding the overuse of electronic devices before bedtime may prove to be effective strategies to preserve both sleep and psychological health. It is also necessary to implement psychological interventions that, in turn, can support sleep health.

The pandemic continues to plague the daily routine of the general population worldwide. Further research is recommended to evaluate the differential long-term repercussions among late adolescents and the elderly population. This unprecedented period is having a persistent negative impact on the sleep and mental health of the Italian population, as evidenced by the increased perceived stress, and the unchanged prevalence of poor sleepers and moderate/severe depression conditions during the second contagion wave of Winter 2020 compared with the first one (Salfi, D'Atri, et al., 2021). Therefore, we suggest the development of prompt supportive strategies focused on young people, who appeared to be the most vulnerable population group. On the other hand, it is also recommended monitoring older adults' sleep health and psychological status, as they may develop a concomitant vulnerability over time.

Chapter 3

Sleep quality, insomnia symptoms, and depressive symptomatology among Italian university students before and during the COVID-19 lockdown

3.1 Abstract

The COVID-19 pandemic led world authorities to adopt extraordinary measures to counteract the spread of the virus. The Italian government established a national lockdown from 9 March to 3 May 2020, forcing people in their homes and imposing social distancing. During the pandemic emergency, university students emerged as a vulnerable category. Indeed, higher rates of sleep problems and mental disorders were reported in this population. However, these outcomes were derived from cross-sectional investigations adopting retrospective assessments. Retrospective evaluations suffer from different biases, putatively leading to erroneous outcomes.

To overcome this limitation, we adopted a between-subject approach comparing a sample of 240 Italian undergraduate university students assessed in 2016 (mean age ± SD, 20.39 ± 1.42 years; range 18–25; 80.42% females), with an age/gender-matched sample of university students assessed during the third week of lockdown in Spring 2020. We evaluated sleep quality, insomnia symptoms, and depressive symptomatology using validated questionnaires.

We found worse sleep quality, a delayed bedtime, and more severe insomnia and depression symptoms in the students sampled under COVID-19 restrictive measures. We suggest paying special attention to this at-risk population during the current pandemic emergency and applying preventive and supportive interventions to limit the exacerbation of sleep and psychological problems.

3.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *International Journal of Environmental Research and Public Health* (Viselli et al., 2021). As described in previous Chapters (1 and 2), some population groups demonstrated a greater susceptibility to the effects of the restrictive measures. The university students emerged as one of the most affected. Elmer and colleagues (2020) reported a worsening in depressive and anxiety symptoms, and higher levels of stress and loneliness among the university student population during the restrictive measures, compared with pre-lockdown assessments. Moreover, recent cross-sectional investigations focused on students have showed high rates of depression, anxiety, stress, and suicidal thoughts during the pandemic emergency worldwide (Elmer et al., 2020; Kaparounaki et al., 2020). These findings are consistent with several Italian reports (Giusti et al., 2020; Marelli et al., 2021; Meda et al., 2021). Worldwide, the confinement measures also seemed to have a detrimental effect on sleep in the university students (Martínez-Lezaun et al., 2020; Wright et al., 2020). This evidence has been confirmed by cross-sectional investigations among the Italian population (Giusti et al., 2020; Marelli et al., 2021).

In order to better understand the effects of home confinement on sleep and mental health among this specific population, it would be useful to have a direct comparison between data collected during the lockdown and the pre-outbreak period. However, current literature focused on students that adopts a longitudinal approach using a pre-pandemic baseline is limited (Elmer et al., 2020; Evans et al., 2021; Wright et al., 2020). For the Italian university student population, only one study had pre-outbreak data on mental health (Meda et al., 2021). However, this investigation did not assess possible changes in sleep variables. On the other hand, several cross-sectional studies employed a retrospective approach referred to the pre-pandemic period to investigate the impact of restraining measures due to the COVID-19 outbreak (Ammar et al., 2020; Cellini et al., 2020; Marelli et al., 2021). This methodology could be questionable as the retrospective symptom evaluations are frequently biased, and subjects tend to overestimate the current symptomatology (Hipp et al., 2020; Van Den Bergh & Walentynowicz, 2016). Moreover, depression and anxiety affect the accuracy of the retrospective recalls (Van Den Bergh & Walentynowicz, 2016). These biases were confirmed by the findings of Gao and Scullin (C. Gao & Scullin, 2020), who adopted both retrospective and longitudinal approaches and found a worsening of sleep quality only in the first case. One way to partially overcome the limitations of retrospective studies is to compare the data obtained during the pandemic with those previously collected on a different sample from the same population. Although useful in this unprecedented period, this study typology is limited (Benham, 2021; Elmer et al., 2020), and even absent among the Italian student population.

Based on the above-mentioned evidence, we evaluated the effects of the lockdown on sleep quality/patterns, insomnia symptoms, and depression symptomatology in undergraduate students by comparing data from a previous study (Lauriola et al., 2019), collected in October 2016, with data from an age/gender-matched sample of undergraduate university students collected in the first week of our investigation held during the lockdown period of Spring 2020 (25–31 March 2020) (Salfi, Lauriola, et al., 2021).

Considering the peculiar and vulnerable life condition of the university students under restrictive measures, we hypothesized that students assessed during lockdown showed worse sleep quality and a higher level of insomnia and depression symptoms compared to students assessed during the pre-pandemic period. Finally, the lack of social impositions due to the restrictive measures could lead undergraduate students to follow their well-documented evening circadian preference (Adan et al., 2012; Núñez et al., 2019). Therefore, we hypothesized that there would be a delayed bedtime and get up time in the sample evaluated during the lockdown.

3.3 Materials and methods

3.3.1 *Participants and procedure*

In the present study, data derived from two different samples of undergraduate university students are reported. The first one (pre-pandemic group) consisted of a sample of 240 Italian students (mean age ± SD, 20.39 ± 1.42 years, range 18–25; 80.42% females) who participated in a data collection held from 6 to 11 October 2016 at the University of L'Aquila (Lauriola et al., 2019). The second sample (lockdown group) comprised a total of 240 Italian students evaluated during the third week of home confinement period (25–31 March 2020), matched for age and gender with the pre-pandemic group. Specifically, the lockdown group was randomly selected from our nationwide dataset described in 1.3.1 section, using a custom-made MATLAB script (MATLAB R2021a, The MathWorks Inc., Natick, MA, USA). We chose to match for age and gender as the two demographic factors are associated with different sleep characteristics (L. Li et al., 2021).

In both the surveys, we collected demographic factors (age, gender), and we evaluated sleep quality, insomnia symptoms, and depression symptoms using the PSQI, the ISI, and the BDI-II, respectively (see 1.3.2 section for a description of questionnaires).

The studies (Lauriola et al., 2019; Viselli et al., 2021) were approved by the Institutional Review Board of the University of L'Aquila (protocol n. 23038/2016; protocol n. 43,066/2020, respectively) and were performed according to the principles established by the Declaration of Helsinki.

3.3.2 *Statistical analysis*

We performed independent sample t-tests comparing the PSQI, ISI, and BDI-II scores of the two student groups (pre-pandemic group, lockdown group) to evaluate possible differences in sleep quality, insomnia, and depression symptoms due to the lockdown period. The same analysis was performed for each sub-component of the PSQI (subjective sleep quality; sleep latency; sleep duration; habitual sleep efficiency; sleep disturbance; sleep medication; daytime dysfunction) to provide a fine-grained overview of the sleep differences between the two conditions. We also extracted from the PSQI questionnaire two crucial variables, such as bedtime (hh:mm) and get up time (hh:mm) to evaluate possible differences in sleep schedule. Independent sample t-test analyses were applied to the above-mentioned sleep pattern variables (bedtime, get up time). All the analyses were two-tailed, and the level of significance was set at $p < 0.05$. All *p*-values were corrected for multiple comparisons with false discovery rate (Benjamini & Hochberg, 1995).

Furthermore, we carried out an analysis of variance (ANOVA) on PSQI, ISI, and BDI-II scores, with "*Gender*" (male, female) and "*Condition*" (pre-pandemic, lockdown) as two level between-subjects factors. Such analysis was performed both to assess possible gender effects on sleep quality, insomnia, and depression symptoms and to explore putative interactions between the two factors ("*Gender*", "*Condition*").

3.4 Results

The results of the comparisons between pre-pandemic and lockdown groups on the PSQI, ISI, and BDI-II scores, PSQI sub-components, and bedtime and get up time are summarized in Table 3.1.

Table 3.1. Mean ± standard deviation of questionnaire scores (PSQI, ISI, BDI-II), PSQI sub-components, bedtime, and get up time of the two groups (pre-pandemic, lockdown). Results of t-test comparisons are also reported (*t*, *p*).

Variable	Pre-pandemic	Lockdown	*t*	*p*
	Mean ± SD			
PSQI total score	5.96 ± 2.64	6.61 ± 2.92	−2.55	**0.03**
PSQI sub-component				
Subjective sleep quality	1.14 ± 0.59	1.34 ± 0.74	−3.34	**0.004**
Sleep latency	1.54 ± 0.84	1.56 ± 0.97	−0.25	0.80
Sleep duration	0.48 ± 0.65	0.52 ± 0.69	−0.61	0.70
Habitual sleep efficiency	0.70 ± 0.88	0.55 ± 0.85	1.79	0.14
Sleep disturbance	1.33 ± 0.50	1.35 ± 0.57	−0.34	0.80
Sleep medications	0.10 ± 0.41	0.16 ± 0.57	−1.39	0.27
Daytime dysfunction	0.80 ± 0.70	1.21 ± 0.78	−4.80	**< 0.001**
ISI total score	7.33 ± 4.40	8.34 ± 4.93	−2.35	**0.04**
BDI-II total score	10.17 ± 8.55	14.18 ± 8.97	−5.02	**< 0.001**
Bedtime (hh:mm)	00:27 ± 01:15	00:52 ± 01:38	−3.11	**0.007**
Get up time (hh:mm)	09:26 ± 01:29	09:34 ± 01:33	−1.02	0.44

Notes: Bold values are statistically significant. All *p*-values were corrected for multiple comparisons with false discovery rate.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; BDI-II, Beck Depression Inventory-Second Edition; SD, standard deviation.

As shown in Figure 3.1, the students under lockdown reported poorer sleep quality, and more severe insomnia and depression symptoms than the pre-pandemic group. Moreover, the lockdown group displayed a delayed bedtime compared to the pre-pandemic group (Figure 3.2), but no differences in get up time were obtained.

In addition, students assessed under lockdown reported significantly poorer subjective sleep quality and greater daytime dysfunction than students evaluated during the pre-pandemic period (Table 3.1).

Finally, the female gender emerged as the most compromised in sleep quality, insomnia, and depression symptoms, as the "*Gender*" factor was significant in all the analyses (PSQI: $F_{1,476}$ = 7.28, p = 0.007; ISI: $F_{1,476}$ = 9.40, p = 0.002; BDI: $F_{1,476}$ =

15.91, $p < 0.001$). However, no "*Gender*" × "*Condition*" interaction was significant for the assessed variables (PSQI: $F_{1,476} = 0.36$, $p = 0.55$; ISI: $F_{1,476} = 1.78$, $p = 0.18$; BDI: $F_{1,476} = 3.14$, $p = 0.08$).

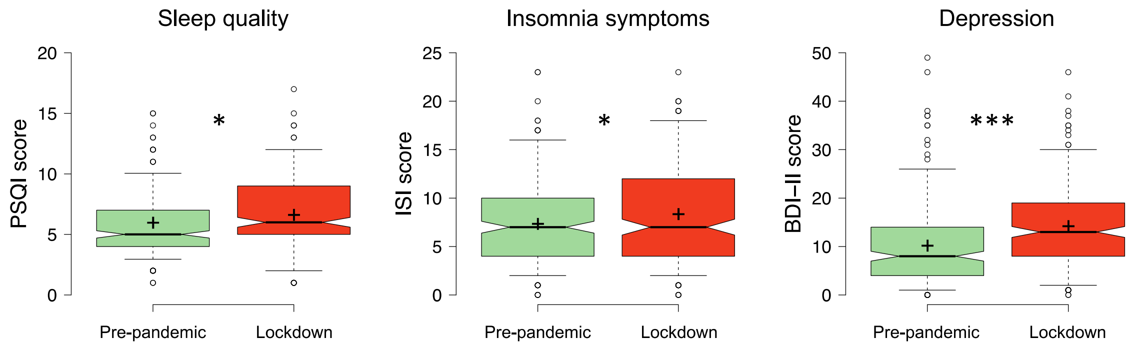

Figure 3.1. Sleep quality (PSQI), severity of insomnia (ISI), and depression symptoms (BDI-II) of the students in pre-pandemic group (assessed in 2016) and the group of students evaluated during the COVID-19 lockdown.

Notes: Center lines show the medians; box limits indicate the 25th and 75th percentiles; whiskers extend to 5th and 95th percentiles, outliers are represented by dots; crosses represent sample means. Significant differences between groups of students [pre-pandemic (green), lockdown (red)] are indicated with asterisks (*$p < 0.05$, ***$p < 0.001$).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; BDI-II, Beck Depression Inventory-Second Edition.

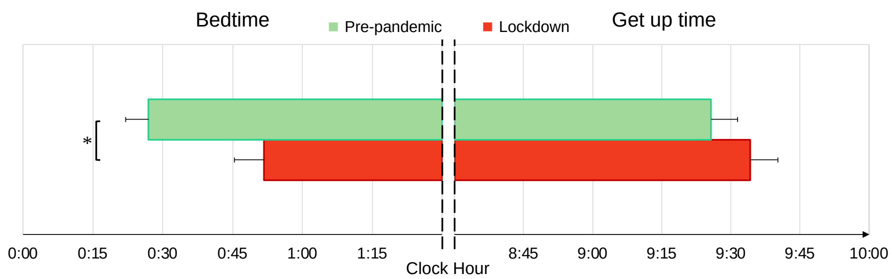

Figure 3.2. Sleep patterns of the two student samples (pre-pandemic, lockdown).

Notes: Mean (and standard errors) of bedtime and get up time and significance of statistical comparisons between pre-pandemic (green) and lockdown (red) groups are reported (*$p < 0.05$).

3.5 Discussion

In the present study, we showed significantly worse sleep quality and more severe insomnia and depression symptoms among undergraduate university students during the COVID-19 lockdown compared to an age/gender-matched sample of students assessed four years before the pandemic period. The analysis of the PSQI sub-components identified daytime dysfunction and subjective sleep quality as the most affected sleep quality facets during the lockdown. Moreover, we reported that restraining measures negatively affected sleep quality, insomnia, and depression symptoms of male and female students in the same way. However, women reported higher scores in all the questionnaires regardless of the assessment period. These findings are not surprising since females show more severe sleep problems and depression symptoms both before (Malhi & Mann, 2018; B. Zhang & Wing, 2006) and during the COVID-19 lockdown (Salfi et al., 2020). As hypothesized, we also found a significantly delayed bedtime in the sample evaluated during the home confinement. On the other hand, we did not find any significant difference in get up time. So, our second hypothesis is only partially confirmed.

Several cross-sectional investigations reported a high level of insomnia symptoms and poor sleep quality in the university student population (Cellini et al., 2021; Gualano et al., 2020; Marelli et al., 2021). Moreover, a longitudinal study highlighted worsened sleep quality among students during the COVID-19 lockdown (Martínez-Lezaun et al., 2020), pointing out a negative effect of the restrictive measures. To the best of our knowledge, before the current study, there was only one study (Benham, 2021) that assessed insomnia symptoms using validated questionnaires both before and during home confinement among independent samples of undergraduate university students. In contrast with our results, Benham did not find any significant difference in insomnia symptoms, while we highlighted more severe insomnia symptomatology during the lockdown. However, the data from Benham (2021) were collected in the Southwestern United States, i.e., a region where the number of deaths was substantially lower than in Italy when data were collected. Furthermore, data collection was not performed during a period of restrictive measures, but during the spread of the virus before the lockdown. These factors could explain the inconsistent results.

High daytime dysfunction in students during lockdown has been repeatedly documented (Benham, 2021; Saadeh et al., 2021) together with low subjective sleep quality (Saadeh et al., 2021). For example, in Saadeh and colleagues (2021) about half of the sample reported both difficulties staying awake during the day and poor subjective sleep quality. Moreover, in the same study, up to 80% of the respondents did not have enough enthusiasm for daily activities, showing an altered daily functioning. Similarly, Benham and collaborators (2021) highlighted a worsening in diurnal functionality relative to a pre-pandemic condition. Daytime sleepiness during lockdown may have played a role in the students' perception of poor sleep quality. Furthermore, daytime functioning may have been affected by different factors, such as stress (Campbell et al., 2018; Ribeiro et al., 2018), loneliness (Hawkley et al., 2010), and worries about COVID-19 (Pellegrini et al., 2020). The current literature also showed a delayed bedtime and get up time during home confinement relative to the pre-pandemic period among university students (Marelli et al., 2021; Wright et al., 2020). However, the results of our study supported only the first assumption, pointing out a delayed bedtime in the student population. University students typically show an evening chronotype, preferring to go to sleep and wake up later (Adan et al., 2012; Núñez et al., 2019). Consequently, we hypothesized that the students assessed during the lockdown, free from university (i.e., lessons) and social demands, aligned their sleep rhythm more strictly with their biological rhythm, moving bedtime forward. On the other hand, the lack of a significant effect on get up time in our lockdown group could be attributed to seasonal influences on awakening times, due to the different assessment period in the two samples, as spring season is associated with earlier wake up times (Mattingly et al., 2021).

As far as depressive symptomatology is concerned, the literature highlighted high rates of students who reported depression symptoms during home confinement worldwide (Elmer et al., 2020; Giusti et al., 2020; Kaparounaki et al., 2020; Majumdar et al., 2020). Furthermore, several longitudinal studies indicated a putative role of restrictive measures in exacerbating the depression symptoms among the university population (Evans et al., 2021; Marelli et al., 2021; Meda et al., 2021). Therefore, our results are consistent with the above-mentioned literature.

The restrictive measures obligated people to spend all days in their homes without social interaction and face-to-face peer contact. The university years coincide with a period of life characterized by important personal life events where social interactions are fundamental (Sussman & Arnett, 2014). Poor social life is associated with negative health outcomes (Alsubaie et al., 2019; Buote et al., 2007; Diehl et al., 2018), and a change in social activities is considered an important stressor in this population (Acharya et al., 2018). During the lockdown, an additional detrimental factor was the concern about COVID-19, which negatively impacted mental well-being (Pellegrini et al., 2020). Based on this evidence, it is not surprising that recent studies showed that the collapse of social interactions during the pandemic emergency, and the worries (e.g., about close friends, or COVID-19), impacted the student's mental health and sleep (Chaturvedi et al., 2021; Elmer et al., 2020; Pellegrini et al., 2020; Villani et al., 2021).

Students' problems could also be caused by the influence of the pandemic emergency on their future carrier. During this unexpected situation, universities switched exams and lessons to online modalities. However, online education could have negatively affected student sleep and mental well-being (Biwer et al., 2021). Online learning has been proposed to exacerbate depression and anxiety symptoms (Fawaz & Samaha, 2021). Together with the desire to maintain social interactions and to counteract boredom, online learning led students to increase the use of electronic devices drastically (Majumdar et al., 2020). Remarkably, the increased use of electronic devices before bedtime during lockdown was associated with worsened sleep quality and insomnia symptoms, as well as altered sleep-wake patterns (Salfi, Amicucci, et al., 2021). This evidence was confirmed also during the second contagion wave during Winter 2020 (Salfi, D'Atri, et al., 2021).

Moreover, a good amount of physical activity is known to positively affect sleep and mental health (Allen et al., 2019; Ekelund et al., 2016). However, during the home confinement students showed decreased physical activity and increased time spent sitting during the day (Gallè et al., 2020; Luciano et al., 2021; Y. Zhang et al., 2020). The above-mentioned factors were associated with inadequate sleep and the development of psychological and health problems among the student population (Allen et al., 2019; Memon et al., 2021). Interestingly, Caldwell and colleagues (2022) highlighted a negative influence of the COVID-19 lockdown on dietary intake. Indeed, energy intake increased in university students during the lockdown, especially due to increased snacking frequencies (Gallo et al., 2020). Considering the consumption of fatty/sugary foods is associated with sleep problems in students populations (Nisar et al., 2019; St-Onge et al., 2016), it is plausible that the variation in eating habits also influenced sleep quality during the lockdown.

Furthermore, younger people generally showed a tendency to evening chronotype (Adan et al., 2012). Eveningness is associated with mental health problems and sleep disorders (Adan et al., 2012), and this relationship was also confirmed during the pandemic scenario (Salfi, Lauriola, et al., 2021). In addition, younger people typically have the lowest level of resilience (Gooding et al., 2012), and this feature was confirmed during the pandemic (Rossi et al., 2021). Rossi and colleagues (2021) highlighted that age moderated the mediation role of resilience in the relationship between pandemic-associated stressful experience and depression, anxiety, and perceived stress. Overall, this evidence supported the idea that problems of young people may be attributable also to the lower resilience attitude (Amicucci et al., 2021).

Some limitations of the present study should be reported. We acknowledge that the non-probabilistic sampling technique adopted, and the use of self-report questionnaires may limit the generalization of our findings. Furthermore, we did not assess the socioeconomic status of participants, their study fields, data about physical activity and dietary intake, or the presence of concomitant disease/treatment that could interfere with sleep problems. Moreover, a longitudinal approach with a pre-pandemic baseline would have been more accurate in highlighting the detrimental effects of the restrictive measures due to the COVID-19 outbreak. However, the unexpected nature of the pandemic made such a study hardly feasible, and the matching of age and gender between the two samples should increase the reliability of our results.

In conclusion, in light of our findings and considering the bidirectional relationship between sleep and mental (Dinis & Bragança, 2018; Freeman et al., 2020), we encourage paying special attention to university students during the current emergency period. Moreover, considering that the above-reported vulnerability of this population was also present before the COVID-19 outbreak, we suggest the implementation of preventive interventions focused on this specific group. This is of particular importance, as depression is associated with elevated probability of dropping out of the university (Eisenberg et al., 2009), in addition to being related to suicidal ideation (Klonsky et al., 2016). Indeed, the suicide rates showed an increase during the pandemic emergency among students (Kaparounaki et al., 2020). Finally, supportive interventions could be particularly important as the detrimental impact of the COVID-19 pandemic on sleep and mental health seems to persist in the long run (Salfi, D'Atri, et al., 2021), in order to avoid the chronicity of such disorders among this at-risk population.

Chapter 4

Gender-related time course of sleep disturbances and psychological symptoms during the COVID-19 lockdown: A longitudinal study on the Italian population

4.1 Abstract

Italy was the first western hotspot of the COVID-19 pandemic. In order to contain the spread of the virus, the Italian government imposed home confinement to the entire population for almost two months. The present study is the first large-scale longitudinal report of the sleep and mental health changes during the prolonged lockdown due to the COVID-19 outbreak. We focused on the gendered vulnerability in a sample of the Italian population since cross-sectional research identified women to be more at-risk than men during this unprecedented situation.

A total of 2701 individuals (mean age ± SD, 32.37 ± 11.62 years; range, 18–82 years) participated in a web-based longitudinal survey consisting of two measurements. Participants were first-time recruited on social networks and via telephone messages through a snowball sampling and tested during the third week of the lockdown period. Subsequently, a follow-up evaluation was carried out during the seventh week of restraining measures. The survey assessed sleep quality, insomnia and depression symptoms, perceived stress, and anxiety, using the following questionnaires: the Pittsburgh Sleep Quality Index, the Insomnia Severity Index, the Beck Depression Inventory-second edition, the 10-item Perceived Stress Scale, and the State-Anxiety Inventory.

Female gender showed the worst condition for all the examined dimensions in both the assessments. Nevertheless, at the follow-up women reported a reduction in insomnia and depression severity symptoms, perceived stress, and anxiety. On the other hand, male participants showed a worsening of sleep quality, insomnia symptoms, and perceived stress. Consequently, the gender prevalence gap of clinical conditions such as insomnia and depression was largely reduced under lockdown.

Our investigation pointed to a different time course of sleep and mental health between genders during the home confinement period. Women seemed to show greater long-term resilience during the lockdown. Meanwhile, the male gender emerges as the most vulnerable category to the extension of the restraining measures. Our results suggest that there is no "weaker gender" after a prolonged lockdown. Indeed, the Italian population transversely presented signs of psychological suffering and significant sleep disturbances after the protracted and stressful lockdown period due to the COVID-19 pandemic.

4.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Neurobiology of Stress* (Salfi et al., 2020).

Italy was the first western hotspot of COVID-19. The Italian Government adopted extraordinary measures aimed at limiting the contagion. Since March 9, 2020, a total lockdown was imposed, which forced the entire population into home confinement. The restraining measures were extended until May 4, 2020, resulting in approximately two months of confinement. This unprecedented situation profoundly impacted the everyday life of all Italian citizens. The limitation of social interaction and the restriction of movement freedom could be linked to consistent psychological impact among the general population (Brooks et al., 2020).

Increased stress and exacerbation of depression and anxiety symptomology was reported in China as in the rest of the world during the COVID-19 pandemic (Rajkumar, 2020; Vindegaard & Benros, 2020). Moreover, in a situation where the rhythms of life were deeply altered, sleep has been proposed as one of the primary targets to be impacted, as well as a crucial mediator of mental health outcomes (Altena et al., 2020). Recent cross-sectional studies on the psychological impact of the COVID-19 pandemic focused on specific at-risk groups, such as healthcare professionals (Pappa et al., 2020) and referred to limited periods. Some studies addressed longitudinally the impact of the current situation but used pre-outbreak baselines (Cellini et al., 2020; Pierce et al., 2020; Wright et al., 2020). Therefore, the large-scale temporal impact of the restraining measures within the general population has been scarcely studied. Because of the protracted duration of the home confinement, it is fundamental to investigate the long-term consequences of this extraordinary situation. To our knowledge, this is the first study that longitudinally addresses the within-subject psychological impact of seven weeks of home confinement in the same large sample of the general population during a public pandemic catastrophe. Two thousand seven hundred one Italian citizens were tested using a web-based survey in two time periods: during the third and the seventh week of lockdown. The survey assessed sleep quality, insomnia and depression symptoms, perceived stress, and anxiety. This study aimed at investigating the changes in the above-mentioned variables during the extended lockdown, to address the hypothesis that the restraining measures could have had a cumulative negative impact on the mental health of the general population. Different from previous research works, we took into account gender differences to evaluate if men and women suffered differently from this situation. The importance of gender-disaggregated data was strongly suggested as regards COVID-19 vulnerability (Wenham et al., 2020). This is also crucial on the psychological side since the risk for psychopathology markedly differs between men and women, and women represent a high-risk category for mental health problems such as depression, anxiety, and PTSD (Malhi & Mann, 2018; Olff et al., 2007). In this view, women could suffer the COVID-19 lockdown more severely, and preliminary cross-sectional studies reported female gender to be a vulnerability factor for developing psychological symptoms during the early stage of the pandemic (Casagrande et al., 2020; Léger et al., 2020; C. Mazza et al., 2020; Özdin & Bayrak Özdin, 2020; Vindegaard & Benros, 2020; C. Wang, Pan, Wan, Tan, Xu, Ho, et al., 2020)

The present investigation has two main peculiarities. First, we showed the trajectories of sleep and psychological well-being within the same population during the extended lockdown period. Second, it is the first investigation to address the different progression of sleep disturbances and psychological symptoms for men and women. Our results are useful to identify gender-specific timing of intervention to prevent and counteract the long-term development of mental health problems during this unprecedented situation.

4.3 Materials and methods

4.3.1 *Participants and procedure*

7107 Italian citizens (mean age ± SD, 32.38 ± 11.38; range, 18–84; 1616 men) completed a web-based survey during the third week of the home confinement (Test 1; 25–31 March 2020), the days immediately following the peak of contagion (Istituto Superiore di Sanità, 2020). The data collection procedure is detailed in 1.3.1 section. After four weeks, the website link of the follow-up survey was provided to the participants via email address/telephone number. A total of 2701 individuals (mean age ± SD, 32.37 ± 11.62; range, 18–82; 491 men) participated in the follow-up assessment (Test 2) in seven days (21–27 April 2020), completing the same questionnaires of the first measurement time (see 1.3.2 section). Demographic and COVID-related characteristics of the sample participating in both the measurements are reported in Table 4.1. The local Institutional Review Board at the University of L'Aquila approved the current study (protocol n. 43,066/2020). Online informed consent was obtained from the participants.

Table 4.1. Demographic and COVID-related characteristics of the sample participating in both the measurements (Test 1: 25-31 March 2020; Test 2: 21-27 April 2020).

Variable	Overall follow-up sample (n = 2701)	Men (n = 491)	Women (n = 2210)
		N (%)	
Age			
18–30 years	1617 (59.9)	280 (57.0)	1337 (60.5)
31–50 years	783 (29.0)	137 (27.9)	646 (29.2)
> 50 years	301 (11.1)	74 (15.1)	227 (10.3)
Education			
Until middle school	36 (1.3)	10 (2.0)	26 (1.2)
High school	851 (31.5)	182 (37.1)	669 (30.3)
Graduated	1814 (67.2)	299 (60.9)	1515 (68.5)
Occupation			
Unemployed	231 (8.6)	36 (7.3)	195 (8.8)
Employed	1545 (57.2)	299 (60.9)	1246 (56.4)
Student	925 (34.2)	156 (31.8)	769 (34.8)
Geographical location			
Northern Italy[a]	991 (36.7)	175 (35.6)	816 (36.9)
Central Italy[b]	800 (29.6)	144 (29.3)	656 (29.7)
Southern Italy[c]	910 (33.7)	172 (35.0)	738 (33.4)
COVID-19 infection			
Yes	7 (0.3)	1 (0.2)	6 (0.3)
No	2673 (99.0)	484 (98.6)	2189 (99.0)
No response	21 (0.8)	6 (1.2)	15 (0.7)
Forced Quarantine			
Yes	97 (3.6)	17 (3.5)	80 (3.6)
No	2601 (96.3)	474 (96.5)	2127 (96.2)
No response	3 (0.1)	0 (0)	3 (0.1)
Relative/friend with COVID-19			
Yes	600 (22.2)	97 (19.8)	503 (22.8)
No	2085 (77.2)	391 (79.6)	1694 (76.7)
No response	16 (0.6)	3 (0.6)	13 (0.6)

Notes: [a]Northern Italy: Aosta Valley, Emilia Romagna, Friuli-Venezia Giulia, Liguria, Lombardy, Piedmont, Trentino-Alto Adige, and Veneto. [b]Central Italy: Lazio, Marche, Tuscany, and Umbria. [c]Southern Italy: Abruzzo, Apulia, Basilicata, Calabria, Campania, Molise, Sardinia, and Sicily.

4.3.2 *Statistical analysis*

We carried out several preliminary analyses to assess the robustness and reliability of the data. To control for potential selection bias of the follow-up respondents based on the examined variables (PSQI, ISI, BDI-II, PSS-10, STAI-

X1), we performed mixed-model analyses on the questionnaire scores of all participants who took the Test 1, using "*Test 2 participation*" (yes, no), "*Gender*" (man, woman) and their interaction as predictors. Neither significant effect of "*Test 2 participation*" nor an interaction between the two predictors has been highlighted by the analyses (all $p > 0.10$). Additionally, because of the facultative nature of the last three questionnaires tapping into mental health problems, we performed the Little's MCAR test on these variables, which showed that missing questionnaires occurred completely at random, both at Test 1 ($\chi^2 = 1.78$, $p = 0.63$) and Test 2 ($\chi^2 = 3.64$, $p = 0.30$).

To evaluate the changes between Test 1 and Test 2, the questionnaire scores (PSQI, ISI, BDI-II, PSS-10, STAI-X1) were submitted to mixed model analyses with a random intercept per participant, to account for the correlation of questionnaire scores within each subject and intraindividual variability. The main models included "*Time*" (Test 1, Test 2), "*Gender*" (man, woman), and their interaction as predictors. Explorative analyses taking into account the interaction between "*Gender*", "*Time*", and the other demographic and COVID-related variables did not yield any significant effect (all $p > 0.10$). Therefore, the other demographic factors were collapsed and are not reported in the results. Analyses were performed using the "*lme4*" R package (Bates et al., 2015) weighting the estimates according to the gender prevalence within the Italian population. Models were fitted using *REML*, and *p*-values were obtained using the Satterthwaite approximation. Bonferroni *post hoc* tests were computed using the "*emmeans*" R package (Lenth et al., 2022). Statistical significance was set at $p < 0.05$, and all tests were 2-tailed. To check for potential biases due to the unbalanced gender composition of the sample, a randomized female sample corresponding to an equal number of male participants (n = 491) was extracted from the overall follow-up sample using SPSS v.22 (IBM Corp, Armonk, NY, USA). Then, the mixed model analyses applied to the total sample were replicated, confirming the outcomes of the main models.

Finally, the prevalence of moderate/severe insomnia and severe depression were computed according to the validated cut-off scores (see 1.3.2 section). Subsequently, logistic regression analyses were performed to evaluate the difference between genders of the prevalence of insomnia and depression clinical conditions at the two measurement times.

4.4 Results

The follow-up measurement was characterized by higher scores in all the questionnaires, except for the PSQI. Specifically, the "*Time*" factor was significant for ISI ($B = -0.33$, $t_{2825.60} = -2.86$, $p = 0.004$), BDI-II ($B = -0.37$, $t_{2300.62} = -2.23$, $p = 0.026$), PSS-10 ($B = -0.83$, $t_{2772.82} = -4.37$, $p < 0.001$), and STAI-X1 ($B = -1.40$, $t_{2378.21} = -5.93$, $p < 0.001$), while PSQI did not ($B = 0.04$, $t_{2669.22} = 0.48$, $p = 0.63$).

Gender was significant in all the analyses, showing higher mean scores of women in all the examined dimensions (PSQI: $B = -1.90$, $t_{5105.86} = -8.33$, $p < 0.001$; ISI: $B = -2.69$, $t_{5397.85} = -8.04$, $p < 0.001$; BDI-II: $B = -4.72$, $t_{4390.48} = -8.22$, $p < 0.001$; PSS-10: $B = -7.35$, $t_{4059.06} = -15.20$, $p < 0.001$; STAI-X1: $B = -5.06$, $t_{4337.02} = -7.48$, $p < 0.001$).

Finally, all the mixed model analyses highlighted significant interactions between "*Time*" and "*Gender*" factors (PSQI: $B = 0.47$, $t_{2649.43} = 3.99$, $p < 0.001$; ISI: $B = 0.82$, $t_{2825.60} = 4.86$, $p < 0.001$; BDI-II: $B = 0.74$, $t_{2288.67} = 2.97$, $p = 0.003$; PSS-10: $B = 3.24$, $t_{2769.66} = 11.47$, $p < 0.001$; STAI-X1: $B = 0.86$, $t_{2360.38} = 2.45$, $p = 0.014$). Interaction plots and *post hoc* results are reported in Figure 4.1.

Post hoc comparisons showed that, after four weeks of home confinement, male participants exhibited an increment in PSQI, ISI, and PSS-10 scores (all $p < 0.001$). On the other hand, women reported a reduction in insomnia and depression symptoms, perceived stress, and anxiety ($p = 0.025$; $p = 0.045$; $p < 0.001$; $p < 0.001$, respectively). Notwithstanding this, in both the measurement occasions, female participants reported significantly higher scores on all the variables (PSS-10 at Test 2: $p = 0.005$; all the other $p < 0.001$).

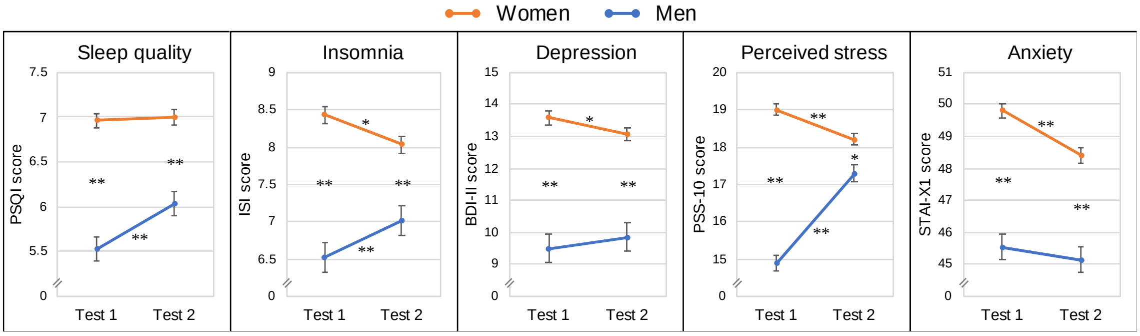

Figure 4.1. Interaction between "*Time*" (Test 1, Test 2) and "*Gender*" (man, woman) factors for the PSQI (sleep quality), ISI (insomnia), BDI-II (depression), PSS-10 (perceived stress), and STAI-X1 (anxiety) questionnaires.

Notes: Figure reports mean (and standard errors) of questionnaires scores in the two assessments (Test 1: 25-31 March 2020; Test 2: 21-27 April 2020) for men (in blue) and women (in orange). Bonferroni *post hoc* results are reported with asterisks (**p* < 0.05; ***p* < 0.001).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; BDI-II, Beck Depression Inventory-second edition, PSS-10, Perceived Stress Scale-10; STAI-X1, state-anxiety subscale of the State-Trait Anxiety Inventory.

Logistic regression analyses (Figure 4.2) revealed a higher female prevalence of moderate/severe insomnia and severe depression at Test 1 (moderate/severe insomnia: 13.12% vs. 9.37%, *odd ratio* (*OR*) = 0.68, $p = 0.023$; severe depression: 7.20% vs. 4.47%, *OR* = 0.60, $p = 0.049$). The gap in gender prevalence was no longer present at Test 2 both for moderate/severe insomnia (women: 11.63%, men: 12.02%; *OR* = 1.04, $p = 0.81$) and severe depression (women: 6.50%, men: 5.71%; *OR* = 0.87, $p = 0.56$). Indeed, men tended to worsen their condition during the lockdown (moderate/severe insomnia: +2.65%; severe depression: +1.24%), while women tended to improve it (moderate/severe insomnia: −1.49%; severe depression: −0.70%). Further analyses of the modifications of the clinical status by gender confirmed that the changes from Test 1 to Test 2 differed according to the gender (moderate/severe insomnia: $\chi^2 = 6.49$, $p = 0.04$, severe depression: $\chi^2 = 9.16$, $p = 0.01$; respectively).

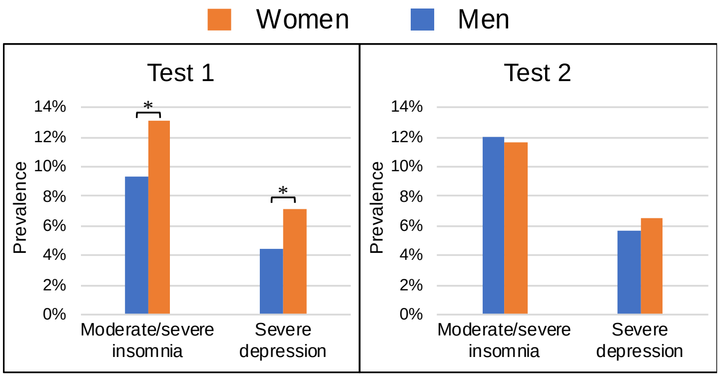

Figure 4.2. Prevalence rates of men (in blue) and women (in orange) reporting moderate to severe insomnia and severe depression at the two assessments.

Notes: Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section). Test 1: 25–31 March 2020; Test 2: 21–27 April 2020. Logistic regression significance is reported with asterisks (*$p < 0.05$).

4.5 Discussion

Our longitudinal study showed a different time course of sleep disturbances and mental health problems in men and women during the COVID-19 lockdown in Italy.

Women had consistently higher scores than men on sleep and mental health scales, especially at the beginning of the lockdown period. It should be noted that this is not a peculiarity of this extraordinary period. Previous research showed that women score is higher on PSQI in a wide range of countries and cultures (Curcio et al., 2013; Hinz et al., 2017; Wong & Fielding, 2011) and the female population typically has the highest prevalence of insomnia symptoms (B. Zhang & Wing, 2006). The prevalence of depression and anxiety is also higher for women (Malhi & Mann, 2018). Furthermore, women are marked by higher stress perception and have an increased likelihood of developing PTSD symptoms (Olff et al., 2007). Consequently, our results are in line with the literature of the pre-outbreak period.

However, the prolonged period of home confinement reduced the gender gap in two important ways. On one hand, women seemed to be more resilient than men, in the long run, exhibiting a slight trend toward improvement of insomnia, depression, anxiety, and distress at the end of the seven weeks covered by the present research. On the other hand, men showed an exacerbation of insomnia symptoms and a deterioration of sleep quality during the lockdown. Furthermore, male participants reported a substantial increment of perceived stress at the end of the study. In addition, although women reported a higher prevalence of clinical conditions such as insomnia and depression in the first part of the lockdown, the gender gap was narrowed after four weeks.

A recent study (C. Wang, Pan, Wan, Tan, Xu, McIntyre, et al., 2020) evaluated stress, anxiety, and depression in two samples of the general Chinese population that was assessed four weeks apart during the COVID-19 outbreak. No significant changes were reported at the overall-sample level. However, gender differences were not considered, participants were not forced into home confinement, and the study used a cross-sectional design. All these factors could explain the inconsistencies with our results.

The differential trend of mental health indicators in women and men during the long confinement period was peculiar and unexpected. Of note, the difference among gender trajectories was confirmed controlling for the other demographic variables such as age, education, and occupation. Because none of the variables collected in the present study could explain this effect, we believe that dispositional or sociocultural gender differences interacted with the extended period of restraining measures.

Men and women respond to stress differently, at both physiological and behavioral levels. According to an evolutionary perspective, the primary response aimed at reducing stress in men is a 'fight-or-flight' reaction, whereas women are likely to adopt a 'tend-and-befriend' one (Taylor et al., 2000). These patterns are supported by neuroendocrine and behavioral evidence (Verma et al., 2011). In this view, the dispositional stress response of women may have proven to be more appropriate when dealing with the current challenging time since the importance of community support and prosocial behaviors has been repeatedly emphasized to cope with the forced home confinement situation (Courtet et al., 2020; Holmes et al., 2020).

From a sociocultural perspective, our results could reflect deep-rooted differences in gender roles within western societies. Particularly in Italy, women have traditionally held a prominent position in the domestic environment compared to men. The gendered time course of the impact of the prolonged lockdown might be explained because the extended home confinement period largely compromised everyone's public life, preserving and emphasizing the domestic one at the same time.

Another possible interpretation is that men might manifest the psychological impact of the lockdown only after a prolonged period. On the other hand, women may have been the first to suffer the consequences of the home confinement situation because of their front-line role in the family care typical of Italian society. Consequently, women might have already reached the peak of psychological distress during the first days of the lockdown, subsequently adapting better to this extraordinary situation.

A final consideration refers directly to the gendered vulnerability to COVID-19. In Italy, as in the rest of the world, the progress of contagion was accompanied by the awareness of a higher prevalence of hospitalizations and deaths among men. This information was widely disseminated by the media during the period from the first to the second measurement time of our study and may have evoked a more danger in the male population, putatively contributing to explain our pattern of results.

Our findings are inconsistent with a general framework that predicts female gender to be a vulnerability factor *tout court* (Casagrande et al., 2020; Léger et al., 2020; C. Mazza et al., 2020; Özdin & Bayrak Özdin, 2020; Vindegaard & Benros, 2020; C. Wang, Pan, Wan, Tan, Xu, Ho, et al., 2020). A crucial point to stress is that, to date, studies based on a single measurement could be elusive concerning the actual psychological suffering of men. The well-known difference between genders in all the examined dimensions could lead to focus the psychological support on women. Instead, our investigation suggests that there is no "weaker gender" under lockdown and, sooner or later, both men and women can be strongly affected by this unprecedented situation.

Furthermore, our investigation did not confirm recent cross-sectional studies highlighting occupation or age as vulnerability factors (Casagrande et al., 2020; Cellini et al., 2020; Marelli et al., 2021). Because this is a longitudinal study, we investigated the presence of predictors which explained the changes over time in the examined variables. This peculiarity can explain the inconsistencies with the current literature based on a single measurement. Although the number of infections in Italy is declining at the moment, with a consequent relaxation of the restraining measures, our results could be of particular interest to the countries around the world where the contagion is ongoing, and home confinement measures still are an integral part of everyday life. The second wave of infections is also feared at the end of the summer or during the fall (Horton, 2020), and a further period of home confinement cannot be excluded.

The present findings could help to identify the timing for therapeutic interventions aimed at boosting coping skills and resilience and protecting the psychological well-being, counteracting the risk of developing mental health problems among the general population. In particular, our investigation highlights two crucial points. First of all, it confirms the urgency to predispose immediate psychological support focused on women since the beginning of the lockdown. Secondly, the present findings suggest that, with the advancement of the weeks, it is essential to shift the attention to men, who seem to be the primary category to suffer from the cumulative effects of the prolonged restraining measures during the COVID-19 pandemic. The sleep dimension emerges as the most affected by the lockdown extension among the male population. In this view, our results suggest predisposing specific sleep-focused interventions. This could be particularly important when considering the contribution of sleep disturbances in the development of mental health problems (Freeman et al., 2017). Finally, our investigation confirms the assumption that the governments should keep the lockdown as short as possible and avoid an overly precautionary approach (Brooks et al., 2020) to limit long-term psychological consequences, especially on male citizens.

To our knowledge, this is the first study reporting large-scale longitudinal changes of sleep disturbances and the risk of mental health deterioration among the same population under home-confinement. However, some limitations need to be reported. The main one is the impossibility of determining the sampling bias in Test 1 because of the sampling technique. We cannot exclude that the present study inadvertently attracted individuals reporting the most serious conditions as regards the examined dimensions. Nevertheless, this bias would be expected at the overall sample level, putatively not affecting the gendered trajectories here highlighted. Secondly, it should be acknowledged that the composition of the experimental sample is substantially unbalanced towards the female gender. Finally, our results were obtained in an Italian sample. Deep-rooted social gender inequities mark Italian society. Further longitudinal investigations could confirm our pattern of results within other populations.

Chapter 5

Changes of evening exposure to electronic devices during the COVID-19 lockdown affect the time course of sleep disturbances

5.1 Abstract

During the coronavirus disease 2019 (COVID-19) lockdown, there was a worldwide increase in electronic devices' daily usage. Prolonged exposure to backlit screens before sleep influences the circadian system leading to negative consequences on sleep health. We investigated the relationship between changes in evening screen exposure and the time course of sleep disturbances during the home confinement period due to COVID-19.

A total of 2,123 Italians (mean age ± SD, 33.1 ± 11.6 years) were tested longitudinally during the third and the seventh week of lockdown. The web-based survey evaluated sleep quality and insomnia symptoms through the Pittsburgh Sleep Quality Index and the Insomnia Severity Index. The second assessment survey inquired about intervening changes in backlit screen exposure in the two hours before falling asleep.

Participants who increased electronic device usage showed decreased sleep quality, exacerbated insomnia symptoms, reduced sleep duration, prolonged sleep onset latency, and delayed bedtime and rising time. In this subgroup, the prevalence of poor sleepers and individuals reporting moderate/severe insomnia symptoms increased. Conversely, respondents reporting decreased screen exposure exhibited improved sleep quality and insomnia symptoms. In this subgroup, the prevalence of poor sleepers and moderate/severe insomniacs

decreased. Respondents preserving screen time habits did not show variations of the sleep parameters.

Our investigation demonstrated a strong relationship between modifications of evening electronic device usage and time course of sleep disturbances during the lockdown period. Monitoring the potential impact of excessive evening exposure to backlit screens on sleep health is recommendable during the current period of restraining measures due to COVID-19.

5.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Sleep* (Salfi, Amicucci, et al., 2021) and reproduced with permission from *Oxford University Press.*

The forced social isolation and the limitations of outdoor activities led to a worldwide increase in web-based social communication. In the countries hit hardest by the virus, the total messaging and the time spent on social network increased more than 50%, while the time in video calling increased tenfold (Meta, 2020). In Italy, during the lockdown, the daily internet traffic volume almost doubled compared to the previous year (AGCOM, 2020). Most people spent more time on smartphones and computers (DATAREPORTAL, 2020; The Washington Post, 2020), and, for example, in the UK adults spent 40% of their day facing a screen during confinement (Ofcom, 2020). Electronic devices daily usage increased to compensate for the limited social interactions, fill up free time, and ward off boredom. Furthermore, working from home has become the norm for millions of workers worldwide, and 40% of those currently working in the European Union began to telework full-time due to the pandemic (Eurofound, 2020). The implementation of these habits may have helped to cope with the challenging and stressful isolation period. Nevertheless, the increase of screen exposure in the hours before bedtime could have determined adverse consequences on sleep health. Epidemiological and cross-sectional studies indeed showed a strong relationship between the use of electronic devices after sundown and alterations of sleep patterns (Christensen et al., 2016; Exelmans & van den Bulck, 2016; Fossum et al., 2014; Gradisar et al., 2013; Johnson et al., 2004; Lastella et al., 2020; Rafique et al., 2020; Šmotek et al., 2020). Firstly, the usage of electronic devices may displace sleep time (Cain & Gradisar, 2010). Moreover, screen-based activities are related to digital engagement, and the activity type plays a role in the digital media effects on sleep (Orzech et al., 2016). The screen-mediated contents could be emotionally or psychologically arousing, making it more difficult for individuals to relax before bedtime and, thus, interfering with sleep (Cain & Gradisar, 2010; Higuchi et al., 2005a; Orzech et al., 2016). In particular, portable mobile and media devices allow real-time interactions and hence continuous stimulation (Carter et al., 2016). Finally, sleep rhythms are intimately linked with the ambient light, which represents a crucial regulator of the biological clock (Brown, 1994; Cajochen, 2007). The evening exposure to short-wavelength-enriched light emitted from most screens of modern electronic devices (computer, smartphone, tablet, television) can have alerting effects suppressing melatonin release. This assumption has been confirmed by investigations that experimentally manipulated the evening light exposure of tablet (Wood et al., 2013), eReader (Chang et al., 2015), and computer screen (Cajochen et al., 2011; A. Green et al., 2017), showing a concomitant decrease of objective and self-reported sleepiness, higher sleep onset latency, and altered sleep architecture.

Therefore, light per se and the stimulating content of electronic devices during the hours preceding habitual bedtime may interfere with sleep patterns intervening on biological and cognitive mechanisms simultaneously (Woods & Scott, 2019).

Difficulties in falling asleep (e.g., in insomnia), on the other hand, may lead to longer time spent engaging with screens in the evening hours, establishing a vicious circle.

Based on this evidence, the present study aimed to shed light on the relationship between the longitudinal changes of sleep disturbances between the third (March 25–28, 2020) and the seventh week (April 21–27, 2020) of home confinement in Italy and the retrospectively reported modifications of the exposure to electronic devices before falling asleep during the same lockdown period. We hypothesized that changes in electronic device usage could be a crucial moderator of the lockdown-related sleep alterations over time. We expected that individuals who increased screen exposure in the two hours before sleep onset should have shown the largest sleep impairments and the most marked alterations of the sleep/wake schedule. On the other hand, subjects who reduced evening screen time should have exhibited a positive time course of sleep disturbances.

5.3 Materials and methods

5.3.1 *Participants and procedure*

From the large follow-up sample described in 4.3.1 section, we included in the reported analyses only the 2,123 respondents (mean age ± SD, 33.1 ± 11.6; range, 18–82; 401 men, see Table 5.1) who completed the first survey during the four days preceding the daylight-saving time (March 25–28, 2020; Survey wave 1). This allowed us to avoid interfering and confounding effects at the baseline measurement due to the summertime beginning (for a review, see Harrison 2013). During the follow-up survey (Survey wave 2), participants completed the same questionnaires of Survey wave 1 (see 1.3.2 section). Moreover, they were asked to retrospectively evaluate the changes (increase, maintenance, reduction) from the first assessment in the usage duration of electronic devices (smartphone, computer, tablet, television, eReader) in the 2 h before falling asleep.

At Survey wave 1, a total of 1,783 respondents completed the BDI-II, 1,697 filled in also the PSS-10, and 1,675 completed all the questionnaires, while at Survey wave 2 the number of respondents for the last three optional questionnaires (BDI-II, PSS-10, STAI-X1) was 1,873, 1,811, and 1,789, respectively. The study was approved by the Institutional Review Board of the University of L'Aquila (protocol n. 43,066/2020) and carried out according to the principles established by the Declaration of Helsinki. Online informed consent to participate in the whole research was obtained from all the respondents during the first assessment.

Table 5.1. Sociodemographic composition of the sample participating in both the first and the second measurement (Survey wave 1: 25–28 March 2020; Survey wave 2: 21–27 April 2020).

Variable	N (%)
Gender	
Male	401 (18.9%)
Female	1722 (81.1%)
Age	
18–30 years	1263 (59.5%)
31–50 years	598 (28.2%)
> 50 years	262 (12.3%)
Education	
Until middle school	31 (1.5%)
High school	686 (32.3%)
Graduated	1406 (66.2%)
Occupation	
Unemployed	184 (8.7%)
Employed	1172 (55.2%)
Student	767 (36.1%)
Geographical location	
Northern Italy[a]	767 (36.1%)
Central Italy[b]	593 (27.9%)
Southern Italy[c]	763 (35.9%)
Electronic device usage	
Increased	751 (35.4%)
Unchanged	1221 (57.5%)
Reduced	151 (7.1%)

Notes: [a]Northern Italy: Aosta Valley, Emilia Romagna, Friuli-Venezia Giulia, Liguria, Lombardy, Piedmont, Trentino-Alto Adige, and Veneto. [b]Central Italy: Lazio, Marche, Tuscany, and Umbria. [c]Southern Italy: Abruzzo, Apulia, Basilicata, Calabria, Campania, Molise, Sardinia, and Sicily.

5.3.2 *Statistical analysis*

In order to control for potential selection bias of the follow-up participants, we performed preliminary mixed model analyses comparing the Survey wave 1 questionnaire scores of respondents who participated only to the first assessment and those who attended both the measurements (Survey wave 1 and Survey wave 2). These control analyses did not highlight significant differences (all $p > 0.10$).

According to the purpose of the present study, the main variables were the PSQI and ISI scores. Additionally, from the PSQI questionnaire, we extracted other variables such as total sleep time (TST, min), sleep onset latency (SOL, min), bedtime (BT, hh:mm), and rise time (RT, hh:mm). To evaluate the time course of the sleep dimensions as a function of the reported changes of exposure to electronic devices, all the above variables were submitted to mixed model analyses with a random intercept per participant, accounting for the expected intraindividual variability. The models comprised "*Survey wave*" (Survey wave 1, Survey wave 2), "*Screen exposure*" (Increased, Unchanged, Reduced), and their interaction as predictors. Additionally, "*Gender*" (male, female) was included as a factor, and *"Age"* as a covariate, to control for putative effects of these demographic variables on the main outcomes of the present study. Subsequently, explorative analyses were carried out, adding to the models the Survey wave 1 and Survey wave 2 scores of MEQr, BDI-II, PSS-10, and STAI-X1 as time-varying covariates. These further analyses aimed at controlling for the effects of chronotype, depression, stress, and anxiety on sleep measures, in order to isolate the effects of the screen exposure changes from the effects of these psychological dimensions in explaining the time course of sleep variables.

Mixed model analyses were performed using the "*lme4*" R package (Bates et al., 2015). Models were fitted using *REML*, using the Satterthwaite approximation to compute *p*-values. Bonferroni *post hoc* tests were obtained using the "*emmeans*" R package (Lenth et al., 2022). Finally, the validated cut-off scores of PSQI and ISI were used to determine the prevalence of poor sleepers and moderate/severe insomnia condition (see 1.3.2 section). Subsequently, McNemar's tests were performed to evaluate the modifications of the prevalence of sleep disturbances between Survey wave 1 and Survey wave 2 in the three groups characterized by different changes of exposure to electronic devices before falling asleep. For all the analyses, statistical significance was set at $p < 0.05$, and all tests were two-tailed.

5.4 Results

5.4.1 *Relationships between screen exposure and sleep variables*

The results of the mixed model analyses on the sleep variables (PSQI and ISI scores, TST, SOL, BT, RT) are reported in Table 5.2. The analyses did not highlight significant effects of the "*Survey wave*" factor for all the sleep variables (all $p \geq 0.24$). "*Screen exposure*" was significant for all the variables (all $p \leq 0.005$). The analyses yielded a significant effect of the interaction between "*Survey wave*" and "*Screen exposure*" predictors for all the variables (all $p \leq 0.001$). The *"Age"* covariate was significant for PSQI, TST, SOL, BT, and RT (all $p \leq 0.03$), and "*Gender*" was significant for PSQI, ISI, SOL, BT (all $p \leq 0.001$).

Table 5.2. Results (*F* and *p*) of the mixed model analyses on PSQI score (sleep quality), ISI score (insomnia severity symptoms), total sleep time, sleep onset latency, bedtime, and rise time.

Predictor	PSQI score		ISI score		Total sleep time		Sleep onset latency		Bedtime		Rise time	
	F	*p*	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*p*
Survey wave	.11	.75	.75	.39	1.37	.24	.49	.49	.10	.76	.14	.71
Screen exposure	29.57	**<.001**	32.51	**<.001**	6.74	**.001**	6.14	**.002**	7.14	**<.001**	5.26	**.005**
Survey wave × Screen exposure	20.29	**<.001**	23.70	**<.001**	9.07	**<.001**	6.70	**.001**	30.11	**<.001**	20.63	**<.001**
Age	46.64	**<.001**	0.95	.33	247.5	**<.001**	4.60	**.03**	184.9	**<.001**	397.5	**<.001**
Gender	16.62	**<.001**	11.64	**<.001**	.89	.35	19.14	**<.001**	13.01	**<.001**	.02	.89

Notes: The models comprised *"Survey wave"* (Survey wave 1, Survey wave 2), "*Screen exposure*" (Increased, Unchanged, Reduced) as predictors, their interaction, and *"Age"* and *"Gender"* (Male, Female) as covariates. Bold values are statistically significant.

Post hoc comparisons between Survey wave 1 and Survey wave 2 (Figures 5.1 and 5.2) suggested that participants who reported an increase of electronic device usage before falling asleep also showed a significant increase over time of PSQI (mean change ± SE, +1.01 ± 0.15; $p < 0.001$) and ISI scores (+1.26 ± 0.21; $p < 0.001$), a reduction of TST (−16.70 ± 3.22 min; $p < 0.001$), a prolongation of SOL (+4.08 ± 1.31 min; $p = 0.03$), and delayed BT (+23.08 ± 3.13 min; $p < 0.001$) and RT (+18.92 ± 2.83 min; $p < 0.001$). On the other hand, participants who reduced the screen exposure showed concurrent decreases of PSQI (−1.00 ± 0.33; $p = 0.04$) and ISI scores (−1.44 ± 0.42; $p = 0.02$), earlier BT (−23.25 ± 6.70 min; $p = 0.009$), and no changes in TST, SOL, and RT ($p = 1.00$, $p = 0.58$, $p = 0.11$; respectively). No differences in all the variables were obtained for the participant who maintained unchanged electronic device use habits (all $p = 1.00$). Although the mean PSQI and ISI changes between the two survey waves for the groups increasing or reducing the exposure to electronic devices could appear small, they proved to have a clinical significance, as emerged in the analyses on the prevalence of poor sleepers and clinical insomniacs (see 5.4.2 section).

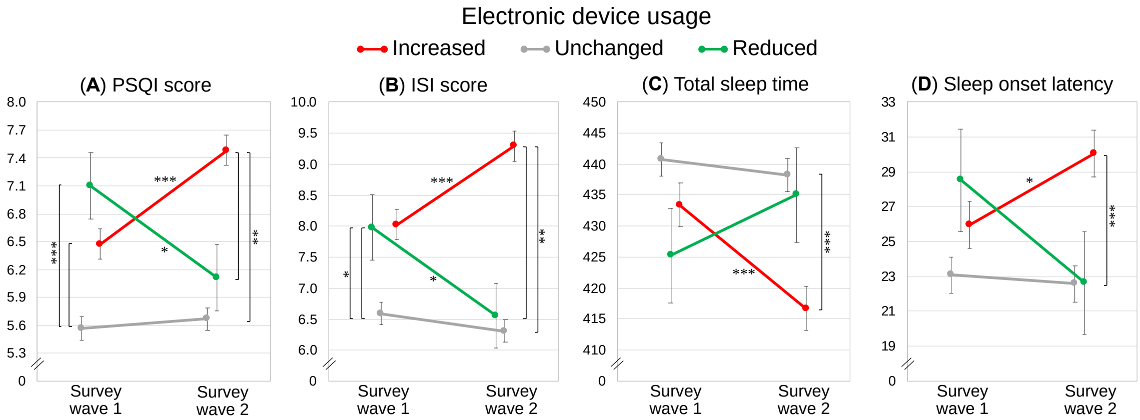

Figure 5.1. "*Survey wave*" × "*Screen exposure*" interaction for PSQI and ISI scores, total sleep time (min), and sleep onset latency (min).

Notes: Figure reports mean ± standard error of the PSQI and ISI scores (A, B), total sleep time (C), and sleep onset latency (D) at the two assessments (Survey wave 1, Survey wave 2) for respondents who declared an increase, preservation, or reduction of the electronic device usage duration before falling asleep. Each analysis was adjusted for age and gender. Bonferroni significant *post hoc* comparisons are reported with asterisks (**p* < 0.05, ***p* < 0.01, ****p* < 0.001).

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index.

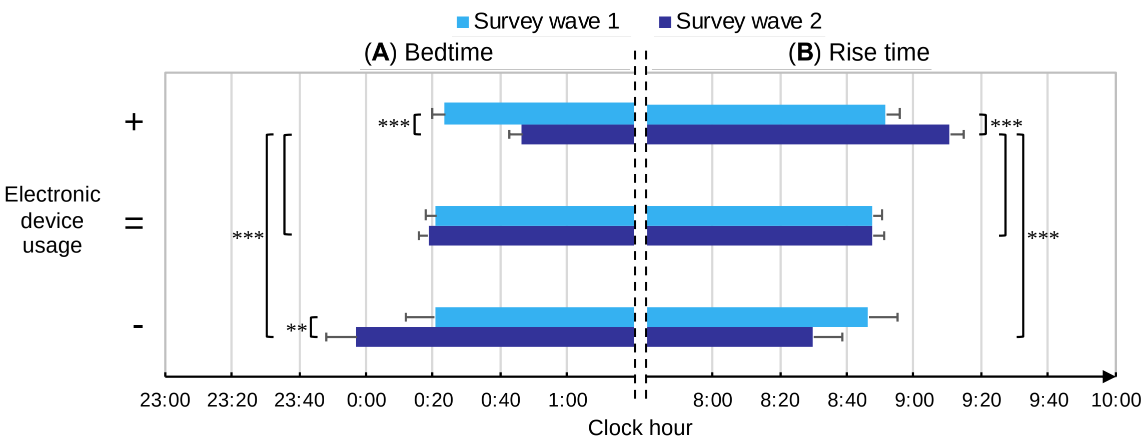

Figure 5.2. "*Survey wave*" × "*Screen exposure*" interaction for bedtime and rise time (hh:mm).

Notes: Mean ± standard error of bedtime (A) and rise time (B) at the two assessments (Survey wave 1, Survey wave 2) for participants who declared an increase (+), preservation (=), or reduction (−) of the electronic device usage duration before falling asleep. Each analysis was adjusted for age and gender. Bonferroni *post hoc* results are reported with asterisks (***p* < 0.01, ****p* < 0.001).

At Survey wave 1, there were no differences in PSQI and ISI scores between respondents who later reported an increase or reduction of screen exposure (both $p = 1.00$). Participants maintaining device use habits showed lower PSQI scores at Survey wave 1 than those who increased or reduced the exposure to backlit screens (both $p < 0.001$). ISI scores were lower at Survey wave 1 for subjects who did not change the screen exposure than participants who increased or reduced it ($p < 0.001$, $p = 0.04$; respectively). The three groups did not differ at Survey wave 1 on TST, SOL, BT, and RT (all $p > 0.85$).

Participants who reported an increase of screen exposure also showed higher PSQI and ISI scores at Survey wave 2, and delayed BT and RT compared to the other two groups (all $p < 0.01$), as well as shorter TST and longer SOL compared to the group that did not change the device usage habits (both $p < 0.001$, see Figure 5.2). No differences for all the variables were obtained at Survey wave 2 between subjects who reduced or maintained the device usage duration before falling asleep (all $p > 0.32$).

Further control analyses confirmed the above-reported pattern of results, controlling for the covariance of age, gender, chronotype, depression, perceived stress, and anxiety. In particular, the interaction between "*Survey wave*" and "*Screen exposure*" remained significant for all the variables (PSQI: $F_{2,1605.95} = 17.50$, $p < 0.001$; ISI: $F_{2,1685.08} = 14.20$, $p < 0.001$; TST: $F_{2,1694.81} = 8.37$, $p < 0.001$; SOL: $F_{2,1711.04} = 4.53$, $p = 0.01$; BT: $F_{2,1664.94} = 17.11$, $p < 0.001$; RT: $F_{2,1645.32} = 12.70$, $p < 0.001$), confirming the crucial role of the changes in screen exposure in explaining the time course of the sleep outcomes during the lockdown.

5.4.2 *Relationships between screen exposure and sleep disturbance prevalence*

McNemar's tests highlighted a significant prevalence increase of poor sleepers (+11.4%) and of moderate/severe insomnia condition (+3.6%) in the group of respondents reporting an increased usage of electronic devices before falling asleep (χ^2 = 108.23, p < 0.001, Cohen's g = 0.21; χ^2 = 149.73, p = 0.01, Cohen's g = 0.15; respectively) (Figure 5.3). On the other hand, there was a significant decrease of poor sleepers (−10.7%) and of moderate/severe insomnia condition (−7.3%) in the group reporting a reduction of the device usage (χ^2 = 19.90, p = 0.04, Cohen's g = 0.18; χ^2 = 12.21, p = 0.04, Cohen's g = 0.24; respectively). Finally, in the group of participants who maintained screen habits unchanged there was a reduction of clinical insomnia prevalence (−2.8%; χ^2 = 188.51, p = 0.002, Cohen's g = 0.13), but not of poor sleepers' prevalence (−2.3%; χ^2 = 200.25, p = 0.17, Cohen's g = 0.04). According to the standard interpretation of Cohen's g (J. Cohen, 1988), all the variations in the groups of respondents who increased or reduced the screen exposure was of medium extent, while the effect size of the insomnia condition reduction among those who maintained unchanged the use of electronic devices was small.

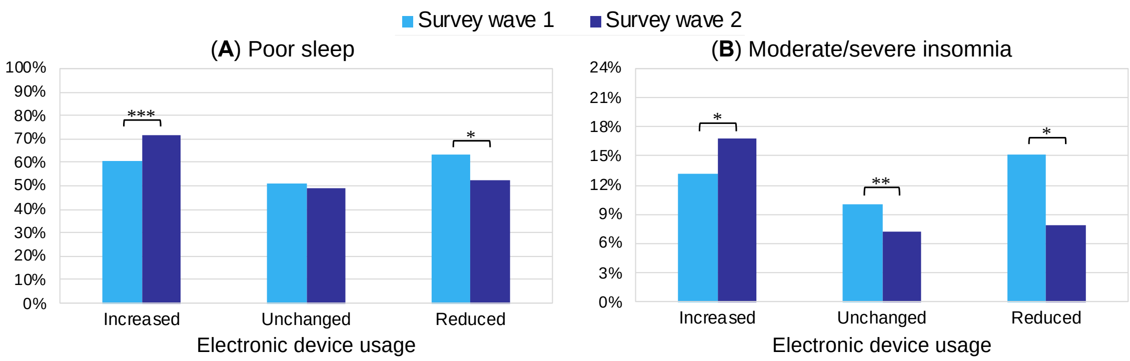

Figure 5.3. Prevalence of poor sleepers (A) and moderate/severe clinical insomnia condition (B) at the two assessments (Survey wave 1, Survey wave 2) for the respondents who increased, maintained unchanged, or reduced the usage of electronic devices before falling asleep.

Notes: Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section). Significant results of the McNemar's tests are reported with asterisks (*p < 0.05, **p < 0.01, ***p < 0.001).

5.5 Discussion

In the present study, we showed a strong relationship between changes in evening screen exposure and time course of sleep parameters during the COVID-19 lockdown.

In line with the initial assumption, individuals declaring increased electronic device usage before falling asleep showed a general sleep impairment over time (from the third to the seventh week of home confinement). This outcome is exemplified by decreased sleep quality, exacerbation of insomnia symptoms, reduced sleep duration, and longer sleep onset latency. Consistently, we found an increased prevalence of poor sleepers and moderate/severe insomnia condition only within this group of respondents. Increased screen exposure was also linked to delayed bedtime and rising time, outlining the delayed sleep phase across the home confinement period. Furthermore, individuals who increased the device usage showed the poorest sleep quality, the most severe insomnia symptoms, the lowest sleep duration, the highest sleep onset latency, and they went to bed and woke up later compared to the other participants during the seventh week of lockdown.

In addition, participants reporting decreased evening screen exposure showed the opposite time course of sleep disturbances. They indeed exhibited improved sleep quality and mitigation of insomnia symptoms, which turned into a prevalence reduction of poor sleepers and clinical insomnia condition. This group of respondents went to bed earlier after four weeks of home confinement.

Finally, the respondents who maintained unchanged electronic device usage habits did not show any modification in all the examined dimensions, except for a prevalence reduction of moderate/severe insomnia conditions.

Remarkably, we obtained the present findings controlling for the effects of gender and age, and they were confirmed also controlling for the covariance of chronotype, depression, stress, and anxiety. Therefore, our results suggest a direct relationship between evening device usage and time course of sleep disturbances during the home confinement period, independent of other psychological and circadian dimensions.

The pattern of results of our longitudinal investigation is consistent with a large pre-outbreak cross-sectional literature addressing the relationship between sleep and evening electronic device usage. In particular, higher screen time has been associated with reduced sleep duration (Bhat et al., 2018; Gamble et al., 2014; Hysing et al., 2015; Lastella et al., 2020), prolongation of sleep onset latency (Christensen et al., 2016; Exelmans & van den Bulck, 2016; Hysing et al., 2015; Rafique et al., 2020; Šmotek et al., 2020), later sleep onset and waking up (Exelmans & van den Bulck, 2016; Gamble et al., 2014; Lastella et al., 2020), poor sleep quality (Christensen et al., 2016; Exelmans & van den Bulck, 2016; Lastella et al., 2020; Rafique et al., 2020; Šmotek et al., 2020), and insomnia symptoms (Bhat et al., 2018; Exelmans & van den Bulck, 2016; Fossum et al., 2014).

The COVID-19 pandemic has affected all the world, and home confinement constitutes the most widely used measure to contrast the spread of the contagion. In modern societies, the increase of screen-based device usage could represent an unavoidable consequence of the pandemic-related home confinement periods. Indeed, more than one-third of our sample reported an increase in electronic device usage in the two hours before falling asleep. On the other hand, only a small percentage of the sample (7.1%) reduced the evening screen time between the third and the seventh week of lockdown. This evidence suggests that the reduction of screen time and the associated sleep improvement during a prolonged confinement period were rare, while the opposite situation was quite common. Consequently, our findings have substantial large-scale implications when contextualized to the current unprecedented situation.

Adequate sleep quantity/quality is essential to deal with stressful events (Leggett et al., 2016) and preserve mental health (Freeman et al., 2017; Pigeon et al., 2017), and it plays a crucial role in emotional processing (Tempesta et al., 2018, 2020) and mood regulation (Fairholme & Manber, 2015). The increased screen time and its consequences on sleep health may negatively affect psychological well-being increasing anxiety, depression, and stress symptoms during the current pandemic period. Indeed, aberrant light exposure and excessive screen time were associated with sleep and mental health problems (Bedrosian & Nelson, 2017; Wu et al., 2015). Consistently, blocking screen-emitted blue light has proved to be effective in promoting both sleep quality and mood (Burkhart & Phelps, 2009; Janků et al., 2020) and it was proposed as a useful approach to treat both clinical insomnia (Janků et al., 2020; Shechter et al., 2018) and mood disorders (Bedrosian & Nelson, 2017; Phelps, 2008), although the current literature presents inconsistencies (Heath et al., 2014).

Finally, sleep and the circadian system support the proper functioning of the immune system (Besedovsky et al., 2012; Bryant et al., 2004). Short sleep duration and poor sleep continuity are associated with increased vulnerability to infectious illness, including higher susceptibility to the common cold and greater symptom reporting (S. Cohen et al., 2009; Irwin, 2015; Prather et al., 2015). The largest vaccination campaign in human history is around the corner, and studies have clearly shown that sleep is an important factor in determining the effectiveness of vaccinations, for example, against influenza viruses (Spiegel et al., 2002; Zimmermann & Curtis, 2019). In light of these considerations, the relationship between screen time and sleep outcomes has a broad spectrum of implications, configuring a major public health concern during the COVID-19 outbreak.

The present results were obtained in an Italian sample, but they could be generalized to other modern societies since the putative underlying mechanisms involve a disruption of circadian physiology due to evening light exposure (Cajochen et al., 2011; Chang et al., 2015; A. Green et al., 2017; Wood et al., 2013), increased arousal caused by the stimulating content of the screen-mediated material before bedtime (Cain & Gradisar, 2010; Higuchi et al., 2005; Orzech et al., 2016), and a direct displacement of sleep time (Cain & Gradisar, 2010). However, we cannot infer the causality of this relationship since this is an observational study, and the measurement of screen exposure changes has been retrospectively reported during the second assessment. Notwithstanding that comprehensive literature supported the detrimental effect of electronic devices' evening usage on sleep patterns, we cannot exclude reverse causation. Nevertheless, the two interpretations are not mutually exclusive, and a bidirectional model of causation has been suggested (Magee et al., 2014). We propose that a vicious circle during the confinement period was established, in which the increased screen exposure before falling asleep negatively impacted the sleep parameters, which in turn supported the overuse of electronic devices after the sunset. Notably, participants who did not change the screen exposure during the examined four weeks of lockdown exhibited the lowest PSQI and ISI scores at the first assessment (Survey wave 1). This outcome could be interpretable as a tendency to maintain unchanged screen habits among individuals with fewer sleep disturbances.

In conclusion, our findings corroborate the assumption that the governments should pursue policies aimed at raising public awareness on healthy sleep behaviors during confinement due to the COVID-19 pandemic, discouraging the excessive use of electronic devices before falling asleep (Johns Hopkins Medicine, 2020; Sleep Foundation, 2020). The evening use of blue-light blocking glasses and the application of a blue wavelength light filter (night shift settings) on the electronic screens should be encouraged to mitigate the well-known detrimental consequences of bright light exposure. In addition, the implementation of psychophysiologically and emotionally arousing screen-based activities such as computer work and surfing the Internet (Orzech et al., 2016), playing videogames

(Higuchi et al., 2005), and overuse of media to obtain information about COVID-19 (Léger et al., 2020) should be discouraged before the sleep onset.

To date, the feared risk of a second wave of contagion has become a concrete reality, and hundreds of thousands of people are subjected to home confinement measures worldwide. In light of our results, the above-mentioned interventions focused on sleep hygiene are fundamental to counteract the occurrence and exacerbation of sleep disturbances and foster the general well-being during the period of social distancing and restraining measures due to the COVID-19 pandemic.

To the best of our knowledge, the present investigation is the first to provide insights into the relationship between electronic device usage and the time course of sleep disturbances during the COVID-19 lockdown. However, it should be acknowledged that we used a non-probabilistic sampling technique, and the sample comprised a higher prevalence of women and young people. Moreover, under-eighteen years-old individuals were not included. However, the relationship between evening screen time and sleep disturbances was widely shown in adolescents (Cain & Gradisar, 2010; Carter et al., 2016; Hale & Guan, 2015). We hypothesize that our results could be generalizable to younger people. Further research focused on the younger population is necessary as children and adolescents are spending increasingly more time on electronic devices during the pandemic emergency (Montag & Elhai, 2020). Additionally, the electronic device category of our survey included a broad set of devices, and we cannot discern the relationship between the usage of each device (i.e., smartphone, computer, tablet, television, eReader) and the time course of the sleep outcomes. Finally, in our survey, we did not assess the extent of the screen exposure changes, the use of bright/dim screens, the room lighting, and the implementation of blue-light blocking glasses or blue light filter technology, thus we cannot estimate their contribution to the present findings. Further research should be performed accounting for these limitations to disentangle the causal relationship between sleep patterns and the increased digital device usage before sleep onset during the current pandemic period. Future longitudinal investigations should include a detailed day-by-day quantification of screen time for each device (e.g., using daily diaries and/or specific applications), an objective estimation of sleep patterns (e.g., through actigraphy), and an evaluation of the screen-mediated contents as well as the use of blue-light blocking approaches.

Part 2

The second wave

As described in Part 1, the first COVID-19 contagion wave in the Spring of 2020 and the adopted restraining measures have deeply affected the sleep and mental health of the general population.

Like other coronaviruses (Monto et al., 2020), SARS-CoV-2 behaves seasonally, being more prevalent in Winter and less so during the hot season (X. Liu et al., 2021). Indeed, during the Summer of 2020, the virus circulation substantially declined, with a consequent lifting of the stay-at-home orders. However, the subsequent cold season was characterized by a new global surge in COVID-19 cases, leading international governments to apply again large-scale intervention to manage the novel public health crisis. The strict lockdown measures adopted to face the first contagion wave had dramatic societal and economic costs. Therefore, lighter restraining measures were applied to cope with the second wave in most countries, where several business and school activities remained open, freedom of movement was partially ensured, and people began co-existing with the virus without any vaccine for COVID-19 still available.

This stressful scenario again challenged the sleep and mental health of the general population while the aftermath of the first lockdown continued to be felt worldwide.

In Chapter 6, we reported the results of the first longitudinal investigation aimed at understanding the consequences of the second contagion wave on Italians' sleep and psychological well-being. We provided a fine-grained overview of the behavioral and sociodemographic risk factors for sleep disturbances during the second contagion wave. Driven by the results shown in Part 1, we evaluated the effect of age, gender, chronotype, working status, and digital screen time. Moreover, we addressed the social and economic impact and the repercussion of living constantly surrounded by the COVID-19 threat. Furthermore, we compared the sleep features between the two contagion peaks of infection, evaluating the changes in sleep disturbances and sleep habits/schedules due to the partial resumption of daily working and activity routines.

Finally, Chapter 7 addressed one of the main characteristics of the second wave of COVID-19, the large-scale transition to a new working approach named *remote working*, and how this societal change interacted with the different chronotypes' sleep and mental health.

Chapter 6

Sleeping under the waves: A longitudinal study across the contagion peaks of the COVID-19 pandemic in Italy

6.1 Abstract

After the March–April 2020 coronavirus disease 2019 (COVID-19) outbreak, a second contagion wave afflicted Europe in the autumn. The present study aimed to evaluate sleep health/patterns of Italians during this further challenging situation.

A total of 2,013 Italians longitudinally participated in a web-based survey during the two contagion peaks of the COVID-19 outbreak. We investigated the risk factors for sleep disturbances during the second wave, and we compared sleep quality and psychological well-being between the two assessments (March–April and November–December 2020).

Female gender, low education, evening chronotype, being a high-risk person for COVID-19 infection, reporting negative social or economic impact, and evening smartphone overuse predicted a higher risk of poor sleep and insomnia symptoms during the second wave. Advanced age, living with a high-risk person for COVID-19 infection, and having a relative/friend infected with COVID-19 before the prior 2 weeks were risk categories for poor sleep quality. Living with children, having contracted COVID-19 before the prior 2 weeks, being pessimistic about the vaccine and working in healthcare, were risk factors for insomnia symptoms. The follow-up assessment highlighted reduced insomnia symptoms and anxiety. Nevertheless, we found reduced sleep duration, higher daytime dysfunction, advanced bedtime and get up time, and a shift to

morningness, confirming the alarming prevalence of poor sleepers (~60%) and severe depression (~20%) in a context of increased perceived stress.

The present study showed a persistent impact of the COVID-19 pandemic on sleep and mental health. Large-scale interventions to counteract the chronicity and exacerbation of sleep and psychological disturbances are necessary, especially for the at-risk categories.

6.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Journal of Sleep Research* (Salfi, D'Atri, et al., 2021) and reproduced with permission from *John Wiley and Sons.*

From December 2019, coronavirus disease 2019 (COVID-19) began to spread worldwide rapidly. The Italian government reacted to the first contagion wave (March–April 2020) implementing a total lockdown involving home confinement and social distancing for the entire population, and the closure of most business activities. The lockdown started on 9 March and lasted until 3 May 2020. Many studies reported a pervasive impact of the lockdown period during the first wave of the COVID-19 outbreak on sleep and psychological health of the general population (Jahrami et al., 2021; Rajkumar, 2020; Salfi, Lauriola, et al., 2021). In the autumn, a second contagion outbreak occurred in Italy, leading the government to adopt new restraining measures to control the virus propagation. A regional approach was adopted this time: restrictions to freedom of movement, business and school activities were imposed according to the local infection diffusion and the pressure on the regional healthcare system. On 6 November 2020, Italian regions were classified across three risk levels (yellow, orange, and red, ordered in terms of the severity of the restrictions), periodically updated based on the COVID-19-related data monitoring. In the present study, we provide the first evaluation of sleep health of the general population during the second wave of the COVID-19 emergency, identifying the at-risk categories for sleep disturbances during this further challenging period. Moreover, we longitudinally compared the outcome of the current period in a large Italian sample with the situation of the first pandemic wave using a web-based survey administered during 2 weeks around the two contagions peaks.

6.3 Materials and methods

6.3.1 *Participants and procedure*

A total of 8,798 Italian citizens participated in a web-based survey during the first wave of COVID-19 (Test 1: 25 March–7 April 2020, the third and fourth week of lockdown; Figure 6.1). The data collection procedure is detailed in 1.3.1 section. The Test 1 respondents were invited by email to participate in a follow-up assessment on 28 November 2020, corresponding to the contagion peak of the second wave of the COVID-19 outbreak. A total of 2,013 individuals participated in the second measurement in a 2-week time window (Test 2: 28 November–11 December 2020; Figure 6.1). The follow-up measurement comprised the same questionnaires as Test 1 (see in 1.3.2 section). Additionally, we collected the following sociodemographic and COVID-19-related information as continuous or categorical variables: age, gender, education, occupation, geographical region used to derive the restraining measures in force (yellow, orange, or red zone), living with children, being a high-risk person for COVID-19 infection, living with a high-risk person for COVID-19 infection, COVID-19 infection, forced quarantine, infection or death of a relative/close friend due to COVID-19, perspective on vaccination, negative economic and social impact of the current situation, and mean exposure (min) to smartphone, personal computer (PC)/tablet, television, and e-reader in the 2 hours before falling asleep during the previous 2 weeks. The available choices for each categorical variable along with the sociodemographic composition of the follow-up sample, and the COVID-related responses are reported in Table 6.1. The compilation of the last three questionnaires (BDI-II, PSS-10, STAI-X1) was optional to ensure reliable unforced responses. A total of 1,847, 1,790, and 1,784 participants completed the BDI-II, the PSS-10, and the STAI-X1, respectively, during Time 1 and Time 2. The study was approved by the Institutional Review Board of the University of L'Aquila (protocol n. 43,066/2020). Online informed consent was obtained from participants.

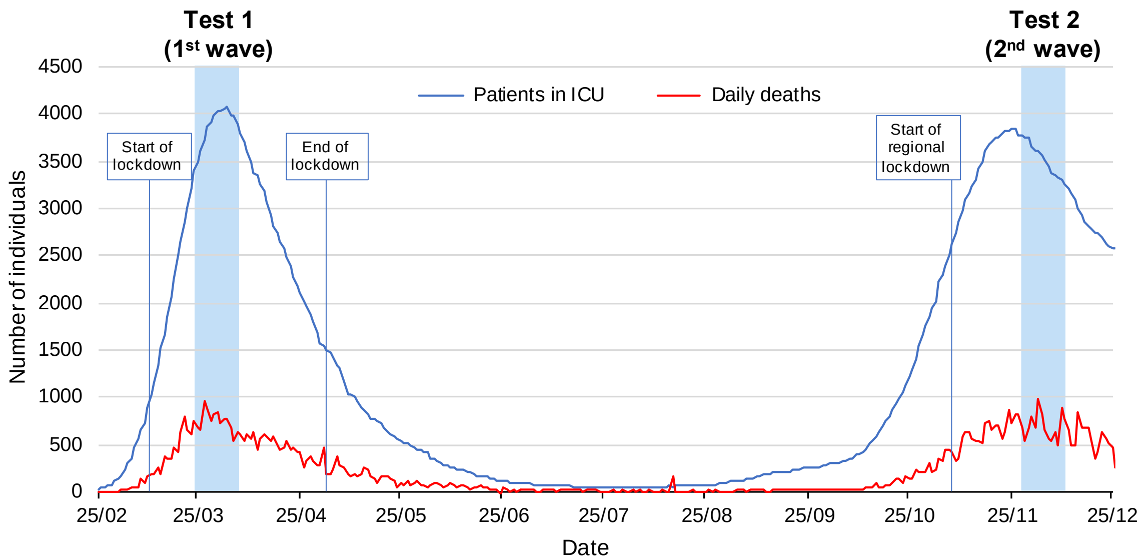

Figure 6.1. Italian national trend of daily deaths (blue line) and patients in the Intensive Care Unit (ICU; red line) due to COVID-19 infection across the pandemic period (Istituto Superiore di Sanità, 2020).

Notes: The two assessment periods (Test 1: 25 March–7 April 2020, Test 2: 28 November–11 December 2020) are marked by the light blue areas.

6.3.2 *Statistical analysis*

Prevalence of poor sleepers, moderate/severe insomnia, and severe depression symptoms were computed according to the conventional cut-off scores (see 1.3.2

section). To provide a comprehensive overview of the sociodemographic and COVID-related factors influencing the risk of poor sleep quality and moderate/severe insomnia during the second pandemic wave, we performed binomial logistic regressions on PSQI (> 5) and ISI (> 14) scores including the available sociodemographic and COVID-19-related variables as predictors.

The investigation on possible changes in sleep quality, insomnia symptoms, chronotype, depression, perceived stress, and anxiety between the two infection waves was performed contrasting the questionnaire scores (PSQI, ISI, MEQr, BDI-II, PSS-10, STAI-X1, respectively) at the two time-points by Wilcoxon signed-rank tests, due to violation of the normality assumption. The analysis was replicated for specific items (bedtime and get up time) and each sub-component of the PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medications, and daytime dysfunction) to further detail the specific dimensions of sleep habits/quality possibly changed between the two assessments. All *p*-values were corrected for multiple comparisons by false discovery rate (Benjamini & Hochberg, 1995).

The prevalence of poor sleep quality, moderate/severe insomnia, and severe depression were compared between the two time-points using the McNemar's test.

All tests were two-tailed and statistical significance was set to $p < 0.05$. We excluded 153 respondents from the PSQI analyses due to compilation errors (they declared longer total sleep time than the reported total time in bed).

6.4 Results

6.4.1 *At-risk categories for sleep disturbances during the second wave*

The results of the logistic regression models are reported in Table 6.1. Female gender, evening chronotype, being a high-risk person for COVID-19 infection, reporting negative social or economic impact of the current situation, and higher smartphone usage in the 2 hours before falling asleep predicted a higher risk of poor sleep and moderate/severe insomnia symptoms during the second wave of COVID-19. On the other hand, higher education level and morning chronotype emerged as protective factors against poor sleep quality and insomnia symptoms.

Advanced age, living with a high-risk person for COVID-19 infection, and having a relative/close friend infected with COVID-19 were at-risk categories for poor sleep quality, while living with children, having contracted COVID-19 before the prior 2 weeks, being pessimistic about the vaccination prospective, and being a healthcare worker, were risk factors for developing moderate/severe insomnia symptoms.

Table 6.1. Sociodemographic composition and COVID-related responses of the Test 2 sample and results (*B*, odds ratio [*OR*], 95% confidence interval [*CI*], *p*-value) of the logistic regression analyses on PSQI and ISI scores.

Predictor	*N* (%) or *mean (SD)	Poor sleep (PSQI > 5)			Moderate/severe Insomnia (ISI > 14)		
		B	*OR* (95% *CI*)	*p*	*B*	*OR* (95% *CI*)	*p*
Intercept		−1.99	0.14 (0.06–0.32)	**< .001**	−4.36	0.01 (0.002–0.07)	**< .001**
Age	*34.84 (12.37)	0.02	1.02 (1.01–1.03)	**< .01**	−0.01	0.99 (0.97–1.01)	.35
Gender							
Female	1,648 (81.87)		*Reference*			*Reference*	
Male	365 (18.13)	−0.39	0.68 (0.52–0.87)	**< .01**	−0.45	0.64 (0.41–0.998)	**< .05**
Education							
Middle/High school	586 (29.11)		*Reference*			*Reference*	
Graduate	1,163 (57.77)	−0.22	0.80 (0.64–1.01)	.06	−0.47	0.62 (0.45–0.87)	**< .01**
Postgraduate	264 (13.12)	−0.33	0.72 (0.51–0.99)	**< .05**	−0.31	0.73 (0.44–1.21)	.22
Occupation							
Unemployed	151 (7.50)		*Reference*			*Reference*	
Student	521 (25.88)	−0.20	0.82 (0.53–1.28)	.38	0.13	1.13 (0.60–2.13)	.70
Healthcare worker	159 (7.90)	−0.36	0.70 (0.42–1.18)	.18	0.86	2.36 (1.15–4.83)	**.02**
Self-employed	340 (16.89)	−0.33	0.72 (0.46–1.13)	.15	0.31	1.36 (0.71–2.60)	.35
Employed	772 (38.35)	−0.16	0.86 (0.56–1.30)	.46	0.43	1.53 (0.84–2.78)	.16
Retired	70 (3.48)	−0.26	0.77 (0.36–1.66)	.51	0.86	2.36 (0.76–7.37)	.14
Restraining measures							
Red zone	1,046 (51.96)		*Reference*			*Reference*	
Orange zone	451 (22.40)	−0.07	0.93 (0.73–1.20)	.58	0.11	1.12 (0.77–1.62)	.55
Yellow zone	516 (25.63)	0.05	1.06 (0.83–1.34)	.66	−0.08	0.92 (0.64–1.33)	.67

Predictor	*N* (%) or *mean (SD)	Poor sleep (PSQI > 5)			Moderate/severe Insomnia (ISI > 14)		
		B	*OR (95% CI)*	*p*	*B*	*OR (95% CI)*	*p*
Chronotype							
Neither-type	1,289 (64.03)		*Reference*			*Reference*	
Morning-type	487 (24.19)	−0.44	0.65 (0.51–0.82)	**< .001**	−0.48	0.62 (0.41–0.94)	**.03**
Evening-type	237 (11.77)	0.42	1.53 (1.10–2.13)	**.01**	0.71	2.03 (1.36–3.03)	**< .001**
Living with children							
No	1,566 (77.79)		*Reference*			*Reference*	
Yes	447 (22.21)	0.12	1.13 (0.89–1.45)	.32	0.41	1.50 (1.06–2.13)	.02
Being a high-risk person for COVID-19 infection							
No	1,812 (90.02)		*Reference*			*Reference*	
Yes	201 (9.99)	0.49	1.64 (1.13–2.38)	**< .01**	0.59	1.80 (1.16–2.81)	**< .01**
Living with a high-risk person for COVID-19 infection							
No	1,493 (74.17)		*Reference*			*Reference*	
Yes	520 (25.83)	0.31	1.36 (1.07–1.71)	**.01**	0.01	1.01 (0.72–1.41)	.96
COVID-19 infection							
No	1,887 (93.74)		*Reference*			*Reference*	
Yes (prior two weeks)	34 (1.69)	0.92	2.50 (0.87–7.17)	.09	0.84	2.32 (0.78–6.86)	.13
Yes (before the prior 2 weeks)	92 (4.57)	0.18	1.20 (0.71–2.02)	.50	0.66	1.94 (1.02–3.70)	**.04**
Forced quarantine							
No	1,513 (75.16)		*Reference*			*Reference*	
Yes (prior two weeks)	128 (6.36)	0.12	1.13 (0.70–1.81)	.62	0.01	1.01 (0.51–2.01)	.98
Yes (before the prior 2 weeks)	372 (18.48)	−0.02	0.98 (0.74–1.30)	.89	0.05	1.05 (0.69–1.58)	.83
COVID-19 infection of a relative/close friend							
No	823 (40.88)		*Reference*			*Reference*	
Yes (prior 2 weeks)	541 (26.88)	0.17	1.19 (0.92–1.52)	.19	-0.02	0.99 (0.68–1.44)	.94
Yes (before the prior 2 weeks)	649 (32.24)	0.31	1.36 (1.06–1.74)	**.01**	−0.10	0.90 (0.62–1.30)	.59
Death of a relative/close friend due to COVID-19							
No	1,832 (91.01)		*Reference*			*Reference*	
Yes	181 (8.99)	−0.04	0.96 (0.67–1.37)	.82	0.06	1.06 (0.64–1.77)	.81
Perspective on vaccination							
Optimistic	853 (42.38)		*Reference*			*Reference*	
Undecided	887 (44.06)	0.19	1.21 (0.98–1.49)	.08	0.29	1.33 (0.95–1.86)	.09
Pessimistic	273 (13.56)	0.20	1.22 (0.89–1.67)	.23	0.61	1.84 (1.20–2.81)	**< .01**
Economic impact							
None	1,055 (52.41)		*Reference*			*Reference*	
Negative	712 (35.37)	0.47	1.60 (1.27–2.01)	**< .001**	0.57	1.78 (1.28–2.46)	**< .001**
Positive	246 (12.22)	−0.08	0.92 (0.68–1.26)	.61	−0.17	0.85 (0.49–1.47)	.56
Negative social impact							
None	74 (3.68)		*Reference*			*Reference*	
A little	760 (37.76)	0.79	2.21 (1.28–3.80)	**< .01**	0.85	2.35 (0.55–10.02)	.25
A lot	1,179 (58.57)	1.46	4.29 (2.50–7.36)	**< .001**	1.59	4.93 (1.18–20.65)	**.03**
Electronic device usage in the 2 hours before falling asleep (min)							
Smartphone	*55.25 (37.96)	0.009	1.009 (1.006–1.012)	**< .001**	0.009	1.009 (1.005–1.013)	**< .001**
PC and tablet	*37.02 (44.00)	0.002	1.002 (1.000–1.005)	.11	0.001	1.001 (0.998–1.004)	.57
Television	*50.11 (45.96)	−0.001	0.999 (0.996–1.001)	.27	<0.001	0.999 (0.996–1.003)	.70
E-reader	*6.08 (19.53)	0.003	1.003 (0.997–1.008)	.32	0.002	1.002 (0.996–1.009)	.51

Notes: Sleep quality and insomnia ranges were established according to the validated cut-off scores (see 1.3.2 section). Numbers preceded by an asterisk (*) are mean values (standard deviation). Bold values are statistically significant.
Abbreviations: ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index; PC, Personal computer; SD, Standard deviation; OR, Odd ratio.

6.4.2 *Sleep and psychological differences between the waves*

Results of the Wilcoxon signed-rank tests between Test 1 and Test 2 are reported in Table 6.2. The sample went to bed and got up earlier at Test 2. Notwithstanding the lack of significant changes on PSQI total score, the analyses on PSQI sub-components highlighted several differences between the two measurements. Subjective sleep quality improved and was accompanied by a decrease in sleep latency and sleep disturbances. On the contrary, respondents slept less, tended to increase sleep medications use, and showed higher daytime dysfunction. Moreover, the participants reported reduced severity of insomnia symptoms and increased MEQr scores, pointing to a morning chronotype. Finally, depressive symptomatology remained stable, while perceived stress increased, and anxiety declined. The prevalence comparisons showed that the percentage of poor sleepers remained stable, insomniacs declined, and the individuals reporting severe depression symptoms remained unchanged over time.

Table 6.2. Descriptive statistics (mean and standard deviations) of questionnaire scores assessing sleep/chronobiological habits and quality, and psychological condition for Test 1 (25 March–7 April) and Test 2 (28 November–11 December), and the corresponding statistical comparisons (Wilcoxon signed-rank test: *Z*, *p*). Prevalence (%) of sleep disturbances and severe depression at the two time points and the corresponding statistical comparisons (McNemar's test: χ^2, *p*) are also reported.

Sleep/chronotype features	Test 1	Test 2	*Z*	*p*
	Mean (SD)			
Bedtime (hh:mm)	00:14 (1:25)	23:38 (1:17)	21.13	**< 0.001**
Get up time (hh:mm)	8:44 (1:38)	7:50 (1:22)	25.72	**< 0.001**
PSQI total score	6.95 (3.67)	6.90 (3.54)	0.47	0.64
PSQI sub-component				
Subjective sleep quality	1.39 (0.78)	1.34 (0.72)	2.52	**0.02**
Sleep latency	1.43 (1.04)	1.27 (1.02)	6.60	**< 0.001**
Sleep duration	0.70 (0.81)	0.79 (0.78)	−5.21	**< 0.001**
Habitual sleep efficiency	0.79 (1.00)	0.81 (1.00)	−0.47	0.64
Sleep disturbances	1.41 (0.60)	1.38 (0.57)	2.25	**0.03**
Sleep medications	0.29 (0.80)	0.33 (0.86)	−1.96	0.059
Daytime dysfunction	0.85 (0.71)	0.92 (0.70)	−4.17	**< 0.001**
ISI score	8.34 (5.45)	7.73 (5.39)	5.61	**< 0.001**
MEQr score	15.31 (3.66)	15.44 (3.68)	−2.36	**0.03**
Psychological status	Mean (SD)		*Z*	*p*
BDI-II score	12.46 (8.96)	12.35 (9.41)	0.65	0.60
PSS-10 score	17.99 (7.41)	18.70 (3.74)	−4.16	**< 0.001**
STAI-X1 score	48.58 (9.17)	46.78 (9.39)	8.13	**< 0.001**
Sleep/psychological disturbances	N (%)		χ^2	*p*
Poor sleep	1116 (60.16)	1110 (59.84)	0.04	0.84
Moderate/severe insomnia	270 (13.41)	226 (11.23)	6.56	**0.01**
Severe depression	352 (19.06)	370 (20.03)	0.90	0.34

Notes: Sleep quality, insomnia, and depression ranges were established according to the validated cut-off scores (see 1.3.2 section). Bold values are statistically significant. All *p*-values were corrected for multiple comparisons with false discovery rate.

Abbreviations: SD, Standard deviation; PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version; BDI-II, Beck Depression Inventory-second edition; PSS-10, Perceived Stress Scale-10 item; STAI-X1, State-anxiety subscale of the State-Trait Anxiety Inventory.

6.5 Discussion

Consistent with the literature about the first wave, we confirmed a higher predisposition of female gender (Cellini et al., 2021; Salfi et al., 2020) and low education level (Kokou-Kpolou et al., 2020) to develop sleep disturbances during our second-wave assessment. The healthcare workers confirmed their vulnerability to insomnia symptomatology during the second wave (Pappa et al., 2020) while the elderly emerged as a risk factor for poor sleep quality.

The circadian preference was a crucial predictor of sleep outcome, consistent with the pre-pandemic literature (Adan et al., 2012). Evening-type individuals showed a greater predisposition to poor sleep quality and moderate/severe insomnia symptoms, while morning chronotype emerged as a protective factor. The follow-up assessment of our investigation took place during a period of lighter restraining measures. In Italy, during the second wave of contagion, a regional lockdown was adopted, and we failed to highlight any difference according to the rigidity of the restraining measures adopted. This result pointed to a detrimental effect of the pandemic period itself, regardless of the restrictions in force.

The present findings showed a higher risk of insomnia in individuals who lived with children. In-person school activities were suspended in Italy during the follow-up measurement, while working activities partially continued (especially in the orange and yellow zones). This may have created a difficult situation to manage for parents, explaining the present results.

Being a high-risk person for COVID-19 infection was associated with a higher predisposition to poor sleep quality and moderate/severe insomnia symptoms, while living with a high-risk person for COVID-19 infection predicted a higher probability of experiencing poor sleep quality. These results could reflect a greater fear of infection and worries experienced by these individuals, which triggered sleep disturbances. Having contracted the COVID-19 or having a relative/close friend infected before the prior 2 weeks of the survey participation constituted a risk factor for insomnia and poor sleep quality, respectively, pointing to a long-term impact of these events. Notably, optimism for the future due to the arrival of a vaccine emerged as a protective factor against the insomnia exacerbation. Therefore, it seems that the vaccination campaign prospective could be itself beneficial for sleep health.

The pandemic has lasted for many months, and the healthcare emergency has been accompanied by unprecedented economic and social crises. In this context, more than one-third of the sample reported a negative economic impact of the current situation, and six out of ten of the respondents reported a consistent impairment of their social relationships. Both these outcomes turned out to be risk factors for exacerbation of sleep disturbances. Finally, smartphone overuse before sleep onset emerged as a risk factor for sleep disturbances. This finding is putatively ascribable to the well-known detrimental effect of backlit screen exposure before sleep time on the circadian system, as well as to the alerting effects of digital engagement. Notably, the increased evening usage of electronic devices has already been proposed as a mediator of sleep deterioration during the March–April lockdown (Salfi, Amicucci, et al., 2021).

Comparisons between data from the two outbreak waves displayed an articulated framework. We showed improved insomnia symptoms, reduced prevalence of moderate/severe insomnia conditions, and reduced anxiety. However, the present investigation confirmed the alarming situation highlighted during the first wave of COVID-19 (Jahrami et al., 2021; Salfi, Lauriola, et al., 2021) as the majority of the sample consisted of poor sleepers and this prevalence (~60%) remained stable between the two pandemic waves.

Despite the invariance of sleep quality between the two assessments, we showed several differences as concerns the PSQI sub-components. The subjective sleep quality, sleep latency, and sleep disturbances dimensions improved. However, the improvements were compensated by reduced sleep duration, more severe daytime dysfunction, and a trend to higher sleep medication use. Moreover, the participants went to bed more than half an hour earlier and woke-up almost an hour earlier than during the March–April lockdown. These results were accompanied by a significant shift towards the morning chronotype. In light of these results, it should be acknowledged that the first lockdown period was characterized by a substantial reduction of the *social jetlag* due to weaker social and working obligations (Korman et al., 2020). The present findings suggest that the *social jetlag* returned to negatively influence Italians' sleep, as the second assessment period was marked by a substantial resumption of daily working and activity routine.

Finally, we confirmed the severity of depressive symptomatology and the alarming prevalence of severe depression conditions (~20%) of the March–April lockdown. Remarkably, all these results were obtained in a context of increased perceived stress, putatively ascribable to the prolonged emergency period.

In conclusion, the present study found that the impact of the COVID-19 pandemic persists on both sleep and mental health, although the second wave of contagion has been faced using lighter restraining measures. Therefore, vigilance is still required, and large-scale interventions should be implemented to counteract the chronicity and exacerbation of sleep and psychological disturbances, especially for the categories identified as at-risk in the present study.

Chapter 7

The fall of vulnerability to sleep disturbances in evening chronotypes when working from home and its implications for depression

7.1 Abstract

Eveningness is distinctively associated with sleep disturbances and depression symptoms due to the misalignment between biological and social clocks. The widespread imposition of remote working due to the COVID-19 pandemic allowed a more flexible sleep schedule. This scenario could promote sleep and mental health in evening-type subjects. We investigated the effect of working from home on sleep quality/quantity and insomnia symptoms within the morningness-eveningness continuum, and its indirect repercussions on depressive symptomatology.

A total of 610 Italian office workers (mean age ± SD, 35.47 ± 10.17 years) and 265 remote workers (40.31 ± 10.69 years) participated in a web-based survey during the second contagion wave of COVID-19 (28 November–11 December 2020). We evaluated chronotype, sleep quality/duration, insomnia, and depression symptoms through validated questionnaires. Three moderated mediation models were performed on cross-sectional data, testing the mediation effect of sleep variables on the association between morningness-eveningness continuum and depression symptoms, with working modality (office vs. remote working) as moderator of the relationship between chronotype and sleep variables.

Remote working was associated with delayed bedtime and get up time. Working modality moderated the chronotype effect on sleep variables, as eveningness was related to worse sleep disturbances and shorter sleep duration among the office

workers only. Working modality also moderated the mediation of sleep variables between chronotype and depression. The above mediation vanished among remote workers.

The present study suggests that evening-type people did not show their characteristic vulnerability to sleep problems when working from home. This result could imply a reduction of the proposed sleep-driven predisposition to depression of late chronotypes. A working environment complying with individual circadian preferences might ensure an adequate sleep quantity/quality for the evening-type population, promoting their mental health.

7.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Scientific Reports* (Salfi, D'Atri, et al., 2022) and reproduced with permission from *Springer Nature*.

Since the first months of 2020, the COVID-19 outbreak has deeply impacted the everyday life of the world population. After a summer period of reduced contagion and death rates, Winter 2020 was marked by a new exacerbation of the pandemic emergency (World Health Organization, 2023). This scenario radically affected the labor market as millions of workers were subjected to exceptional measures worldwide. The most widespread way to cope with the pandemic crisis has been a rapid transition to the remote work modality. According to a recent Eurofound report (Eurofound, 2020), there was an upsurge in teleworking across all European countries during the COVID-19 pandemic. Approximately 40% of the European workforce began to work from home full-time. Similarly, in the United States, 35% of the population shifted from commuting to working remotely (Brynjolfsson et al., 2020).

Notwithstanding the large-scale nature of the remote working implementation, the consequences on sleep health of this unprecedented situation have been scarcely addressed. Remote working removed the need to spend time commuting between home and work, and it could be associated in some cases with greater flexibility of working hours. This situation allowed a better organization of the daily activities, leading to delayed and extended sleep time (Leone et al., 2020; Salfi, Lauriola, et al., 2021; Staller & Randler, 2021). Consistently, we recently reported a beneficial effect of working from home on sleep quality, insomnia symptoms, and sleep duration among a large sample of the Italian population during the first contagion wave of COVID-19 (Salfi, Lauriola, et al., 2021). A positive effect of the transition to remote working on sleep quality and duration was also documented by other investigations (Conroy et al., 2021; Leone et al., 2020; Raman & Coogan, 2021; Staller & Randler, 2021). However, some reports suggested that sleep quality (Barrea et al., 2020) and insomnia (McCall et al., 2021) could worsen while working from home. The inconsistencies could be attributed to the lack of an evaluation of possible circadian typology effects in the available studies, considering that chronotype has been demonstrated to modulate the influence of the working schedule on sleep quality and duration (Juda et al., 2013; Vetter et al., 2015).

In our modern society, the issue of the misalignment between the daily social/working schedule and the internal biological clock is a long-standing controversy (Roenneberg et al., 2019; Wittmann et al., 2006). In 2006, Wittmann and colleagues (2006) coined the term *social jetlag* to give a face to this phenomenon. Consistent evidence pointed to a reduction of the *social jetlag* among the general population during the pandemic, when weaker social and working obligations led to a loosening of rigorous sleep/wake schedules (Blume et al., 2020; Korman et al., 2020; Leone et al., 2020; Raman & Coogan, 2021; Staller & Randler, 2021). Remarkably, *social jetlag* is intrinsically linked with the circadian typology, being typically more pervasive in the evening chronotype (the so-called *night owls*). Among this group of people, who tend to go to bed and wake up later in a free-living condition, the mismatch between the endogenous biological and the exogenous social clock is the most pronounced (Roenneberg et al., 2019). This scenario lead to an accumulated sleep debt and more sleep problems during the working days in the evening chronotype (Adan et al., 2012; Fabbian et al., 2016; Merikanto et al., 2012)

An adequate quantity/quality of sleep is crucial for emotional regulation (Tempesta et al., 2018, 2020) and to preserve mental health (Freeman et al., 2017; Pigeon et al., 2017), and an extensive literature supports a determining role of both sleep disturbances and short sleep duration in the onset and exacerbation of depressive symptoms (Baglioni et al., 2011; Buysse et al., 2008; Hertenstein et al., 2019; Watson et al., 2014; Zhai et al., 2015). In this view, it is unsurprising that the evening chronotype has been systematically associated with a mood disturbance propensity (Adan et al., 2012; Au & Reece, 2017). Indeed, several recent reports suggested a causal role of sleep problems in accounting for the association between eveningness and depression (Bakotic et al., 2017; Bradford et al., 2021; Chiu et al., 2017; Hou et al., 2020; Selvi et al., 2018; van den Berg et al., 2018; Zhou et al., 2020). On the other hand, people tending to go to bed and wake up earlier (*morning larks*) are less affected by *social jetlag*, having their sleep–wake rhythms aligned with the common social clock. This situation results in less severe sleep problems and depression symptoms among morning-type people (Adan et al., 2012).

The large-scale transition toward remote working during the pandemic represented an unprecedented open-air laboratory to study the relationship between chronobiology and sleep health in a naturalistic environment. The current period emerges as an ideal context to address whether a more flexible working routine could influence sleep quality/quantity of the different circadian typologies and modify the mediating role of sleep between chronotype and depression.

In the present cross-sectional study, we investigated the effect of working from home during the second wave of the COVID-19 outbreak (28 November–11 December 2020) on sleep health/habits of almost nine hundred Italian workers placed along the morningness-eveningness continuum. We evaluated the moderator effect of the working modality (office vs. remote working) on the relationship between chronotype and sleep quality, insomnia symptoms, and sleep duration. We expected to confirm the well-known propensity of the evening-type people to experience sleep problems in the office working group. Meanwhile, we hypothesized that working from home could be associated with specific sleep benefits among the *night owls*, flattening the difference in sleep disturbances among the different circadian typologies.

Finally, considering the causal role of sleep disturbances and duration in depressive symptomatology, we investigated the mediation role of sleep in the relationship between chronotype and depression symptoms, evaluating potential differences between office and remote workers. We expected to confirm a significant role of sleep disturbances/duration in accounting for the higher vulnerability to depression of the evening-typology among the office workers. On the other hand, we hypothesized that the mediation effect of sleep could be weakened in the group who worked from home.

7.3 Materials and methods

7.3.1 *Participants and procedure*

Cross-sectional data reported in the present study are referred to the workers (N = 875; mean age ± SD, 36.93 ± 10.57 years; range, 20–76; 729 females) who participated in the assessment carried out during the second contagion wave (28

November–11 December 2020) (see 6.3.1 section for a description of the data collection procedure) The selected sample comprised 610 full-time office workers (35.47 ± 10.17 years; range, 20–68 years; 515 females) and 265 full-time remote workers (40.31 ± 10.69 years; range, 23–76 years; 214 females). In the present study, we evaluated chronotype, sleep quality, insomnia symptoms, and depressive symptomatology using the MEQr, the PSQI, the ISI, and the BDI-II, respectively (see 1.3.2 section for a description of questionnaires). From the PSQI, we further extracted the answers to the items "sleep duration" (min), "bedtime" (hh:mm), and "get up time" (hh:mm), which were used in the analyses described in the next paragraph. The Institutional Review Board of the University of L'Aquila approved the study (protocol n. 43,066/2020), which was carried out according to the principles established by the Declaration of Helsinki. Online informed consent was obtained from all participants.

7.3.2 *Statistical analysis*

We computed group descriptive statistics (office working, remote working) for all the considered variables in the current study. We evaluated potential differences in gender composition between the two groups through Chi-square test. Moreover, we compared office and remote working groups on age and questionnaire scores (MEQr, PSQI, ISI, BDI-II), sleep duration (min), bedtime (hh:mm), and get up time (hh:mm), using Mann–Whitney U test, considering the violation of normality/heteroscedasticity assumptions. All tests were two-tailed, and a p-value < 0.05 was considered significant. All p-values were corrected for multiple comparisons by false discovery rate (Benjamini & Hochberg, 1995). Harman's one-factor test did not show any common method bias in our data. According to the research hypotheses, three moderated mediation analyses were run using model 7 of *PROCESS* macro (version 3.5; Hayes, 2013, 2017) for SPSS (version 22.0). Model 7 assumes that the first stage of the mediation model is moderated. We included MEQr score as independent variable, each sleep outcome [PSQI and ISI scores, sleep duration (min)] as individual mediator, and BDI-II score as dependent variable. All the above outcomes were analyzed as continuous variables. The direction of the effects was established by relying on a consistent meta-analytic literature on longitudinal epidemiological studies supporting a causal role of sleep problems in the development of depressive symptoms (Baglioni et al., 2011; Hertenstein et al., 2019; Zhai et al., 2015), as well as on several studies proposing a mediation effect of sleep variables between chronotype and depression (Bakotic et al., 2017; Bradford et al., 2021; Chiu et al., 2017; Hou et al., 2020; Selvi et al., 2018; van den Berg et al., 2018; Zhou et al., 2020).. We separately included sleep variables as mediators in each model due to violations of the assumptions for alternative parallel mediation analysis (Hayes, 2017). Firstly, mediators are intrinsically related to each other as they evaluate overlapping constructs. Moreover, mediators are strongly correlated (PSQI scores and ISI scores: $r = 0.80$, $p < 0.001$; PSQI scores and sleep duration: $r = -0.67$, $p < 0.001$; ISI scores and sleep duration: $r = -0.53$, $p < 0.001$). This evidence constitutes a second violation of the mediation assumptions because their parallel inclusion in a model would give rise to a multicollinearity problem, which affects the estimation of their partial relationships with the outcome variable (Hayes, 2013).

The working modality factor (office working, remote working) was assumed as a moderator of the first path of the mediation models (chronotype → sleep variables), and it was entered as a dichotomous dummy variable (office working: 0, remote working: 1). Finally, since previous studies indicated that sleep problems and depressive symptoms correlate with age and gender (Amicucci et al., 2021; L. Li et al., 2021; Madrid-Valero et al., 2017; Patel et al., 2018; Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salk et al., 2017; B. Zhang & Wing, 2006), we included them in the models as continuous and dummy coded (female: 0, male: 1) covariates, respectively. A summary of the three theoretical models tested is provided in Figure 7.1.

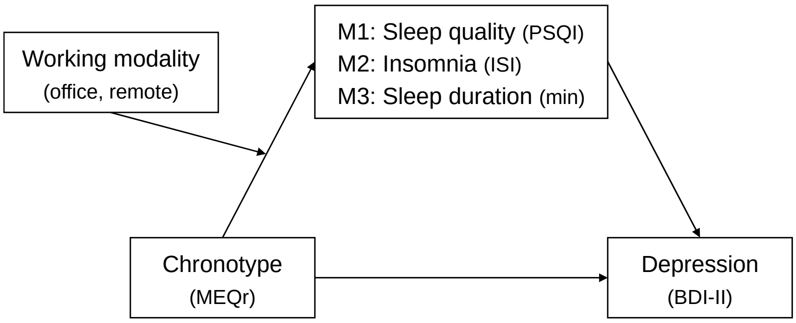

Figure 7.1. The three theoretical moderated mediation models tested (M1, M2, M3). Three mediators (sleep quality, insomnia symptoms, sleep duration) are hypothesized to mediate the relationship between morningness-eveningness continuum and severity of depression symptoms in a context where working modality (office working, remote working) moderate the effect of chronotype on sleep variables.
Notes: Each model was adjusted for age and gender.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version; BDI-II, Beck Depression Inventory- second edition.

Simple slope analyses were performed to explore the nature of the significant interactions between working modality (office working, remote working) and chronotype in predicting sleep variables (sleep quality, insomnia symptoms, sleep duration). The statistical significance of the conditional indirect effects was ascertained by means of 5,000 bootstrap samples to create bias-corrected 95% *CIs* with heteroscedasticity-consistent SEs. Moderated mediation models were considered significant and accepted when the interval between the 95% bootstrapped lower limit (*BootLLCI)* and upper limit of *CIs* (*BootULCI*) of the index of moderated mediation (the difference between conditional indirect effects) does not contain 0.

Finally, to further clarify how remote working affected the sleep schedule within the morningness-eveningness continuum, we analyzed how chronotype scores interact with working modality in predicting sleep onset and offset time. Therefore, two explorative moderation models were tested, hypothesizing that working modality (office working, remote working) moderated the effect of chronotype on bedtime and get up time (see Figure 7.2). These models were tested using model 1 of *PROCESS* macro (version 3.51) for SPSS (version 22.0), including the covariance of age and gender.

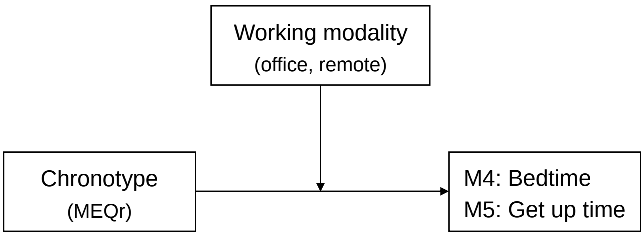

Figure 7.2. The two additional moderation models tested (M4, M5). Chronotype is hypothesized to predict bedtime and get up time, while the working modality (office working, remote working) moderated this relationship.
Notes: Each model was adjusted for age and gender.
Abbreviations: MEQr, Morningness-Eveningness Questionnaire-reduced version.

7.4 Results

7.4.1 *Characteristics of participants*

The demographic composition of the two groups (office working, remote working) and descriptive statistics of the main study variables are shown in Table 7.1. The two samples did not differ in MEQr, PSQI, ISI, and BDI-II scores, as well as in sleep duration and gender proportion. However, the office working group was significantly younger and reported earlier bedtime and get up time.

Table 7.1. Characteristics of participants divided by working modality (office, remote). Results of the comparisons between the working modality groups are also shown.

Variable	Working modality		*Statistic*	*df*	*p*
	Office [n = 610 (69.7%)]	Remote [n = 265 (30.3%)]			
	Mean ± SD				
Gender					
Male	95 (15.6%)	51 (19.2%)	1.791*	1	0.289
Female	515 (84.4%)	214 (80.8%)			
Age	35.467 ± 10.174	40.309 ± 10.694	58326†	873	**< 0.001**
MEQr score	15.867 ± 3.494	15.430 ± 3.850	76014.5†	873	0.289
PSQI score	6.693 ± 3.504	7.015 ± 3.598	76367.5†	873	0.289
ISI score	7.428 ± 5.268	7.815 ± 5.356	77398†	873	0.408
Sleep duration (min)	403.365 ± 66.462	401.624 ± 64.434	79169†	873	0.704
Bedtime (hh:mm)	23:11 ± 1:05	23:37 ± 1:16	63901†	873	**< 0.001**
Get up time (hh:mm)	7:13 ± 1:03	7:41 ± 1:09	56625†	873	**< 0.001**
BDI-II score	11.141 ± 8.620	11.660 ± 9.698	79897†	873	0.787

Notes: * Chi-square, † Mann-Whitney *U*. Bold values are statistically significant. All *p*-values were corrected for multiple comparisons with false discovery rate.
Abbreviations: SD, standard deviation; df, Degrees of freedom; PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version; BDI-II, Beck Depression Inventory-second edition.

7.4.2 *Moderated mediation analyses*

The regressions on mediators (PSQI score, ISI score, sleep duration) including age, gender (male, female), MEQr scores, working modality (office working, remote working), and the interaction between MEQr scores and working modality as predictors were significant for each model (Model 1: $R^2 = 0.069$, $F = 12.856$, $p < 0.001$; Model 2: $R^2 = 0.063$, $F = 11.617$, $p < 0.001$; Model 3: $R^2 = 0.094$, $F = 18.057$, $p < 0.001$). Likewise, the regressions on BDI-II scores including age, gender (male, female), MEQr scores, and sleep variables (Model 1: PSQI score; Model 2: ISI score; Model 3: sleep duration) as predictors were significant for all the models (Model 1: $R^2 = 0.289$, $F = 88.123$, $p < 0.001$; Model 2: $R^2 = 0.373$, $F = 129.62$, $p < 0.001$; Model 3: $R^2 = 0.135$, $F = 33.947$, $p < 0.001$). As showed in Table

7.2, older age was associated with lower sleep quality, more severe insomnia, shorter sleep duration, and lower depressive symptoms in all the models. Male subjects reported better sleep quality and less severe insomnia symptoms than females, while no difference in sleep duration between genders emerged. Men showed a lower severity of depression in each model.

Table 7.2. Unstandardized effects (*B*), *t*-value, and significance of the covariates (age, gender) for the three models including sleep quality (PSQI score; Model 1), insomnia symptoms (ISI score; Model 2), and sleep duration (min; Model 3) as mediators.

Covariate effects	*B*	*t*	*p*
Model 1			
Age → PSQI	0.051	4.480	**< 0.001**
Gender* → PSQI	−1.230	−3.915	**< 0.001**
Age → BDI-II	−2.188	−3.120	**0.002**
Gender* → BDI-II	−0.067	−2.690	**0.007**
Model 2			
Age → ISI	0.052	3.040	**0.002**
Gender* → ISI	−1.943	−4.112	**< 0.001**
Age → BDI-II	−0.054	−2.336	**0.019**
Gender* → BDI-II	−1.820	−2.764	**0.006**
Model 3			
Age → Sleep duration	−1.834	−8.752	**< 0.001**
Gender* → Sleep duration	−6.908	−1.196	0.232
Age → BDI-II	−0.071	−2.493	**0.013**
Gender* → BDI-II	−3.998	−5.217	**< 0.001**

Notes: * Female was used as reference for "*Gender*" factor. Bold values are statistically significant.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; BDI-II, Beck Depression Inventory-second edition.

As reported in Table 7.3, both the MEQr scores and the sleep variables (PSQI score, ISI score, sleep duration) were significantly associated with the BDI-II scores in all the models (direct effects). Tendency to eveningness, lower sleep quality, more severe insomnia, and shorter sleep duration predicted greater depressive symptoms. The conditional direct effects at the value of the moderator (office working, remote working) indicated that the tendency to morningness was associated with better sleep quality, lower severity of insomnia symptoms, and longer sleep duration in the office working group. On the other hand, no significant relationship between chronotype and sleep variables emerged among the remote workers.

Table 7.3. Direct effects and conditional direct effects at the value of the moderator (office working, remote working) for the three models, including sleep quality (PSQI score; Model 1), insomnia symptoms (ISI score; Model 2), and sleep duration (min; Model 3) as mediators, whilst accounting for the effects of age and gender.

Direct effects	*B*	*t*	*p*
Model 1			
MEQr → BDI-II	−0.274	−3.724	**< 0.001**
PSQI → BDI-II	1.245	16.613	**< 0.001**
Model 2			
MEQr → BDI-II	−0.233	−3.376	**< 0.001**
ISI → BDI-II	0.971	20.775	**< 0.001**
Model 3			
MEQr → BDI-II	−0.445	−5.560	**< 0.001**
Sleep duration → BDI-II	−0.038	−8.535	**< 0.001**
Conditional direct effects			
Model 1			
Office working: MEQr → PSQI	−0.247	−6.151	**< 0.001**
Remote working: MEQr → PSQI	−0.101	−1.825	0.068
Model 2			
Office working: MEQr → ISI	−0.374	−6.200	**< 0.001**
Remote working: MEQr → ISI	−0.141	−1.696	0.090
Model 3			
Office working: MEQr → Seep duration	3.023	4.102	**< 0.001**
Remote working: MEQr → Sleep duration	0.151	0.149	0.881

Notes: Bold values are statistically significant.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version; BDI-II, Beck Depression Inventory-second edition.

The working modality moderator was significant in each model (Table 7.4), indicating that remote workers reported higher sleep quality, lower insomnia symptoms, and longer sleep duration than the office working group. The interaction between MEQr scores and the working modality moderator was significant in each model, suggesting a different linear relationship between chronotype and sleep variables comparing the office and remote working groups (Figure 7.3).

Table 7.4. Moderator and interaction effects for the three models, including sleep quality (PSQI score; Model 1), insomnia symptoms (ISI score; Model 2), and sleep duration (min; Model 3) as mediators, whilst accounting for the effects of age and gender.

Moderator effects	*B*	*t*	*p*
Model 1			
Working modality* → PSQI	−2.242	−2.062	**0.039**
Model 2			
Working modality* → ISI	−3.555	−2.175	**0.030**
Model 3			
Working modality* → Sleep duration	53.026	2.654	**0.008**
Interaction effects			
Model 1			
Working modality* × MEQr → PSQI	0.146	2.158	**0.031**
Model 2			
Working modality* × MEQr → ISI	0.233	2.291	**0.021**
Model 3			
Working modality* × MEQr → Sleep duration	−2.872	−2.309	**0.012**

Notes: * Office working was used as reference for "*Working modality*" factor. Bold values are statistically significant.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version.

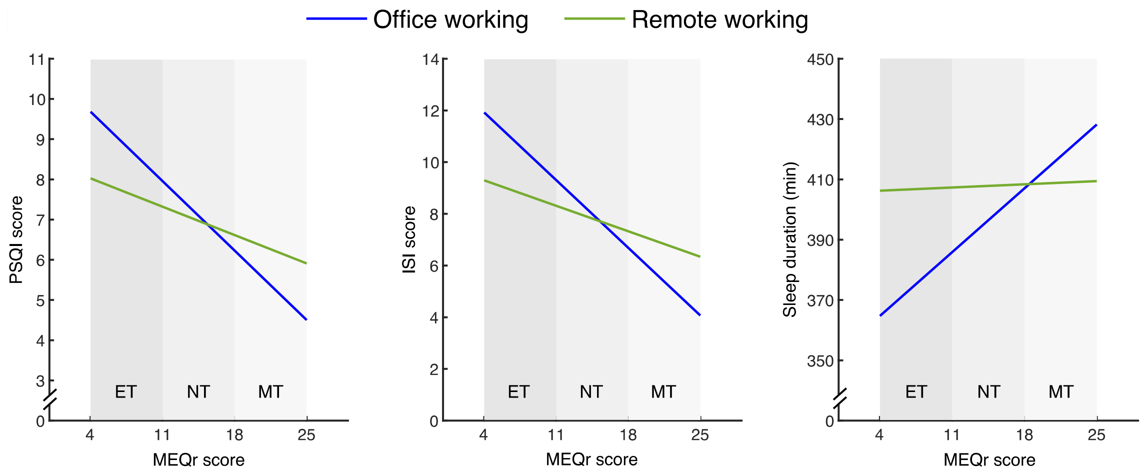

Figure 7.3. Simple slope analyses of the interaction between MEQr scores and working modality (office working, remote working) on sleep quality (PSQI score), insomnia symptoms (ISI score), and sleep duration (min).

Notes: Blue and green lines indicate office and remote working group, respectively. Gray bands discriminate chronotypes according to the validated cut-off scores (see 1.3.2 section).

Abbreviations: ET, evening-type; NT, neither-type; MT, morning-type; PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version.

Finally, as reported in Figure 7.4, all the conditional indirect effects were significant for the office working group, indicating that the sleep variables partially mediated the effect of chronotype on depression symptoms. On the other hand, no significant indirect effect was detected in the remote working group. Consistently, the index of moderated mediation was significant in each model (Model 1: 0.182 [0.008, 0.361]; Model 2: 0.227 [0.031, 0.430]; Model 3: 0.110 [0.015, 0.221]), indicating that working from home suppressed the mediation effect of sleep variables on the association between chronotype and depression. Control analyses including occupation and educational level in the moderated mediation models confirmed all the reported results (data not shown).

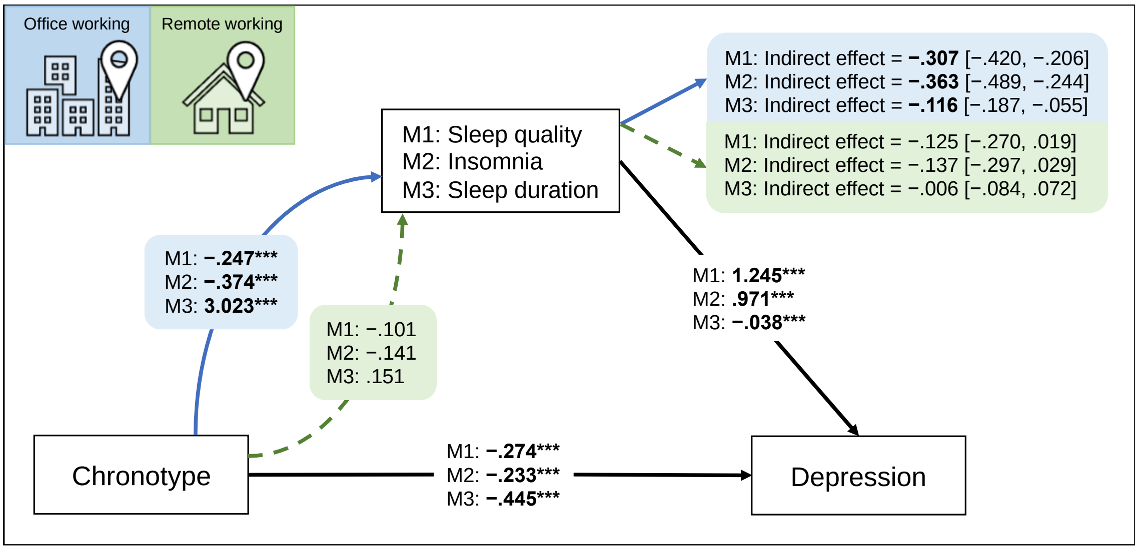

Figure 7.4. Summary of the results of the three moderated mediation models (M1, M2, M3).

Notes: The figure reports the unstandardized coefficients of direct effects, conditional direct effects at the value of moderator, and conditional indirect effects with bootstrapped computed confidence intervals for the two levels of moderator [office working (blue arrow/area), remote working (green arrow/area)]. Significant effects are reported in bold, and the significance level of direct effects is indicated with asterisks (***$p < 0.001$).

7.4.3 *Moderation analyses*

The regressions on bedtime and get up time were significant (Model 4: $R^2 = 0.247$, $F = 56.852$, $p < 0.001$; Model 5: $R^2 = 0.274$, $F = 65.685$, $p < 0.001$). The covariate effect of "*Gender*" emerged significant for the bedtime variable ($B = 14.51$ min, $t = 2.630$, $p = 0.009$), indicating that female respondents went to bed earlier. Age was a significant predictor of get up time ($B = -1.58$ min, $t = -8.509$, $p < 0.001$), indicating that older age was associated with earlier get up time.

The conditional direct effects at both values of the moderator (office working, remote working) were significant in both the models. In particular, MEQr score predicted significantly bedtime (office working: $B = -9.80$ min, $t = -10.029$, $p < 0.001$; remote working: $B = -7.92$ min, $t = -11.154$, $p < 0.001$) and get up time (office working: $B = -8.50$ min, $t = -9.317$, $p < 0.001$; remote working: $B = -6.05$ min, $t = -9.221$, $p < 0.001$), confirming the tendency to delayed sleep time of evening-type people in both the working modality conditions. The "*Working modality*" moderator was significant in both the models (M4: B = 51.55 min, t = 2.682, p = 0.008; M5: B = 69.27 min, t = 3.874, p = 0.001), showing that people working from home went to bed and got up later. Finally, the significant interaction between "*Working modality*" and MEQr score was limited to the get up time variable (M4: B = −1.87 min, t = −1.564, p = 0.118; M5: B = −2.30 min, t = −2.130, p = 0.033), highlighting that the relationship between chronotype and rising time was stronger in those who worked from home than in the office working condition (Figure 7.5).

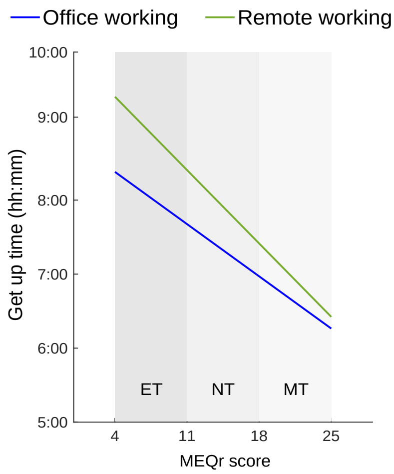

Figure 7.5. Simple slope analysis of the interaction between MEQr scores and working modality (office working, remote working) on get up time (hh:mm).

Notes: Blue and green lines indicate office and remote working group, respectively. Gray bands identify chronotypes according to the validated cut-off scores (see 1.3.2 section).

Abbreviations: ET, evening-type; NT, neither-type; MT, morning-type; MEQr, Morningness-eveningness questionnaire-reduced version.

7.5 Discussion

The COVID-19 emergency pervasively impacted the daily routine of millions of workers worldwide. Consistent with European and American reports during the pandemic (Brynjolfsson et al., 2020; Eurofound, 2020), three out of ten individuals in our sample worked full-time from home. In line with recent investigations (Leone et al., 2020; Massar et al., 2021; Salfi, Lauriola, et al., 2021; Staller & Randler, 2021), the remote working group showed a general delay in bedtime and get up time. We hypothesized that evening-type subjects could have benefited from such a scenario, as their sleep time was better aligned with the endogenous circadian phase than the office working sample. The analyses supported our prediction: the tested models revealed a significant interaction between chronotype scores and working modality (office, remote) in predicting sleep variables. Remarkably, we showed that the well-documented relationship between chronotype and sleep problems/duration (Adan et al., 2012; Fabbian et al., 2016; Merikanto et al., 2012) was limited to the office working group. Therefore, our findings suggest that the propensity to sleep problems and shorter sleep duration of evening-type people may not depend on chronotype per se. Eveningness could represent a risk factor only in the office working condition.

The outcomes of the additional models (see Figure 7.5) contributed to further clarifying the pattern of results. We showed that working from home influenced the relationship between chronotype and get up time but did not affect the association with bedtime. Specifically, eveningness was related to a stronger tendency to get up later in the remote working group than in the office working sample. On the other hand, the inclination of evening-type people to go to bed later than morning-type was comparable in the two working modality groups. Therefore, later bedtimes were not adequately compensated by later get up times when participants had to reach the workplace, giving rise to the shorter sleep duration tendency shown by the late chronotypes. On the other hand, strengthening the association between get up times and chronotype scores implies that the *night owls* slept more when they worked from home, leading to the extinction of the sleep duration differences between circadian typologies.

Our findings are consistent with studies showing that chronotype modulates the effect of the working schedule on sleep patterns (Juda et al., 2013; Vetter et al., 2015). Late chronotypes are characterized by shorter sleep duration and more severe sleep disturbances compared with early ones when working in the morning (Juda et al., 2013). Consistently, a chronotype-based working routine was associated with increased sleep duration and quality by reducing the *social jetlag* among the evening-type population (Vetter et al., 2015).

Several studies demonstrated a positive effect of working from home on sleep patterns during the current pandemic (Conroy et al., 2021; Leone et al., 2020; Massar et al., 2021; Raman & Coogan, 2021; Staller & Randler, 2021). This literature is consistent with investigations on the student population under remote learning due to the COVID-19 emergency, where participants delayed their sleep time and reported longer sleep duration and improved sleep quality (Genta et al., 2021; Gruber et al., 2020; Santos & Louzada, 2022; Stone et al., 2021). Notwithstanding the lack of an evaluation of possible differential effects as a function of circadian typology in these studies, the results were interpreted as a general tendency to synchronize the sleep/wake cycle with the individual biological clock when daily schedules are less strongly dictated by the office/school hours. Interestingly, we did not find significant differences in mean sleep quality, sleep duration, and severity of insomnia symptoms in the preliminary direct between-group comparisons. However, the beneficial effect of remote working on sleep emerged by including the interaction between chronotype scores and working modality in the models. This evidence could account for some of the inconsistencies in the literature addressing remote working effects during the pandemic period (Barrea et al., 2020; McCall et al., 2021). The individual circadian preference could act as a confounding variable, resulting in misleading conclusions when studying the consequences of the working modality on sleep health. Therefore, we caution that future studies in this field duly consider chronotype and its interaction with both working modality and schedule.

As far as the depressive symptomatology is concerned, we confirmed the tendency of the evening-types to experience more severe symptoms (Adan et al., 2012; Au & Reece, 2017), as well as the established relationship between both sleep problems and short sleep duration and more severe depression symptoms (Baglioni et al., 2011; Buysse et al., 2008; Hertenstein et al., 2019; Watson et al., 2014; Zhai et al., 2015). Meanwhile, the loosening of the proposed association between sleep disturbances/duration and chronotype in the group who worked from home corroborated the second goal of this study: determining whether remote working affected the mediation role of sleep between circadian typologies and depression symptoms.

The three moderated mediation models demonstrated that poorer sleep quality, more severe insomnia symptoms, and shorter sleep duration could partially explain the tendency of the late chronotypes to experience depression, but only when they had to reach the workplace.

This outcome is consistent with a growing literature supporting a causative role of sleep disturbances and shorter sleep duration in explaining the eveningness susceptibility to depressive symptomatology (Bakotic et al., 2017; Chiu et al., 2017; Hou et al., 2020; Selvi et al., 2018; van den Berg et al., 2018; Zhou et al., 2020). On the other hand, we showed that the sleep-dependent vulnerability to depression of late chronotypes disappeared under remote working. Therefore, the improvement of sleep problems while working from home could indirectly promote the mental health of evening-type participants, influencing their predisposition to depressive symptoms.

The present results were obtained in a sample where older respondents and females experienced poorer sleep quality and more severe insomnia symptoms, women reported higher depressive symptomatology, and younger people slept longer and showed more severe depression. These results are consistent with an extensive pre-pandemic and pandemic literature showing a tendency of women to report worse sleep disturbances (Madrid-Valero et al., 2017; Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salfi, Lauriola, et al., 2021; B. Zhang & Wing, 2006a) and depression symptoms (Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salk et al., 2017), as well as the predisposition of older age to experience poorer sleep quality (de Pue et al., 2021; Madrid-Valero et al., 2017; Mander et al., 2017; Salfi, Lauriola, et al., 2021), more insomnia (Patel et al., 2018; Salfi, Lauriola, et al., 2021), shorter sleep duration (Amicucci et al., 2021; Mander et al., 2017), and a lower predisposition to mood disorders (Amicucci et al., 2021; Rossi, Socci, Talevi, et al., 2020).

The results of this study solicit a discussion at the community level. Our modern society forces many employees to fit a standard work schedule typically oriented to morningness. Social pressure imposes to get up early in the morning beginning from the school period; this situation limits the time available for sleep and leads adolescents to be awake at an inappropriate circadian phase (Carskadon, 2011). This issue spans to adulthood as early morning working is associated with inadequate sleep, more sleep problems, and fatigue among the general population (Åkerstedt et al., 2010; Kecklund et al., 1997). This situation is even more pronounced when the large and intrinsic variability in the biological circadian predispositions is considered (Juda et al., 2013; Vetter et al., 2015), configuring a latent penalization of evening-type people. Considering the individual circadian predisposition in managing the working environment could promote late chronotypes' sleep and mental health.

The vaccination campaign and the gradual mitigation of the pandemic crisis are leading people to resume their pre-pandemic working routine worldwide. In this vein, our results could have large-scale implications spanning the post-pandemic period, considering that circadian predisposition has a substantial genetic component (Kalmbach et al., 2017; Lane et al., 2016) that could be hardly manipulated, and the current literature estimated a 10–20% prevalence of *night owls* among the adult population (Koskenvuo et al., 2007; Paine et al., 2006; Randler et al., 2016, 2017; Salfi, Lauriola, et al., 2021; Taillard et al., 2004), which is also higher among young people (Adan et al., 2012; Randler, 2015). The outcomes of the present study should be taken into account when designing remote working policies during the current pandemic, as well as in the post-covid era.

Our pattern of results was obtained in a large sample of workers. Moreover, the inclusion of demographic factors (age and gender) in all the tested models confuted the possibility that the younger age of the office working group could have biased our results. However, some limitations should be acknowledged. We adopted a cross-sectional design, the sample comprised a higher prevalence of women, and we did not collect information about pre-pandemic experience of remote work. Furthermore, our findings relied on regression analyses so that the direction of the effects could be only hypothesized. Consequently, caution is required in interpreting the indirect effects, considering the potential bidirectionality between sleep disturbances and depressive symptoms (Fang et al., 2019). A longitudinal analysis might confirm our results clarifying the causal relationship between the investigated variables and evaluating the effects of a change of working modality in a prospective within-subject study design. Additionally, we assessed chronotype, sleep variables, and depression using self-report retrospective questionnaires. Future research should adopt ecological momentary assessment technologies to minimize recall bias and maximize ecological validity to provide more reliable results (Shiffman et al., 2008). Moreover, our evaluation of sleep habits did not discriminate between workdays and free days. However, a sleep evaluation targeted on workdays could have provided even stronger evidence of the interaction between chronotype and working modality, although PSQI scores predominantly reflect sleep quality/patterns of workdays (Pilz et al., 2018). Finally, an ad hoc evaluation of the *social jetlag* phenomenon through, e.g., the Munich Chronotype Questionnaire (Roenneberg et al., 2003), might have contributed to better understand the effect of working from home during this unprecedented pandemic period.

Part 3

Two years later

In the last days of 2020, the administration of the first COVID-19 vaccine (Polack et al., 2020) to the adult population was authorized by international medicine agencies, kicking off the most extensive vaccination campaign in human history. The increased vaccination rates among the world population led to a decline in COVID-19 cases, hospitalizations, and deaths thereby paving the way for the lifting of restrictions and a gradual return to "normal" life. In 2022, business activities and schools re-opened, sporting and cultural events resumed, masks were rarely worn, and people restored their pre-pandemic daily routine, hugging, crowding, and traveling.

This scenario represented a boon for the sleep and mental health of the worldwide population. However, the pandemic left a heavy legacy. Since the first months of the emergency, it became evident that a substantial portion of COVID-19 survivors reported a broad spectrum of symptoms that continued or developed several weeks/months after acute illness. This widespread and poorly understood condition was named *long COVID* and holds the potential to produce a second public health crisis on the heels of the pandemic itself.

In Chapter 8, we reported the results of a longitudinal investigation covering two critical stages of the COVID-19 emergency (the first lockdown and the second contagion wave) and providing the first long-term overview of Italians' sleep and psychological well-being two years after the pandemic outbreak. In line with the studies described in Part 1 and 2, we focused on possible differences in the time course of sleep and mental health outcomes according to age, gender, and chronotype, addressing how these factors interacted with the gradual loosening of the restraining measures until the return to pre-pandemic life.

Chapter 9 explored for the first time the potential role of pre-infection sleep disturbances in the incidence of long COVID symptoms, providing a novel point of view by proposing sleep health as an important *antecedent* of post-COVID-19 manifestations.

Finally, in the conclusive chapter of this Thesis (Chapter 10), we provided a general and updated overview of the accumulated knowledge over two pandemic years, summarizing the main lessons earned from this unprecedented historical period.

Chapter 8

Two years after lockdown: Longitudinal trajectories of sleep disturbances and mental health over the COVID-19 pandemic, and the effects of age, gender, and chronotype

8.1 Abstract

Since the first lockdown of Spring 2020, the COVID-19 contagion waves pervasively disrupted the sleep and mental health of the worldwide population. Notwithstanding the largest vaccination campaign in human history, the pandemic has continued to impact the everyday life of the general population for two years now. The present study provides the first evidence of the longitudinal trajectories of sleep disturbances and mental health throughout the pandemic in Italy, also describing the differential time course of age groups, genders and chronotypes. A total of 1062 Italians participated in a three-time-point longitudinal study covering two critical stages of the emergency (the first lockdown in April 2020 and the second partial lockdown in December 2020) and providing a long-term overview two years after the pandemic outbreak (April 2022). We administered validated questionnaires to evaluate sleep quality/habits, insomnia, depression, stress, and anxiety symptoms. Analyses showed a gradual improvement in sleep disturbances, depression, and anxiety. Conversely, sleep duration progressively decreased, particularly in evening-type and younger people. Participants reported substantial earlier bedtime and get up time. Stress levels increased during December 2020 and then stabilized. This effect was stronger in the population groups apparently more resilient during the first lockdown (older people, men, and morning-types). Our results describe a

promising scenario two years after the pandemic onset. However, the improvements were relatively small, the perceived stress increased, and the re-establishment of pre-existing social/working dynamics led to general sleep curtailment. Further long-term monitoring is required to claim the end of the COVID-19 emergency on Italians' sleep and mental health.

8.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Journal of Sleep Research* (Salfi, Amicucci, et al., 2022) and reproduced with permission from *John Wiley and Sons*.

In the first months of 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started to spread worldwide, giving rise to a pandemic. To deal with the increasing contagion and death rates due to virus propagation, governments around the world started to apply extraordinary containment measures consisting of home confinement, social distancing, and the closure of most business activities.

The lockdown period was associated with raised sleep disturbances and mental health problems among the general population, as reported by consistent meta-analytic literature (AlRasheed et al., 2022; Jahrami et al., 2022; Robinson et al., 2022). Italy was the first European country to handle the contagion wave of COVID-19, implementing a total lockdown lasting 2 months (March–April 2020). Several Italian studies confirmed the pervasive impact of this unprecedented period on sleep quality/habits and psychological well-being (Casagrande et al., 2020; Cellini et al., 2020; Salfi, Lauriola, et al., 2021). After a phase of alleviated pandemic emergency and loosened restrictions (Summer 2020), a second large contagion wave occurred in Autumn 2020. The Italian government promptly reacted to the new exacerbated scenario by applying partial lockdown measures on a regional basis, weighted according to the local load on the healthcare system and infection rates.

Notwithstanding the adoption of this regional approach consisting of lighter restraining measures than the first lockdown, some longitudinal investigations showed a persistent impact of the emergency period on sleep (Conte et al., 2021; Salfi, D'Atri, et al., 2021) and mental health (Salfi, D'Atri, et al., 2021) among the Italian population during the second contagion wave. These results were consistent with the international literature confirming long-lasting repercussions on sleep features (Basishvili et al., 2021; Y. Liu et al., 2022; Trakada et al., 2022) and psychological measures (Benke et al., 2022; Chodkiewicz et al., 2021; Daly & Robinson, 2022; Rus Prelog et al., 2022; Wetherall et al., 2022) during the second COVID-19 wave, suggesting the urgency of large-scale interventions to preserve the general well-being.

Notwithstanding the largest vaccination campaign in human history and the consequent lifting of restraining measures in the subsequent months, COVID-19 has continued to disrupt the everyday life of the worldwide population for two years now. However, the long-term impact of the pandemic on sleep and mental health remains poorly elucidated. In this vein, the first aim of the present study is to identify the longitudinal trajectories of sleep quality, insomnia, depression, stress, and anxiety in the general population across the pandemic in Italy. We surveyed a large sample of Italian citizens (n = 1.062) using validated questionnaires at three time points: during the first weeks of lockdown (April 2020), during the second contagion wave (December 2020) and two years after the first implementation of the lockdown measures (April 2022).

The current literature consistently showed that age groups (Amicucci et al., 2021; Bottary et al., 2022a; Daly et al., 2020; Jahrami et al., 2022; Rossi, Socci, Talevi, et al., 2020), genders (Daly et al., 2020; Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salfi, Lauriola, et al., 2021) and chronotypes (Bottary et al., 2022; Merikanto et al., 2022; Salfi, Lauriola, et al., 2021) reacted differently to the first months of restraining measures. Specifically, younger people (Amicucci et al., 2021; Daly et al., 2020; Jahrami et al., 2022; Rossi, Socci, Talevi, et al., 2020) and women (Daly et al., 2020; Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salfi, Lauriola, et al., 2021) reported higher rates of sleep disturbances and psychological symptoms. These results were confirmed by Italian (Salfi, D'Atri, et al., 2021) and European studies (Benke et al., 2022; Chodkiewicz et al., 2021; Rus Prelog et al., 2022; Wetherall et al., 2022) addressing the effect of the second wave of COVID-19. Similarly, the evening chronotype was associated with more evident changes in sleep patterns and increased sleep and mental health problems both during the lockdown (Bottary et al., 2022a; Merikanto et al., 2022a; Salfi, Lauriola, et al., 2021) and the second contagion wave (Salfi, D'Atri, et al., 2021). Based on this evidence, another objective of the present research is to identify the different time courses of sleep and psychological disturbances between age groups, genders and chronotypes.

8.3 Materials and methods

8.3.1 *Participants and procedure*

The present study consists of a longitudinal web-based survey involving three assessment points. Participants responded using an online platform (Google forms). The first survey wave was held during the third and fourth weeks of the lockdown period of Spring 2020 (25 March–7 April 2020), coinciding with the first contagion peak of COVID-19 (see 1.3.1 section). Subsequently, respondents were invited to participate in the second survey wave by email during the contagion peak of the second pandemic wave (28 November–11 December 2020), as described in 6.3.1 section. Finally, all respondents were re-invited to take part in the third survey wave two years after the first one (9 April–22 April 2022). A total of 1062 Italian citizens participated in all three assessments. The demographic composition of the sample is reported in Table 8.1. All the survey waves comprised an evaluation of sleep quality, insomnia symptoms, chrono- type, depressive symptomatology, perceived stress, and anxiety through the following validated questionnaires: the PSQI, the ISI, the MEQr, the BDI-II, the PSS-10, and the STAI-X1, respectively (see 1.3.2 section for a description of the questionnaires). As detailed in 1.3.1 section, the administration order of mandatory sleep questionnaires was as follows: PSQI, ISI and MEQr. Subsequently, participants could decide whether to continue the compilation of the other three questionnaires (BDI-II, PSS-10, STAI-X1) with the option to stop after each of them to ensure reliable unforced responses due to the burden of testing battery. A total of 71, 43 and 40 subjects did not fill out the BDI-II in the first, second and third survey waves, respectively. A total of 100, 61 and 83 participants did not complete the PSS-10 during the three assessment points, respectively. Finally, 103, 61 and 116 respondents did not fill out the STAI-X1 in the three survey waves. The Institutional Review Board of the University of L'Aquila approved the research project (protocol n. 43,066/2020). The study was performed according to the principles established by the Declaration of Helsinki. Online informed consent was obtained from participants.

Table 8.1. Demographic characteristics of the sample participating in the three survey waves.

Variable	April 2020	December 2020	April 2022
		N (%) or *mean (SD)	
Age	*35.325 (12.59)	*35.985 (12.59)	*37.367 (12.59)
Gender			
Male	202 (19.02)	202 (19.02)	202 (19.02)
Female	860 (80.98)	860 (80.98)	860 (80.98)
Education			
Middle/High school	318 (29.94)	285 (26.84)	238 (22.41)
Graduate	599 (56.40)	629 (59.23)	633 (59.60)
Postgraduate	145 (13.65)	148 (13.94)	191 (17.99)
Occupation			
Unemployed	81 (7.63)	77 (7.25)	95 (8.95)
Student	305 (28.72)	241 (22.69)	167 (15.73)
Healthcare worker	68 (6.40)	90 (8.47)	106 (9.98)
Self-employed	198 (18.64)	189 (17.80)	212 (19.96)
Employed	379 (35.69)	428 (40.30)	443 (41.71)
Retired	31 (2.92)	37 (3.48)	39 (3.67)

Notes: Numbers preceded by an asterisk (*) are mean values (standard deviation).
Abbreviations: SD, Standard deviation.

8.3.2 *Statistical analysis*

The statistical analyses were performed using the "*lme4*" R package (Bates et al., 2015), which provides functions for fitting and analyzing mixed models. Models were fitted using *REML* adopting the Satterthwaite approximation to compute *p*-values (Luke, 2017). Mixed-model analyses included a random intercept per participant to account for the repeated-measures nature of the data and the variability among respondents' scores. Bonferroni *post hoc* tests and simple effect contrasts using the "*emmeans*" R package (Lenth et al., 2022) were computed in the case of significant main effects or interaction effects, respectively. The level of significance was always set at $p < 0.05$.

Firstly, we ran different models including the scores of each sleep and mental health questionnaire (PSQI, ISI, BDI-II, PSS-10, and STAI-X1) as dependent variables, and the "*Survey wave*" factor (April 2020, December 2020, April 2022) as three-level within-subjects predictor. These analyses aimed to explore the general trajectories of sleep and psychological disturbances among the overall sample along the two pandemic years.

Furthermore, the same analysis was performed for specific items of PSQI (total sleep time [min], bedtime [hh:mm] and get up time [hh:mm]) and each sub-component of PSQI (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medications and daytime dysfunction) to describe the time course of specific dimensions of sleep habits/quality across the three assessments. Finally, we ran further mixed models on questionnaire scores (PSQI, ISI, BDI-II, PSS-10 and STAI-X1) including "*Survey wave*" (April 2020, December 2020, April 2022), "*Age*" (continuous time-varying variable), "*Gender*" (male, female), MEQr scores (continuous time-varying variable), and the interaction of survey wave factor with "*Age*", "*Gender*" and MEQr scores as predictors. These analyses aimed at describing possible differences in the trajectories of sleep quality, insomnia, depression, perceived stress, and anxiety depending on the above-mentioned demographic and chrono-psychological factors. Continuous moderators (age and MEQr score) were represented by plotting mean ± SD values to provide a graphical representation of significant interaction effects. As regards the age variable, we coded the mean age − 1 SD (23.612 years) as "younger", the mean age (36.226 years) as "middle-age", and the mean age + 1 SD (48.839 years) as "older". As regards MEQr scores, we labelled the mean MEQr score − 1 SD (11.803) as "evening-type", the mean MEQr score (15.494) as "intermediate-type", and the mean + 1 SD (19.185) as "morning-type".

The analyses involving PSQI scores and one of its sub-components (habitual sleep efficiency) were carried out excluding 44, 36, and 34 participants of the first, second and third survey waves, respectively, due to compilation errors (respondents reported longer total sleep time than time in bed). Due to the optional nature of BDI-II, PSS-10, and STAI-X1, Little's MCAR test was performed using SPSS version 27.0.1.0 (IBM, Armonk, NY, USA), which showed that missing data occurred completely at random over the three survey waves (all $p > 0.241$). Harman's single factor test did not identify common method bias in each survey wave.

8.4 Results

8.4.1 *Sleep variables*

The PSQI overall score did not differ between the three survey waves ($F_{2,2032.77} = 1.637$, $p = 0.195$), indicating that sleep quality was stable over the pandemic. On the other hand, the "*Survey wave*" factor was significant in the analyses on ISI score ($F_{2,2122} = 28.699$, $p < 0.001$) and total sleep time ($F_{2,2122} = 47.751$, $p < 0.001$). Bonferroni *post hoc* comparisons (Figure 8.1) revealed a progressive improvement of insomnia symptomatology and decreased sleep duration. Specifically, the second and third survey waves were characterized by decreased ISI scores (difference of estimated marginal means: −0.617, $p < 0.001$; −1.076, $p < 0.001$; respectively) and total sleep time (−15.395 min, $p < 0.001$; −20.706 min, $p < 0.001$; respectively) than the first one. The third assessment was associated with reduced ISI scores (−0.460, $p = 0.004$) and sleep duration (−5.311 min, $p = 0.048$) compared with the second one.

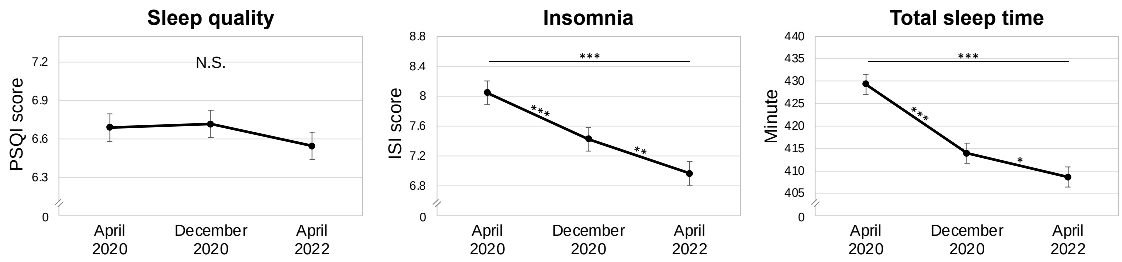

Figure 8.1. Estimated marginal mean ± standard error of PSQI scores (sleep quality), ISI scores (insomnia) and total sleep time (min) during the three survey waves.

Notes: Significant Bonferroni *post hoc* comparisons are indicated with asterisks (**p* < 0.05, ***p* < 0.01, ****p* < 0.001).

Abbreviations: ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index.

Analyses also showed a significant effect of the "*Survey wave*" factor on bedtime ($F_{2,2122}$ = 264.513, $p < 0.001$) and get up time ($F_{2,2122}$ = 430.555, $p < 0.001$). As shown in Figure 8.2, *post hoc* comparisons indicated the progressive advance of bedtime and get up time over the two pandemic years. Specifically, participants reported earlier bedtime and get up time during the second (−34.567 min, $p < 0.001$; −50.400 min, $p < 0.001$; respectively) and third survey waves (−50.400 min, $p < 0.001$; −70.567 min, $p < 0.001$; respectively) than the first one. Bedtime and get up time were also significantly advanced in the third assessment compared with the second one (−15.833 min, $p < 0.001$; −20.167 min, $p < 0.001$; respectively).

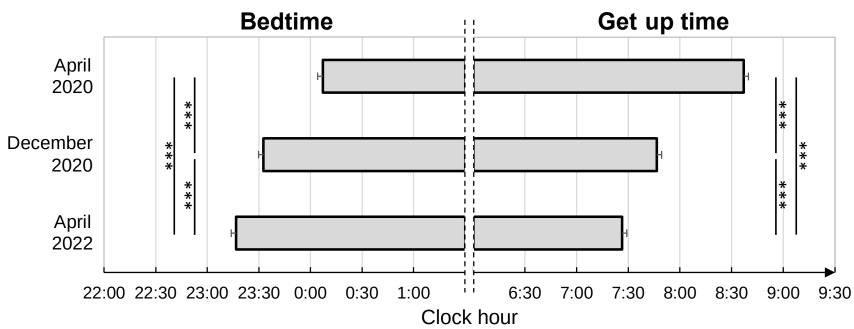

Figure 8.2. Estimated marginal mean ± standard error of bedtime and get up time (hh:mm) during the three survey waves.

Notes: Asterisks indicate significant Bonferroni *post hoc* comparisons (****p* < 0.001)

Results of the analyses on PSQI sub-components are reported in Table 8.2. We highlighted significant differences between survey waves on subjective sleep quality, sleep latency, sleep duration, sleep disturbances and daytime dysfunction. Participants reported better subjective sleep quality and less severe sleep disturbances during the third assessment time compared with the first one ($p < 0.001$, $p = 0.001$, respectively) and the second one ($p = 0.005$, $p = 0.046$, respectively). Sleep-onset latency was reduced over time (all $p < 0.001$). Conversely, *post hoc* comparisons showed reduced sleep duration during the second and third survey waves compared with the first one (both $p < 0.001$), and increased daytime dysfunctions over time (all $p < 0.028$).

Table 8.2. Descriptive statistics [mean (standard deviation)] of PSQI sub-component scores during the three survey waves (survey wave 1: April 2020; survey wave 2: December 2020; survey wave 3: April 2022) and the corresponding statistical comparisons (*F*, *p*, Bonferroni *post hoc*).

PSQI sub-component	April 2020	December 2020	April 2022	*F*	*p*	*Post hoc*
		Mean (SD)				
Subjective sleep quality	1.36 (0.76)	1.30 (0.71)	1.23 (0.66)	14.72	**< 0.001**	SW1>SW3*** SW2>SW3**
Sleep latency	1.36 (1.02)	1.20 (1.01)	1.07 (0.96)	43.61	**< 0.001**	SW1>SW2>SW3***
Sleep duration	0.70 (0.79)	0.81 (0.78)	0.85 (0.77)	21.01	**< 0.001**	SW1<SW2*** SW1<SW3***
Habitual sleep efficiency	0.77 (0.99)	0.79 (0.98)	0.80 (0.97)	0.52	0.59	
Sleep disturbances	1.39 (0.58)	1.37 (0.56)	1.32 (0.55)	6.39	**0.002**	SW1>SW3** SW2>SW3*
Sleep medications	0.26 (0.77)	0.32 (0.85)	0.29 (0.82)	2.18	0.11	
Daytime dysfunction	0.83 (0.71)	0.90 (0.67)	0.97 (0.71)	15.00	**< 0.001**	SW1<SW2<SW3*

Note: Bold values are statistically significant while asterisks indicate significance level of Bonferroni *post hoc* comparisons (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).
Abbreviations: SD, Standard deviation; PSQI, Pittsburgh Sleep Quality Index; SW, Survey wave.

8.4.2 *Age, gender, and chronotype effect on sleep variables*

As reported in Table 8.3, older age was associated with poorer sleep quality, more severe insomnia symptoms, and shorter total sleep time. The interaction between "*Survey wave*" and "*Age*" factors was significant in the analyses of all the sleep variables (PSQI score, ISI score, total sleep time), indicating an age-dependent time course of sleep quality, insomnia symptoms, and sleep duration.

Table 8.3. Results (*F* and *p*) of the mixed model analyses on PSQI score (sleep quality), ISI score (insomnia), and total sleep time (min).

Predictor	PSQI score		ISI score		Total sleep time	
	F	*p*	*F*	*p*	*F*	*p*
Survey wave	1.109	0.330	1.287	0.276	17.363	**< 0.001**
Age	17.215	**< 0.001**	4.506	**0.034**	95.126	**< 0.001**
Gender	19.427	**< 0.001**	9.638	**0.002**	0.468	0.494
MEQr score	59.424	**< 0.001**	77.820	**<0.001**	8.204	**0.004**
Survey wave × Age	3.984	**0.019**	3.843	**0.022**	4.816	**0.008**
Survey wave × Gender	2.145	0.117	0.599	0.549	0.101	0.904
Survey wave × MEQr score	0.001	0.999	0.433	0.649	3.463	**0.031**

Note: The models comprised the following predictors: "*Survey wave*" (April 2020, December 2020, April 2022), "*Age*", "*Gender*" (male, female), MEQr score (chronotype), and the interaction between "*Survey wave*" with "*Age*", "*Gender*", and MEQr score. Bold values are statistically significant.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index; MEQr, Morningness-Eveningness Questionnaire-reduced version.

Simple effect contrasts (Figure 8.3) highlighted significant differences between the survey waves among the older respondents, as shown by increased PSQI scores in December 2020 (+0.336, p = 0.041), and a subsequent significant improvement in sleep quality during the last assessment period (−0.369, p = 0.020). No differences were reported by the middle-age (+0.096, p = 0.452) and the younger participants (−0.144, p = 0.385) during the second survey compared with the first one, and from the second to the third assessment (−0.104, p = 0.417; +0.162, p = 0.338; respectively).

ISI scores decreased during the second survey wave compared with the first one in the middle-age (−0.577, $p = 0.001$) and younger people (−0.952, $p < 0.001$), while insomnia was stable among the older respondents (−0.202, $p = 0.384$). On the other hand, older participants reported a significant reduction in ISI scores from the second to the third survey wave (−0.703, $p = 0.002$). A further decline in ISI scores was observed in April 2022 in the middle-age group compared with December 2020 (−0.386, $p = 0.033$), while the younger population did not show any change in insomnia symptoms comparing the last two survey waves (−0.068, $p = 0.776$). An overall reduction in total sleep time was observed in December 2020 compared with April 2020 (younger: −15.551 min; middle-age: −14.122 min; older: −12.694 min; all $p < 0.001$), and the young population was marked by a further reduction in sleep time during the last assessment (−9.801 min, $p = 0.008$). Older and middle-age respondents reported stable sleep duration in the last two survey waves (+0.635 min, $p = 0.855$; −4.583 min, $p = 0.103$).

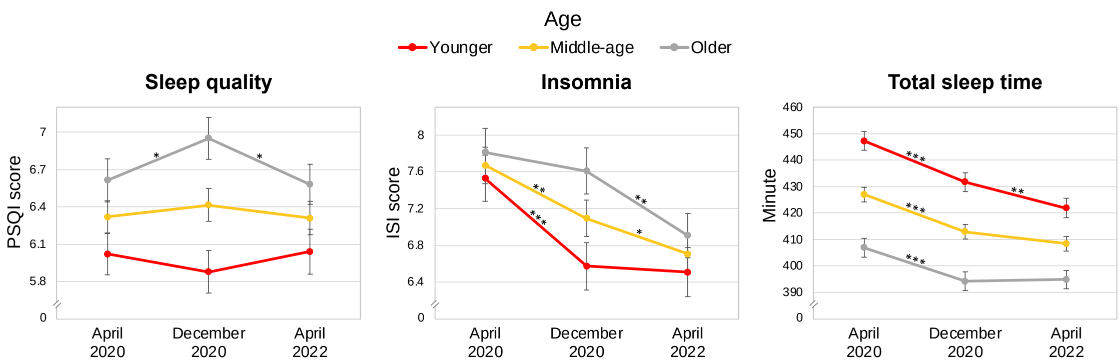

Figure 8.3. Estimated marginal mean ± standard error of PSQI scores (sleep quality), ISI score (insomnia) and total sleep time (min) during the three survey waves according to age.

Notes: Red line: younger; yellow line: middle-age; grey line: older. Significant simple effect contrasts are indicated with asterisks (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

Abbreviations: ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index.

Female participants reported poorer sleep quality and more severe insomnia symptoms than males (Table 8.3). No differences in total sleep time between genders emerged. The interaction between "*Survey wave*" and "*Gender*" factors on sleep variables did not reveal differences between genders in the time course of sleep quality, insomnia symptoms and sleep duration.

Finally, eveningness was associated with lower sleep quality, more severe insomnia symptomatology and shorter total sleep time (Table 8.3). The interaction between "*Survey wave*" and MEQr scores in predicting sleep duration was significant, while no different time course of sleep quality and insomnia symptoms between circadian typologies was highlighted. As shown in Figure 8.4, simple effect contrasts revealed a larger reduction of total sleep time among the evening-type population (−17.068 min, $p < 0.001$) from the first to the second survey wave than among the intermediate-type (−14.122, $p < 0.001$) and morning-type respondents (−11.177, $p = 0.002$). Late chronotypes are associated with a further significant reduction of sleep time from the second to the third assessment point (−7.774 min, $p = 0.028$), while no significant differences were reported by intermediate-type (4.583 min, $p = 0.102$) and morning-type participants (−1.392 min, $p = 0.708$).

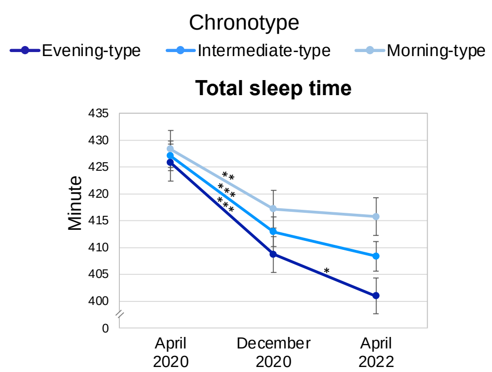

Figure 8.4. Estimated marginal mean ± standard error of total sleep time (min) during the three survey waves according to chronotype.

Notes: Light blue line: morning-type; blue line: intermediate-type; dark blue line: evening-type. Significant simple effect contrasts are indicated with asterisks (*$p < 0.05$, ***$p < 0.001$).

8.4.3 *Psychological variables*

The analyses on BDI-II, PSS-10 and STAI-X1 scores showed significant differences between the three survey waves ($F_{2,2016.04} = 4.142$, $p = 0.016$; $F_{2,1974.17} = 16.576$, $p < 0.001$; $F_{2,1911.25} = 43.850$, $p < 0.001$, respectively). As shown in Figure 8.5, participants reported less severe depressive symptoms during the third survey wave than the first one (−0.661, $p = 0.023$), while the second assessment did not significantly differ from the first (−0.109, $p = 1.000$) and the third ones (+0.552, $p = 0.074$). Perceived stress increased during the second (+1.043, $p < 0.001$) and third survey waves (+1.011, $p < 0.001$) compared with the first one. Anxiety scores began to decline in December 2020 (−1.887, $p < 0.001$), and were further reduced during the last assessment compared with the second one (−0.904, $p = 0.008$).

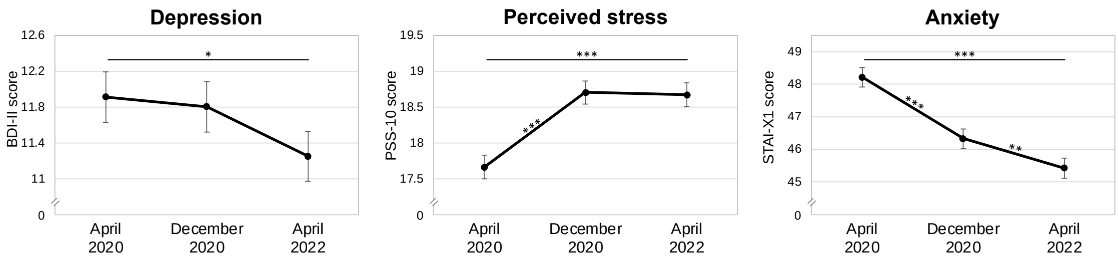

Figure 8.5. Estimated marginal mean ± standard error of BDI-II scores (depression), PSS-10 scores (perceived stress) and STAI-X1 scores (anxiety) during the three survey waves.
Notes: Significant Bonferroni *post hoc* comparisons are indicated with asterisks (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).
Abbreviations: BDI-II, Beck Depression Inventory-second edition; PSS-10, Perceived Stress Scale-10 item; STAI-X1, State–anxiety subscale of the State–Trait Anxiety Inventory.

8.4.4 *Age, gender, and chronotype effect on psychological variables*

Younger age, female gender and eveningness were associated with more severe depressive symptoms and higher perceived stress. Younger respondents and evening-type people reported higher anxiety levels, while no relationship between age and anxiety emerged (Table 8.4). The interaction between "*Survey* *wave*" and chrono-demographic factors ("*Age*", "*Gender*", MEQr score) in predicting PSS-10 was significant. No significant interaction effect for BDI-II and STAI- X1 scores was highlighted, indicating no differences between age groups, genders and chronotypes in the time course of depressive and anxiety symptoms.

Table 8.4. Results (*F* and *p*) of the mixed model analyses on BDI-II score (depression), PSS-10 score (perceived stress), and STAI-X1 score (anxiety).

Predictor	BDI-II score		PSS-10 score		STAI-X1 score	
	F	*p*	*F*	*p*	*F*	*p*
Survey wave	0.949	0.387	26.924	**< 0.001**	27.373	**< 0.001**
Age	8.137	**0.004**	15.065	**< 0.001**	0.134	0.714
Gender	17.034	**< 0.001**	30.345	**< 0.001**	14.842	**< 0.001**
MEQr score	81.224	**< 0.001**	30.133	**< 0.001**	25.545	**< 0.001**
Survey wave × Age	0.404	0.668	7.072	**< 0.001**	0.061	0.941
Survey wave × Gender	1.330	0.265	12.596	**< 0.001**	0.644	0.525
Survey wave × MEQr score	0.484	0.616	3.646	**0.026**	1.182	0.307

Note: The models comprised the following predictors: "*Survey wave*" (April 2020, December 2020, April 2022), "*Age*", "*Gender*" (male, female), MEQr score (chronotype), and the interaction between "*Survey wave*" with "*Age*", "*Gender*", and MEQr score. Bold values are statistically significant.
Abbreviations: BDI-II, Beck Depression Inventory-second edition; PSS-10, Perceived Stress Scale-10 item; STAI-X1, state-anxiety subscale of the State-Trait Anxiety Inventory; MEQr, Morningness-Eveningness Questionnaire-reduced version.

Simple effect contrasts (Figure 8.6) revealed significantly raised stress levels from the first survey wave to the second one in all groups. However, the extent of the effect depended on age, gender and chronotype. Specifically, older participants and morning-type subjects reported the largest increase in perceived stress (+2.461, $p < 0.001$; +2.145, $p < 0.001$; respectively), middle-age and intermediate-type respondents showed an intermediate increase (+1.657, $p < 0.001$; +1.657, $p < 0.001$; respectively), while younger and evening-type subjects were associated with the smallest increase (+0.853, $p = 0.010$; +1.169, $p < 0.001$; respectively). Men reported a greater increase in perceived stress (+2.497, $p < 0.001$) than women (+0.817, $p < 0.001$). Finally, all groups reported unchanged stress levels between the second and the third survey waves (younger: −0.205, p = 0.546; middle-age: −0.012, p = 0.962; older: +0.180, p = 0.572; male: +0.001, p = 0.999; female: −0.025, p = 0.911; evening-type: −0.038, p = 0.907; intermediate-type: −0.012, p = 0.962; morning-type: +0.013, p = 0.969).

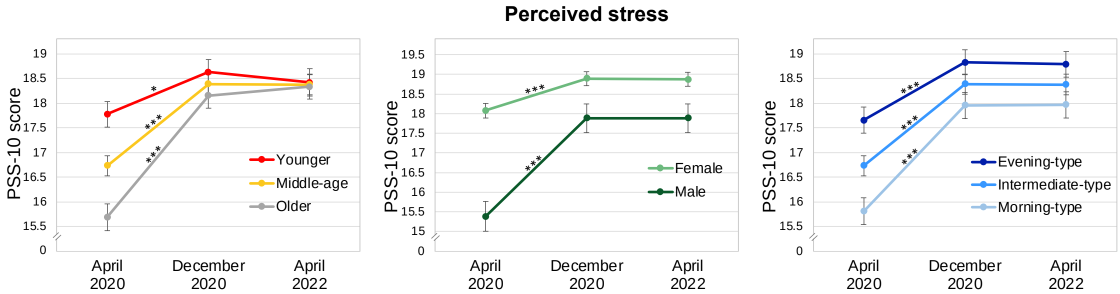

Figure 8.6. Estimated marginal mean ± standard error of PSS-10 scores (perceived stress) during the three survey waves according to age, gender, and chronotype.

Notes: Red line: younger; yellow line: middle-age; grey line: older; light green line: female; dark green line: male; light blue line: morning-type; blue line: intermediate-type; dark blue line: evening-type. Significant simple effect contrasts are indicated with asterisks (*p < 0.05, ***p < 0.001).

Abbreviations: PSS-10, Perceived Stress Scale-10 item.

8.5 Discussion

The present study demonstrated different trajectories of sleep quality, insomnia, depression, stress, and anxiety during the two pandemic years.

As indicated by the PSQI total score, the overall sleep quality was stable across the three assessments. However, an overview of PSQI sub-components suggested a more articulated pattern of results, revealing a clear dissociation of the effects on sleep features depending on the specific domain considered. On the one hand, subjective sleep quality improved, and sleep disturbances and sleep-onset latency decreased two years after the lockdown of Spring 2020. These findings are consistent with the progressive reduction of insomnia symptoms reported by the overall sample. Conversely, we demonstrated a gradual decrease in sleep duration and an increase in sleep-related daytime dysfunctions with the loosening of the restraining measures. Similar results were obtained by our previous investigation (Salfi, D'Atri, et al., 2021) comparing the lockdown scenario and the second contagion wave of COVID-19, and by other studies carried out in the post-lockdown period (Alfonsi et al., 2021; Massar et al., 2021). These results could be ascribable to the peculiar nature of the lockdown. The stressful situation led to worsened sleep disturbances worldwide (AlRasheed et al., 2022; Jahrami et al., 2022). Meanwhile, the strict confinement regimen was associated with unlocked time for sleep and reduced *social jetlag* for most of the population (Kantermann, 2020; Korman et al., 2020; Leone et al., 2020) with a consequent improvement in sleep-related daytime dysfunctions. However, social and working obligations returned to exert their negative effect on sleep during the second survey wave, and even more two years after the lockdown. Consistently, participants reported substantial earlier get up times (~70 min) and a smaller but still important advanced bedtime (~50 min) in April 2022 compared with the first lockdown. The discrepancy between the above-mentioned variations led to an overall reduction in total sleep time, as earlier awakenings were not adequately compensated by a comparable advance in bedtimes.

The improvement in sleep disturbances was accompanied by reduced depressive and anxiety symptoms. However, as far as depression is concerned, we observed a marginal decrease in the BDI-II score, whose effect reached significance only comparing the first and the third assessments. The time course of self-perceived stress was in stark contrast to the other examined psychological dimensions. The stress level increased from the lockdown period, reaching its plateau during the second contagion wave, and then stabilized. As suggested by other investigations (Conte et al., 2021; Salfi, D'Atri, et al., 2021), this outcome could be ascribable to the prolonged nature of the emergency, which was accompanied by a societal and economic crisis. Moreover, after lifting restrictions, the infection risk raised, presumably affecting the perceived stress in the general population.

Demographic factors such as age also influenced the observed effects. Older participants reported poorer sleep quality, more severe insomnia symptoms, and shorter sleep duration than younger respondents. This outcome is consistent with the pre-pandemic (Kamel & Gammack, 2006; Madrid-Valero et al., 2017) literature and is related to the typical sleep changes occurring across the lifespan (J. Li et al., 2018; Patel et al., 2018). Moreover, in line with studies performed during the current period (Amicucci et al., 2021; Manchia et al., 2022; Rossi, Socci, Talevi, et al., 2020), the younger population showed more severe depressive symptoms and no difference in anxiety. Similar trajectories of depression and anxiety were observed over the three assessment points among the different age groups. However, our investigation highlighted an age-dependent time course of sleep quality, insomnia, total sleep time, and perceived stress. Younger and middle-age groups reported unchanged overall sleep quality over the two pandemic years. On the other hand, we observed reduced sleep quality during the second assessment in older participants and a subsequent improvement during the third survey wave. Moreover, the three age groups seemed to report a similar extent of insomnia relief two years after the first lockdown, but this effect was reached at different time points. Younger people reported the maximum improvement already during Winter 2020, middle-age participants gradually improved across the three survey waves, while insomnia symptoms of older respondents were stable until December 2020 and then improved. Finally, we confirmed higher stress levels among young people during the lockdown (Amicucci et al., 2021; Rossi, Socci, Talevi, et al., 2020; Ueda et al., 2020) while we reported a general increase in perceived stress among all age groups, which led to similar stress levels in the overall sample during the second and third survey waves.

The specific characteristics of the pandemic scenario during the three data collections could explain our pattern of results. During the second contagion wave of Winter 2020, the confinement measures were reduced, several business and school activities reopened, and freedom of movement was partially ensured. Therefore, infection risk increased while no vaccine against COVID-19 was still available. Considering that older age is associated with the highest morbidity and mortality rates due to SARS-CoV-2 infection, it is unsurprising that older respondents experienced a substantial increase in stress levels with a concurrent decline in sleep quality and unchanged insomnia severity in December 2020 compared with the first lockdown period. However, the massive vaccination campaign of the subsequent months and the return to an almost normal life after two years could have allowed older participants to experience improved sleep disturbances. On the other hand, several studies suggested that the younger population suffered particularly from the collapse of social interactions during the confinement regimens (Elmer et al., 2020; Sampogna et al., 2021; Viselli et al., 2021; Weissbourd et al., 2020) with well-documented repercussions on sleep and mental health (Amicucci et al., 2021; Daly et al., 2020; Jahrami et al., 2022; Rossi, Socci, Talevi, et al., 2020). Consequently, the loosening of confinement measures and the partial resumption of social interactions could explain the small increase in stress and the concomitant improvement of insomnia symptomatology among the younger people already during Winter 2020.

The present investigation confirmed the vulnerability of women to experience sleep and psychological problems during the pandemic (Daly et al., 2020; Rossi, Socci, Talevi, et al., 2020; Salfi et al., 2020; Salfi, Lauriola, et al., 2021). However, we did not detect differences between genders in the trajectories of sleep quality, insomnia, depression, and anxiety symptoms across the three survey waves. Furthermore, our investigation showed that men reported definitely less stress than women during the first weeks of lockdown, although this difference was largely reduced since Winter 2020. This finding is consistent with the interpretation that females might have already reached the peak of psychological distress during the first weeks of home confinement (Salfi et al., 2020). Conversely, it seems that men reacted better to the lockdown, but the prolonged emergency led them to experience higher distress in the long run. Finally, our study confirmed the well-known vulnerability to sleep disturbances and psychological problems of evening-type people (Adan et al., 2012). This evidence was also reported by investigations carried out during the first stage of the pandemic (Merikanto et al., 2022a; Salfi, Lauriola, et al., 2021). All chronotypes were associated with a similar time course of sleep quality, insomnia, depression, stress, and anxiety across the three periods covered by our study. Meanwhile, the changes in sleep duration differed between circadian typologies. During the lockdown, the typical discrepancy in sleep duration between chronotypes disappeared. However, the progression of the pandemic and the gradual resumptions of social and working obligations reinstated the well-documented misalignment between the evening-oriented biological clock and the morning-oriented social schedule of the so-called *night owls* (Roenneberg et al., 2019). Consequently, this situation led the evening-type participants to sleep less and less as the COVID-19 crisis improved and people resumed their pre-existing daily routine (Salfi, D'Atri, et al., 2022).

8.6 Conclusions

Since the first months of 2020, COVID-19 has pervasively affected every area of life of the worldwide population. A massive amount of literature has been developed during the lockdown period, confirming pervasive repercussions on the sleep and mental health of the general population. The second contagion wave of COVID-19 continued to be characterized by psychological distress and impaired sleep health worldwide.

To the best of our knowledge, the present investigation is the first to longitudinally examine the long-term trajectories of sleep quality/habits, insomnia, depression, stress, and anxiety after two years from the lockdown, providing novel insights on the time course of sleep and mental health according to age, gender, and circadian typology across three critical stages of the COVID-19 outbreak. However, some limitations should be acknowledged. We analyzed a large sample of Italian participants. Nevertheless, the sample comprised a higher prevalence of women, and participants were recruited by adopting a non-probabilistic sampling technique. Moreover, the evaluation of sleep features, chronotype, and psychological well-being relied on self-reported questionnaires. In this view, caution is required in generalizing the present findings due to possible selection and response biases that could affect our data. Future studies should include an objective assessment of sleep patterns (e.g., through actigraphy) to confirm our results. Finally, due to the unpredictable nature of the COVID-19 outbreak, no data that are referred to the pre-pandemic period were available. Longitudinal studies including a pre- pandemic assessment could provide a more comprehensive overview of the situation.

In conclusion, our study described a promising scenario after two years of the pandemic. We demonstrated decreased sleep disturbances, insomnia, depressive, and anxiety symptoms. However, the extent of the improvements was relatively small. Meanwhile, the re-establishment of pre-pandemic social and working dynamics configured a negative effect on sleep duration, which was reduced among the overall sample, and more strongly in particular population groups such as younger and evening-type people. Finally, the persistence of high stress levels and the decreased distress differences between age groups, genders, and chronotypes suggest that people transversely continued to feel the burden of this unprecedented and protracted historical period. In this view, further long-term monitoring of sleep and mental health time course is necessary to claim the end of the COVID-19 emergency on sleep and psychological status of the general population.

Chapter 9

Poor sleep quality, insomnia, and short sleep duration before infection predict long-term symptoms after COVID-19

9.1 Abstract

Millions of COVID-19 survivors experience a wide range of long-term symptoms after acute infection, giving rise to serious public health concerns. To date, few risk factors for post-COVID-19 conditions have been determined. This study evaluated the role of pre-infection sleep quality/duration and insomnia severity in the incidence of long-term symptoms after COVID-19.

This prospective study involved two assessments (April 2020 and 2022). At the baseline, sleep quality/duration and insomnia symptoms in participants without current/prior SARS-CoV-2 infection were measured using the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI). At the follow-up, we asked a group of COVID-19 survivors to retrospectively evaluate the presence of twenty-one symptoms (psychiatric, neurological, cognitive, bodily, and respiratory) that have been experienced one month (n = 713, infection in April 2020–February 2022) and three months after COVID-19 (n = 333, infection in April 2020–December 2021). In April 2022, participants also reported how many weeks passed to fully recover from COVID-19. Zero-inflated negative binomial models were used to estimate the effect of previous sleep on the number of long-term symptoms. Binomial logistic regressions were performed to evaluate the association between sleep variables, the incidence of each post-COVID-19 symptom, and the odds of recovery four/twelve weeks after infection.

Analyses highlighted a significant effect of pre-infection sleep on the number of symptoms one/three months after COVID-19. Previous higher PSQI and ISI scores, and shorter sleep duration significantly increased the risk of almost every long-term symptom at one/three months from COVID-19. Baseline sleep problems were also associated with longer recovery times to return to the pre-infection daily functioning level after COVID-19.

This study suggested a prospective dose-dependent association of pre-infection sleep quality/quantity and insomnia severity with the manifestation of post-COVID-19 symptoms. Promoting sleep health may represent an effective preventive approach to mitigate the COVID-19 sequelae, with substantial public health and societal implications.

9.2 Introduction

All the contents of this Chapter refer to the same-titled article, published in *Brain, Behavior, and Immunity* (Salfi, Amicucci, et al., 2023).

Estimates from the World Health Organization indicate that over 750 million Coronavirus Disease 2019 (COVID-19) cases have been confirmed globally (World Health Organization, 2023). While most individuals experience mild symptoms and recover quickly, recent meta-analyses suggested that 43–45% of COVID-19 survivors report signs and symptoms that continue or develop in the long run (Chen et al., 2022; O'Mahoney et al., 2023). This condition is commonly termed "long COVID" and encompasses over two-hundred long-term clinical manifestations (Davis et al., 2021). General symptoms include fatigue, body aches, fever, ageusia, and anosmia. Other symptoms are related to lung disease (i.e., cough, dyspnea) or involve neurological and cognitive dysfunctions (headache, brain fog, attention/concentration disorders, memory loss) and cardiovascular or gastrointestinal disorders. Moreover, a broad spectrum of psychiatric and psychological manifestations after acute infection were also identified, such as sleep disorders, depression, anxiety, PTSD, obsessive-compulsive disorders (OCD) and psychosis (Badenoch et al., 2021). This disabling condition pervasively impacts the daily life of COVID-19 survivors, also affecting their ability to resume a regular working routine (Davis et al., 2021; O' Mahony et al., 2022).

Identifying potential antecedents of long-term symptoms represents a first-order medical challenge due to the burden on the international healthcare systems and the societal and economic costs (The Lancet, 2021). However, due to the multisystemic and heterogeneous nature of long COVID, its etiology remains poorly understood, and current evidence propose chronic inflammation and immune dysregulation as possible causes of long-term clinical manifestations after acute illness (Crook et al., 2021; M. G. Mazza et al., 2020, 2021; Phetsouphanh et al., 2022).

Sleep plays a crucial role in human immunity (Besedovsky et al., 2012; Bryant et al., 2004), and poor sleep quality and inadequate sleep duration are associated with increased susceptibility to virus infections (S. Cohen et al., 2009; Prather et al., 2015). Moreover, a growing body of evidence linked sleep disturbances and short sleep duration with increased risk for inflammatory diseases due to the relationship between sleep problems and low sleep amount with sustained production of pro-inflammatory cytokines and other circulating markers of inflammation (Garbarino et al., 2021; Irwin et al., 2016).

Based on these assumptions, pre-infection sleep disturbances could play a role in predisposing people to experience long-term symptoms after COVID-19. However, to the best of our knowledge, no prospective studies have addressed this research question. In this study, sleep outcomes of validated questionnaires from a nationwide survey held during the first Italian lockdown (April 2020) were used as predictors of long COVID symptoms, which were retrospectively reported in April 2022 by a group of COVID-19 survivors infected in the previous two years. We hypothesized that sleep disturbances and shorter sleep duration could be prospectively associated with the occurrence of a wide range of long-term symptoms after one and three months from COVID-19 while accounting for established risk factors (age, gender, body mass index – BMI, COVID-19 severity) (Chen et al., 2022; Q. Huang et al., 2022; Sudre et al., 2021; Zeng et al., 2022). Finally, we investigated whether sleep issues before infection were related to longer recovery times to return to the pre-infection daily functioning level.

9.3 Materials and methods

9.3.1 *Participants and procedure*

A total of 13,989 participants were surveyed during the first lockdown period in April 2020 via a web-based set of questionnaires (see 1.3.1 section for a description of the data collection procedure). Subsequently, a total of 2,013 respondents were longitudinally evaluated in December 2020 (see 6.3.1 section). Finally, the overall sample surveyed in April 2020 was re-invited to take part in another longitudinal assessment in April 2022. A total of 2,759 Italians participated in the last data collection, while a total of 1,062 respondents participated in all three survey waves (as detailed in 8.3.1 section). Each assessment comprised an evaluation of sleep quality, insomnia severity, chronotype, depression, perceived stress, and anxiety symptoms via the following questionnaires: the PSQI, the ISI, the MEQr, the BDI-II, the PSS-10, and the STAI-X1, respectively (see 1.3.2 section for a detailed description of questionnaires). Moreover, in each survey wave we collected demographic information and other information (see 1.3.1 and 6.3.1 sections).

During the third time point (April 2022), we asked respondents if they have ever tested positive for COVID-19. If so, participants were asked to answer a set of *ad* *hoc* questions about their infection and symptomatology. We collected information about:

I. the month of detected swab positivity;
II. the COVID-19 severity in the acute stage of illness, using a multiple choice question with four alternative answers (i.e., *no marked symptoms*: absence of any symptom except for smell/taste dysfunctions; *mild disease*: e.g., cough, fever, muscle pains, etc., without pneumonia; *moderate disease*: non-severe pneumonia and having received different medications without the need of extra oxygen treatment; *severe disease*: severe pneumonia requiring extra-oxygen therapy and intravenous lines attached);
III. the presence of long-term symptoms one and three months after the first infection according to Italian National Institute of Health guidelines for long-COVID identification (over-tiredness, muscle weakness, breathlessness/dyspnea, concentration/attention difficulty, headache, asthenia, anxiety, diffuse body pain, sleep problems, memory problems, brain fog, deterioration of perceived health status, persistent cough, small/taste dysfunctions, depression, appetite reduction, fever, PTSD, cardiovascular problems, OCD, psychosis);
IV. the recovery time (in weeks) to return to the pre-infection daily functioning level.

From the overall April 2022 sample, a total of 973 participants (35.00%, mean age ± SD, 33.40 ± 11.40 years; range, 18–81 years; 170 males) reported at least one SARS-CoV-2 infection and provided the above-listed information. The temporal distributions of COVID-19 cases across the pandemic period in our sample and among the over 18-year Italian population are depicted in Figure 9.1.

The flow chart of participants analyzed in the study is reported in Figure 9.2.

To estimate the role of sleep quality/quantity and insomnia severity in predicting long-term symptoms one month after COVID-19 (see 9.3.2.1 and 9.3.2.2 sections) and the odds of recovery in more than four weeks (see 9.3.2.3 section), the analyses were performed excluding 261 individuals. Specifically, we excluded people already infected during the first survey wave (due to possible COVID-19 effects on baseline sleep assessment) and participants who were infected in March/April 2022 (due to the insufficient time elapsed between COVID-19 and the retrospective evaluation in April 2022). Therefore, the analyses were performed on 713 people (33.38 ± 11.40 years; 18–81 years; 122 males) who reported the swab positivity from April 2020 to February 2022.

To evaluate the role of sleep quality/quantity and insomnia severity in predicting long-term symptoms three months after the infection (see 9.3.2.1 and 9.3.2.2 sections) and the risk for recovery in more than twelve weeks (see 9.3.2.3 section), the analyses were performed on the subgroup who reported indicated a swab positivity from April 2020 to December 2021 (n = 333; 33.09 ± 11.80 years; 18–70 years; 60 males). As shown in Figure 9.2, this sample is entirely part of the group in which post-COVID-19 symptoms at one month from infection were analyzed. Specifically, the subgroup was selected by excluding other 380 subjects because they were infected less than three months before the retrospective assessment in April 2022.

The project was approved by the Institutional Review Board of the University of L'Aquila (protocol no. 43,066/2020). Respondents provided electronic consent to participate in the study in each survey wave.

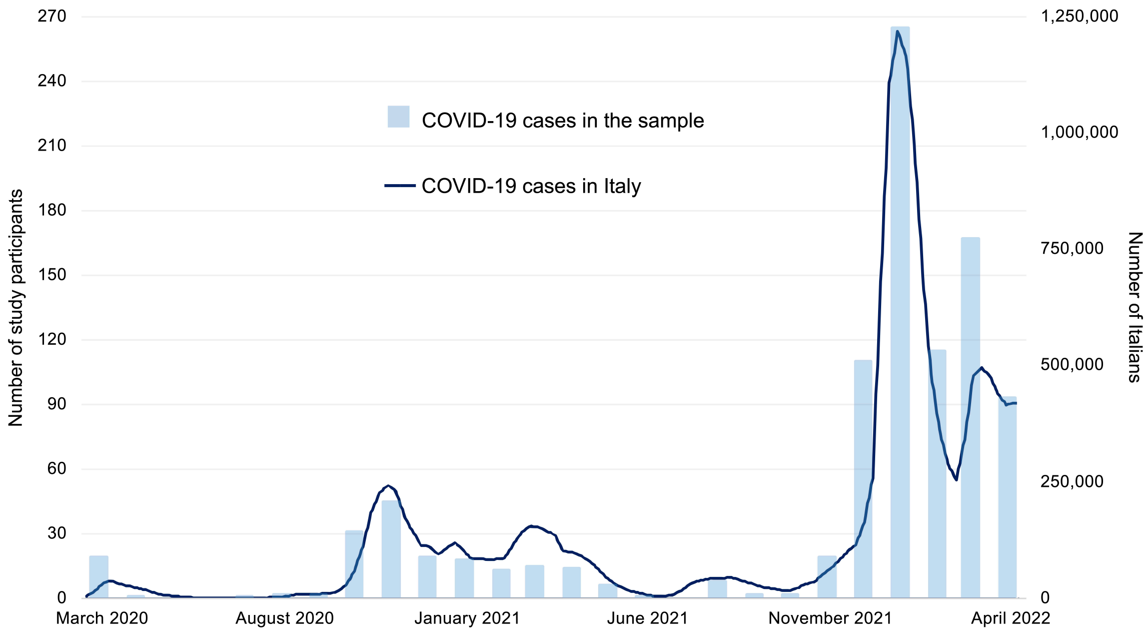

Figure 9.1. Temporal distribution of COVID-19 cases among the over 18-year Italian population (weekly; dark blue line) and in the overall study sample (n= 973; monthly; light blue bars).

Notes: Weekly national trend of COVID-19 cases was derived from the Italian National Institute of Health website.

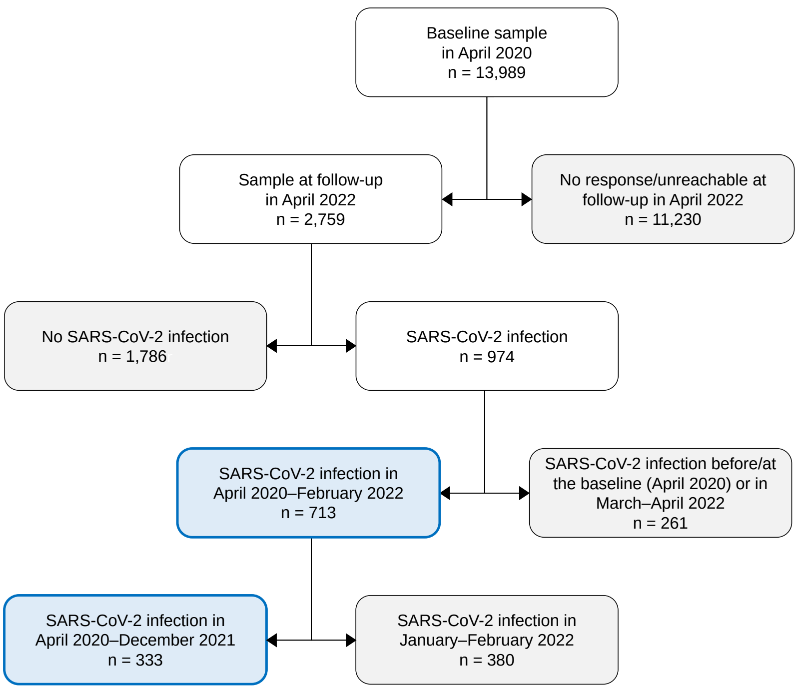

Figure 9.2. Flow chart of study participants.

Notes: Grey boxes indicate missing data or individuals excluded due to the study objectives. Blue boxes indicate analyzed samples. COVID-19 information was collected at follow-up in April 2022.

9.3.2 *Statistical analysis*

We planned three analysis families to evaluate the predictive effect of the sleep variables [PSQI score, ISI score, and total sleep time (TST, extracted from item 4 of PSQI)] on (i) the number of long-term symptoms (9.3.2.1 section), (ii) the odds of each long-term symptom (9.3.2.2 section), and (iii) the odds of recovering the pre-infection daily functioning level in longer times (9.3.2.3 section).

All analyses described in the following sections were adjusted for demographic confounding variables [age, gender, and BMI (weight/height^2)]. All tests were two-tailed and a p-value < 0.05 was considered significant.

9.3.2.1 *Analysis on the number of long-term symptoms after COVID-19*

The numbers of symptoms at one/three months from COVID-19 were entered as dependent variables (range, 0–21), and the sleep variables (PSQI score, ISI score, TST) as separate predictors.

Due to the nature of the dependent variables (count data), linear regressions are unsuitable due to potentially biased results (Coxe et al., 2009; Gardner et al., 1995). Therefore, we evaluated the possibility of performing Poisson regressions, which are typically used to model count data (Coxe et al., 2009; Gardner et al., 1995). However, preliminary analyses highlighted a violation of the equidispersion assumption (Coxe et al., 2009; Long, 1997). In fact, data are overdispersed (χ^2/df ranging from 3.94 to 5.48, which is far greater than the acceptable value of 1.20, Payne et al., 2018).

In this case, a Negative Binomial (NB) regression approach should be used to avoid underestimated standard errors and increased risk of Type 1 errors (Gardner et al., 1995; Hilbe, 2011; Land et al., 2016). NB models are a generalization of the Poisson model, but they include an additional parameter to account for overdispersion, making it more flexible and better able to fit data that deviate from a Poisson distribution (Hilbe, 2011). NB models provide estimates [*exp(B)*] that indicate the rate change of the count variable for a one-unit change in the predictor.

Due to the high prevalence of zero values in count variables (27.9% and 52.6% in 1-month and 3-month symptoms, respectively), data were modeled with Zero-Inflated NB regression (ZINB) (Cameron & Trivedi, 2013; J. A. Green, 2021; Moghimbeigi et al., 2008). The ZINB approach combines two separate models: a ZI model and a NB model. The ZI portion is used to model the probability of a zero count, while the negative binomial portion is used to model the count itself. The ZINB model is useful in analyzing count data that has an excess of zero values because it accounts for this excess in the data and provides more accurate estimates of the underlying distribution. Therefore, the ZINB models allowed us to manage both the excess of zero observations and the overdispersion in the data.

Six ZINB models (M) were tested, evaluating the effect of PSQI, ISI, and TST in predicting the number of symptoms at one month (M1, M2, M3, respectively) and three months from COVID-19 (M4, M5, M6, respectively). The models were fitted using "*countereg*" R package (Zeileis et al., 2008), which provides functions for fitting and analyzing ZINB models. In the results section (9.4.3), we focused on the NB portion of ZINB models for addressing the role of sleep variables in predicting the number of long-term symptoms.

A comparison of relative goodness-of-fit statistics [Akaike information criterion (AIC) and the Bayesian information criterion (BIC)] supported the use of ZINB regressions instead of NB (Table 9.1). Moreover, a visual inspection of Tukey's rootograms (Tukey, 1977) using the "*countereg*" R package (Kleiber & Zeileis, 2016) confirmed ZINB as the best-fit models.

Table 9.1. Information criteria (Akaike and Bayesian) for tested Negative Binomial and Zero-Inflated Negative Binomial models.

Model	AIC	BIC
M1: sleep quality		
NB	3213.221	3240.229
ZINB	3174.956	3224.47
M2: insomnia severity		
NB	3423.114	3450.531
ZINB	3390.338	3440.603
M3: sleep duration		
NB	3452.988	3480.405
ZINB	3425.374	3475.638
M4: sleep quality		
NB	1199.922	1222.399
ZINB	1182.043	1223.251
M5: insomnia severity		
NB	1275.299	1298.147
ZINB	1250.948	1292.837
M6: sleep duration		
NB	1285.192	1308.141
ZINB	1266.241	1308.131

Notes: A lower AIC or BIC value indicates a better fit.
Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; M, Model; NB, Negative Binomial; ZINB, Zero-Inflated Negative Binomial.

Several sensitivity analyses were performed to evaluate the consistency of our results.

First, we fitted M1–6 adjusted for the COVID-19 severity, considering the well-documented relationship between acute illness severity and future long-covid symptoms (Chen et al., 2022; Q. Huang et al., 2022; Taquet et al., 2021; Zeng et al., 2022).

Second, models were fitted including the months from April 2020 to infection as covariate to control for the time distance between actual infection and the first survey wave.

Third, we performed three further ZINB models (M7, M8, M9), testing the effect of sleep variables (PSQI score, ISI score, TST, respectively) collected in December 2020 in predicting the number of long-term symptoms one month from COVID-

19. These models were run on 209 individuals (35.34 ± 11.68 years; range, 18–82 years; 169 females) due to the smaller sample that participated in the last two assessments (December 2020, April 2022, see 9.3.1 section), and because we only included people infected from December 2020 (after the questionnaire compilation) to February 2022. On the other hand, we cannot replicate predictive analyses on the number of symptoms three months after infection due to inadequate sample size of participants (n = 32) infected from December 2020 to December 2022 that reported at least one long-term symptom.

Fourth, we evaluated if the occurred variations in sleep quality, insomnia severity, and sleep duration between the first (April 2020) and the second assessment (December 2020) predicted the number of long-term symptoms by performing separate ZINB models that included baseline (April 2020) PSQI score (M10), ISI score (M11), or TST (M12) and the respective change between the first two survey waves (e.g., Δ PSQI: PSQI in December 2020 − PSQI in April 2020) as independent variables. These models were performed only using the number of symptoms at one month from infection as dependent variable due to inadequate sample size for studying long-term symptoms at three months from COVID-19 in December 2020 sample.

Fifth, control models were performed estimating the relationship between sleep variables and the number of symptoms occurred only one month after the infection, but not three months later. These ZINB models were fitted including participants reporting only transient symptoms (n = 175; 33.56 ± 12.96 years; range, 19–70 years; 135 females). These analyses aimed at confirming the predictive role of sleep features on post-COVID-19 symptoms that may unlikely be interpreted as functional consequences or comorbidities of poor sleep per se, due to their transient occurrence after COVID-19.

9.3.2.2 *Analysis on each long-term symptom after COVID-19*

Binomial logistic regressions were performed to evaluate the association between sleep variables and the future occurrence of each long-term symptom one and three months after COVID-19. Analyses were performed using "*glm*" function of "*stats*" R package (R Core Team, 2022). In detail, each sleep variable was entered as predictor (PSQI score, ISI score, TST), and each long-term symptom as dichotomous dependent variable (yes, no). The criterion of a minimum of five outcome events per predictor variable (EPV) was adopted (Vittinghoff and McCulloch 2007) to identify the analyzable long-term symptoms after infection. Consequently, some symptoms were excluded from the analysis on one-month (psychosis and OCD) and three-month symptoms (PTSD, fever, persistent cough, OCD, appetite reduction, cardiovascular problems, and psychosis) due to insufficient events.

A set of analyses were fitted to confirm the results of the above-described models. Considering the relaxed EPV criterion adopted to maximize the number of analyzable long-term symptoms, sensitivity analyses were performed replicating the binomial logistic models using the Firth's bias reduction method (Firth, 1993; Heinze & Puhr, 2010). This approach allows the parameter estimations to be more efficient and robust to small sample sizes and rare events by penalizing the likelihood function. These control analyses were applied using "*logistf*" R package (Heinze et al., 2022). Furthermore, we replicated the main models adjusting for COVID-19 severity and the time elapsed from the baseline assessment (April 2020) to the virus infection. Finally, binomial logistic regressions were performed using the sleep variables collected in December 2020 as predictors of each symptom. However, based on the above-described EPV criteria, we analyzed only some symptom that has been reported one month after infection (excluded symptoms: smell/taste dysfunctions, appetite reduction, depression, fever, PTSD, cardiovascular problems, OCD, and psychosis), while no 3-month symptoms could be used as dependent variable due to insufficient events.

9.3.2.3 *Analysis on recovery time after COVID-19*

Binomial logistic regressions were performed to test the association between sleep characteristics (quality, duration, insomnia severity,) and the recovery time to return to the pre-infection daily functioning level. The self-reported recovery time was entered as dichotomous dependent variable (≤ 4 weeks vs. > 4 weeks for the 1-month symptoms sample; ≤ 12 weeks vs. > 12 weeks for the 3-month symptoms sample), while sleep variables (PSQI score, ISI score, TST) were used as predictors.

The consistency of results was tested by replicating the above-described regressions adjusted for COVID-19 severity and the time distance between the first assessment (April 2020) and the swab positivity. Finally, the main models were replicated on the sample participating in the survey wave of December 2020. However, only the odds of recovery time after 4 weeks could be tested due to insufficient number of individuals (n = 15) who reported recovering later than 12 weeks.

9.4 Results

9.4.1 *Sample characteristics and COVID-19-related information*

The composition of the analyzed samples is shown in Table 9.2. Most participants were young, females, fell within the healthy weight range, and had at least a bachelor's degree. Most respondents also reported a mild COVID-19 severity in the acute stage and recovered the pre-infection daily functioning level in less than a month. Descriptive statistics of questionnaire scores assessing sleep quality, severity of insomnia symptoms, and sleep duration are also shown.

Table 9.2. Demographic characteristics, information about COVID-19, and descriptive statistics of questionnaire scores evaluating sleep quality, insomnia severity, and sleep duration among participants who were tested positive for SARS-CoV-2 from April 2020 to February 2022, and from April 2020 to December 2021.

Variable	COVID-19 in April 2020–February 2022 (n = 713)	COVID-19 in April 2020–December 2021 (n = 333)
	N (%) or *mean (SD)	
Age (year)		
Younger (18 to 30)	390 (54.7)	194 (58.3)
Middle-aged (31 to 50)	250 (35.1)	100 (30.0)
Older (> 50)	73 (10.2)	39 (11.7)
Gender		
Male	122 (17.1)	60 (18.0)
Female	591 (82.9)	273 (82.0)
BMI		
Underweight range (< 18.5)	48 (6.7)	23 (6.9)
Healthy weight range (18.5 to < 25)	462 (64.8)	205 (61.6)
Overweight range (25 to < 30)	146 (20.5)	69 (20.7)
Obesity (≥ 35)	57 (8.0)	36 (10.8)
Education		
Middle/High school	216 (30.3)	106 (31.8)
Bachelor's degree	171(24.0)	108 (32.4)
Master's degree	229 (32.1)	78 (23.4)
Postgraduate	97 (13.6)	41(12.3)
COVID-19 severity		
No marked symptoms	183 (25.7)	84 (25.2)
Mild disease	490 (68.7)	220 (66.1)
Moderate disease	33 (4.6)	22 (6.6)
Severe disease	7 (1.0)	7 (2.1)
Time to recover the pre-infection daily functioning level		
≤ 4 weeks	479 (67.2)	210 (63.1)
> 4 weeks	234 (32.8)	123 (35.9)
≤ 12 weeks		270 (81.1)
> 12 weeks		63 (18.9)
PSQI score	*6.950 ± 3.575	*6.885 ± 3.694
ISI score	*8.279 ± 5.419	*8.171 ± 5.330
Sleep duration (hour)	*7.205 ± 1.358	*7.215 ± 1.422

Notes: Demographic characteristics and questionnaire scores refer to the first assessment (April 2020), while information about COVID-19 was retrospectively collected in April 2022. Numbers preceded by an asterisk (*) are mean values (standard deviation). BMI ranges were established according to the American Centers for Disease Control and Prevention (2015) guidelines.

Abbreviations: BMI, Body mass index; ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index; SD, Standard deviation.

9.4.2 *Prevalence of long-term symptoms after COVID-19*

The prevalence of each long-term symptom one month and three months after COVID-19 among the analyzed samples is reported in Figure 9.3a. The distribution of the number of symptoms at one month and three months from the infection is shown in Figure 9.3b.

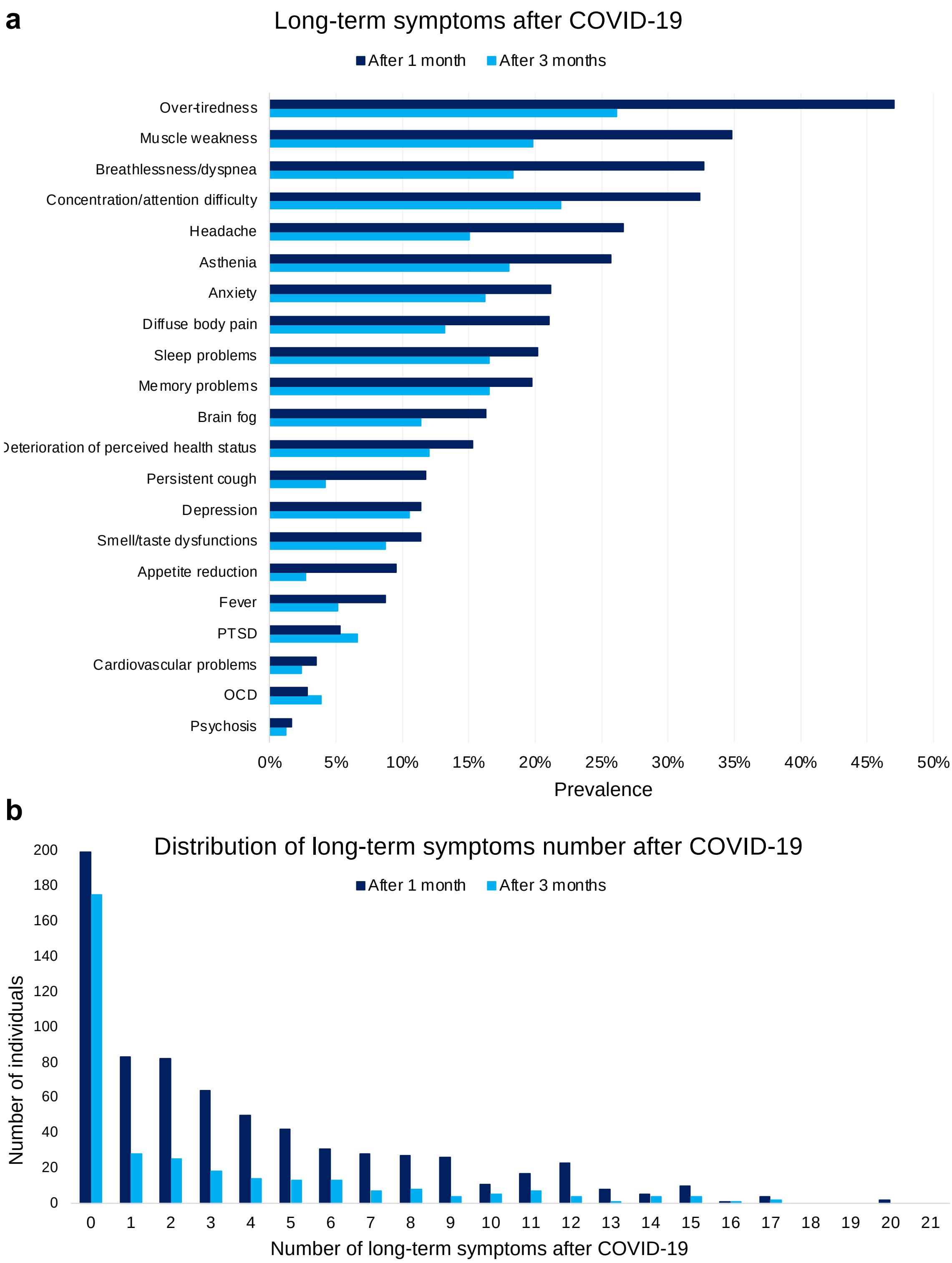

Figure 9.3. Prevalence of long-term symptoms (a) and distribution of symptoms number (b) one month and three months after COVID-19 in the analyzed samples.

Notes: The “After 1 month” group consists of 713 individuals (dark blue bars), while the “After 3 months” group comprises 333 subjects (light blue bars).

Abbreviations: OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder.

9.4.3 *Association between sleep and the number of long-term symptoms after COVID-19*

Results from the NB portion of the ZINB models (Table 9.3) showed that lower sleep quality, more severe insomnia symptoms, and shorter sleep duration significantly predicted a higher number of long-term symptoms at one month and three months after COVID-19. A one-unit increase in PSQI and ISI scores, and a one-hour reduction of sleep duration predicted a 7.0%, 4.9%, and 12.5% increase in the number of symptoms one month after infection, and an increase of 9.1%, 5.4%, and 17.2% in the number of symptoms three months after COVID-19, respectively. A graphical representation of the relationships between sleep variables and the number of long-term symptoms is provided in Figure 9.4.

Table 9.3. Results from the negative binomial portion of the zero-inflated negative binomial regressions [*exp(B)*, 95% confidence intervals, *p*-value] estimating the effect of sleep variables (PSQI score, ISI score, TST) and confounding factors (age, gender, BMI) in April 2020 on the number of long-term symptoms one month (M1, M2, M3) and three months after COVID-19 (M4, M5, M6).

Predictor	M1: sleep quality			M2: insomnia severity			M3: sleep duration		
	exp(B)	95% *CI*	*p*	*exp(B)*	95% *CI*	*p*	*exp(B)*	95% *CI*	*p*
Intercept	2.325	1.461–3.699	**< 0.001**	2.315	1.465–3.658	**< 0.001**	9.182	4.494–18.761	**< 0.001**
Gender*	0.912	0.724–1.149	0.433	0.878	0.701–1.101	0.260	0.819	0.649–1.034	0.093
Age	0.990	0.983–0.998	**0.009**	0.992	0.984–0.999	**0.030**	0.987	0.979–0.995	**0.001**
BMI	1.023	1.006–1.041	**0.008**	1.024	1.006–1.041	**0.008**	1.026	1.008–1.045	**0.004**
PSQI score	1.070	1.046–1.094	**< 0.001**						
ISI score				1.049	1.033–1.064	**< 0.001**			
TST (hour)							0.889	0.840–0.941	**< 0.001**
	M4: sleep quality			M5: insomnia severity			M6: sleep duration		
Intercept	1.312	0.551–3.124	0.540	1.706	0.776–3.752	0.184	8.668	2.478–30.317	**0.001**
Gender*	0.925	0.592–1.446	0.733	0.999	0.644–1.550	0.997	0.816	0.522–1.278	0.375
Age	1.002	0.987–1.018	0.772	1.002	0.988–1.017	0.746	0.996	0.980–1.0120	0.628
BMI	1.021	0.990–1.054	0.184	1.017	0.986–1.048	0.284	1.027	0.995–1.059	0.097
PSQI score	1.091	1.047–1.136	**< 0.001**						
ISI score				1.054	1.027–1.082	**< 0.001**			
TST (hour)							0.853	0.769–0.946	**0.003**

Notes: *Female was used as reference for "*Gender*" factor; significant values are in bold.
Abbreviations: BMI, Body mass index; CI, Confidence interval; ISI, Insomnia Severity Index; M, Model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

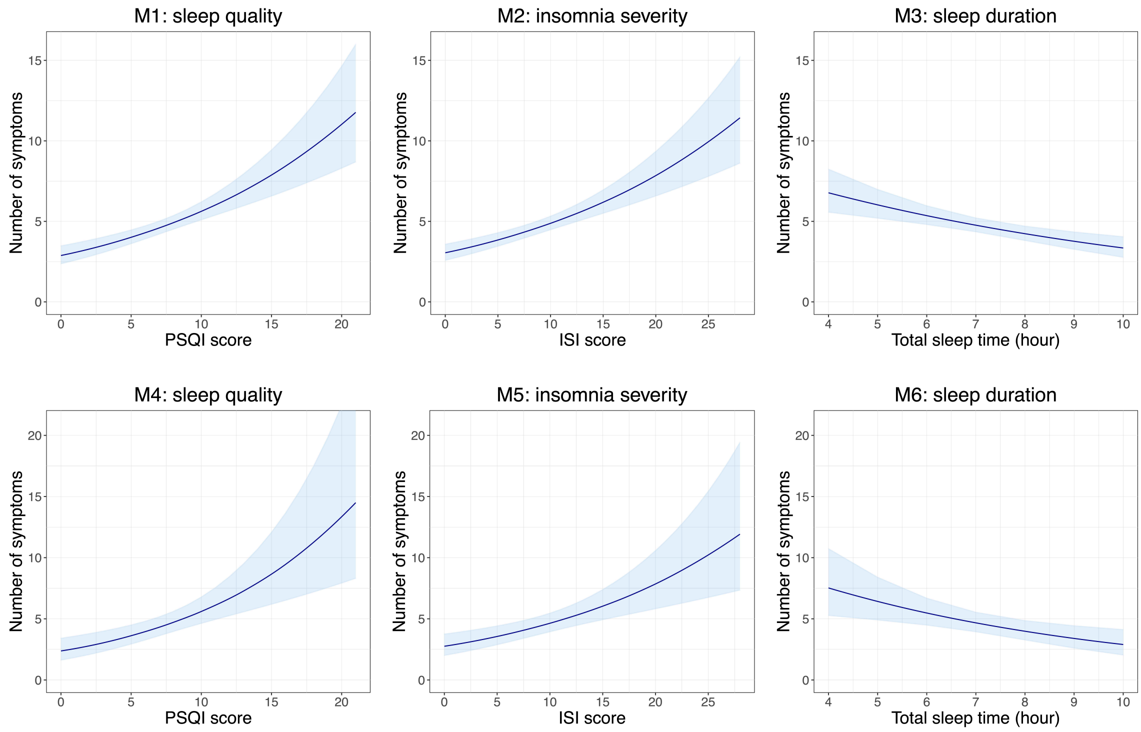

Figure 9.4. Relationships between sleep variables (PSQI score, ISI score, TST) in April 2020 and the number of long-term symptoms one month (M1, M2, M3) and three months after COVID-19 (M4, M5, M6).

Notes: Light blue area represents 95% confidence intervals. Each model was adjusted for age, gender, and body mass index.

Abbreviations: ISI, Insomnia Severity Index; M, Model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

Sensitivity analyses adjusting M1–6 for the COVID-19 severity or the time distance between swab positivity and the baseline assessment (April 2020) confirmed all the significant effects of sleep variables.

Furthermore, analyses using sleep variables collected in December 2020 as predictors confirmed the effect of sleep quality, insomnia severity, and sleep duration on the number of symptoms one month after infection (Table 9.4). A one-unit increase in PSQI and ISI score, and a one-hour reduction of sleep duration predicted an increased number of symptoms by 11.4%, 6.2%, and 27.9%, respectively. The relationships between sleep variables and the number of long-term symptoms are depicted in Figure 9.5.

Table 9.4. Results from the negative binomial portion of the zero-inflated negative binomial regressions [*exp(B)*, 95% confidence intervals, *p*-value] estimating the effect of sleep variables (PSQI score, ISI score, TST) and confounding factors (age, gender, BMI) in December 2020 on the number of long-term symptoms one month after COVID-19.

Predictor	M7: sleep quality			M8: insomnia severity			M9: sleep duration		
	exp(B)	95% CI	*p*	*exp(B)*	95% CI	*p*	*exp(B)*	95% CI	*p*
Intercept	2.209	0.981–4.974	0.056	2.785	1.180–6.574	**0.019**	34.383	9.470–124.838	**< 0.001**
Gender*	0.868	0.591–1.274	0.469	0.953	0.624–1.456	0.825	0.938	0.611–1.442	0.772
Age	0.983	0.971–0.995	**0.006**	0.986	0.974–0.999	**0.035**	0.981	0.968–0.995	**0.006**
BMI	1.023	0.991–1.055	0.162	1.021	0.988–1.056	0.216	1.014	0.980–1.050	0.420
PSQI score	1.114	1.076–1.153	**< 0.001**						
ISI score				1.062	1.035–1.089	**< 0.001**			
TST (hour)							0.782	0.699–0.875	**< 0.001**

Notes: *Female was used as reference for "*Gender*" factor; significant values are in bold.
Abbreviations: BMI, body mass index; CI, Confidence interval; ISI, Insomnia Severity Index; M, Model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

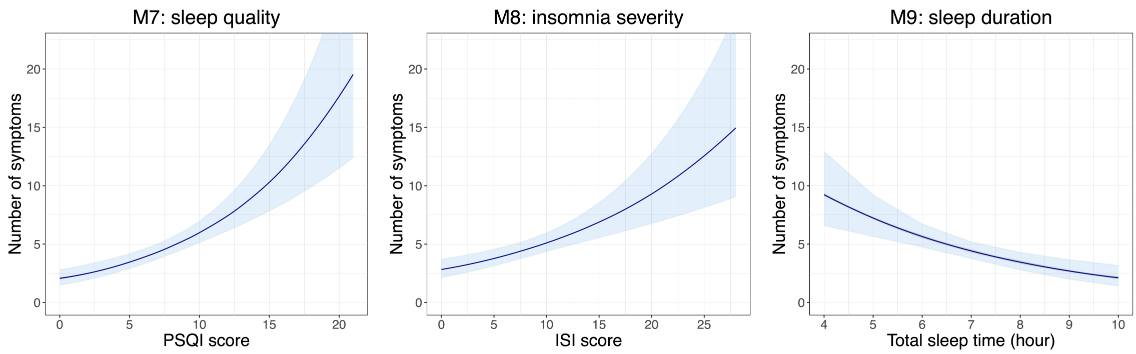

Figure 9.5. Relationships between sleep variables (PSQI score, ISI score, TST) in December 2020 and the number of long-term symptoms one month after COVID-19.
Notes: Light blue area represents 95% confidence intervals. Each model was adjusted for age, gender, and body mass index.
Abbreviations: ISI, Insomnia Severity Index; M, model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

Moreover, M10–12 showed a significant association between the occurred variations in sleep variables from April 2020 to December 2020 and the number of symptoms reported one month after COVID-19 (Table 9.5). A one-unit increase in PSQI and ISI scores, and a one-hour reduction of TST in December 2020 compared to April 2020 predicted higher long-term symptoms after infection by

7.9%, 4.0%, and 17.8%, respectively. The relationship between Δ sleep variables and the number of symptoms after COVID-19 is shown in Figure 9.6.

Sensitivity analyses confirmed the role of sleep variables in predicting transient symptoms that were reported to occur only one month after the infection, but not three months later.

Table 9.5. Results from the negative binomial portion of the zero-inflated negative binomial regressions [*exp(B)*, 95% confidence intervals, *p*-value] estimating the effect of sleep variable variations (Δ PSQI score, Δ ISI score, Δ TST) and confounding factors (age, gender, BMI, sleep variables collected in April 2020) on the number of long-term symptoms one month after COVID-19.

Predictor	M10: sleep quality variation			M11: insomnia severity variation			M12: sleep duration variation		
	exp(B)	*95% CI*	*p*	*exp(B)*	*95% CI*	*p*	*exp(B)*	*95% CI*	*p*
Intercept	2.091	0.929–4.708	0.075	2.582	1.113–5.990	**0.027**	47.563	0.761–177.273	**< 0.001**
Gender*	0.925	0.631–1.356	0.690	0.944	0.624–1.427	0.784	0.954	0.627–1.450	0.825
Age	0.985	0.974–0.997	**0.014**	0.988	0.976–1.000	0.056	0.981	0.968–0.994	**0.004**
BMI	1.017	0.986–1.050	0.289	1.015	0.982–1.049	0.382	1.012	0.978–1.046	0.503
PSQI score	1.131	1.089–1.175	**< 0.001**						
Δ PSQI score	1.079	1.037–1.124	**< 0.001**						
ISI score				1.082	1.050–1.114	**< 0.001**			
Δ ISI score				1.040	1.009–1.072	**0.012**			
TST (hour)							0.995	0.993–0.997	**< 0.001**
Δ TST (hour)							0.849	0.742–0.971	**0.017**

Notes: Δ values are calculated subtracting values collected in December 2020 from those in April 2020. *Female was used as reference for "*Gender*" factor; significant values are in bold.
Abbreviations: BMI, body mass index; CI, Confidence interval; ISI, Insomnia Severity Index; M, model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

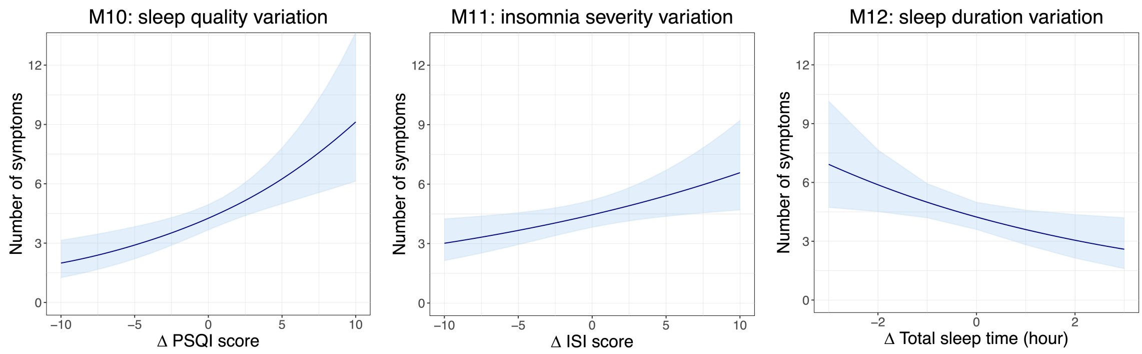

Figure 9.6. Relationships between variation in sleep variables from April 2020 to December 2020 and the number of long-term symptoms one month after COVID-19.

Notes: Δ values are calculated subtracting values collected in December 2020 from those in April 2020. Light blue area represents 95% confidence intervals. Each model was adjusted for age, gender, body mass index, and April 2020 scores.

Abbreviations: ISI, Insomnia Severity Index; M, model; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

9.4.4 *Association between pre-infection sleep and each long-term symptom after COVID-19*

Results of binomial logistic regressions using sleep variables collected in April 2020 as predictors indicated that higher PSQI scores significantly increased the odds of each analyzed long-term symptom at one (Figure 9.7a) and three months from COVID-19 (Figure 9.7b), except for smell/taste dysfunctions, and cardiovascular problems experienced at one month from infection. More severe insomnia symptoms were significantly associated with higher odds of all analyzed long-term symptoms, excluding smell/taste dysfunctions (Figure 9.7c,d). Finally, a one-hour decrease in sleep duration was associated with higher odds of all one-month long-term symptoms, except for asthenia, memory problems, smell/taste dysfunctions, appetite reduction, and cardiovascular problems (Figure 9.7e). Furthermore, reduced sleep duration was associated with increased risk for all symptoms reported after 3 months from infection, excluding over-tiredness, concentration/attention difficulty, anxiety, depression, and smell/taste dysfunctions (Figure 9.7f).

Control analyses using Firth's bias-reduced logistic regressions produced almost identical results to those obtained using the reported binomial logistic regressions, rejecting possible bias due to the low number of events per predictor for some long-term symptoms. Similarly, adjusting for self-reported COVID-19 severity or the time distance between SARS-CoV-2 infection and the baseline assessment (April 2020) confirmed the overall pattern of results.

Moreover, logistic models using PSQI score, ISI score, and TST of December 2020 as predictors of symptoms reported one month after COVID-19 almost completely confirmed the above-described results. Specifically, lower sleep quality (Figure 9.8a) and more severe insomnia symptoms (Figure 9.8b) significantly predicted higher odds of every analyzed symptom, except for persistent cough. Shorter sleep duration led to higher odds of over-tiredness, concentration/attention difficulty, breathlessness/dyspnea, headache, asthenia, sleep problems, anxiety, diffuse body pain, brain fog, and deterioration of perceived health status (Figure 9.8c).

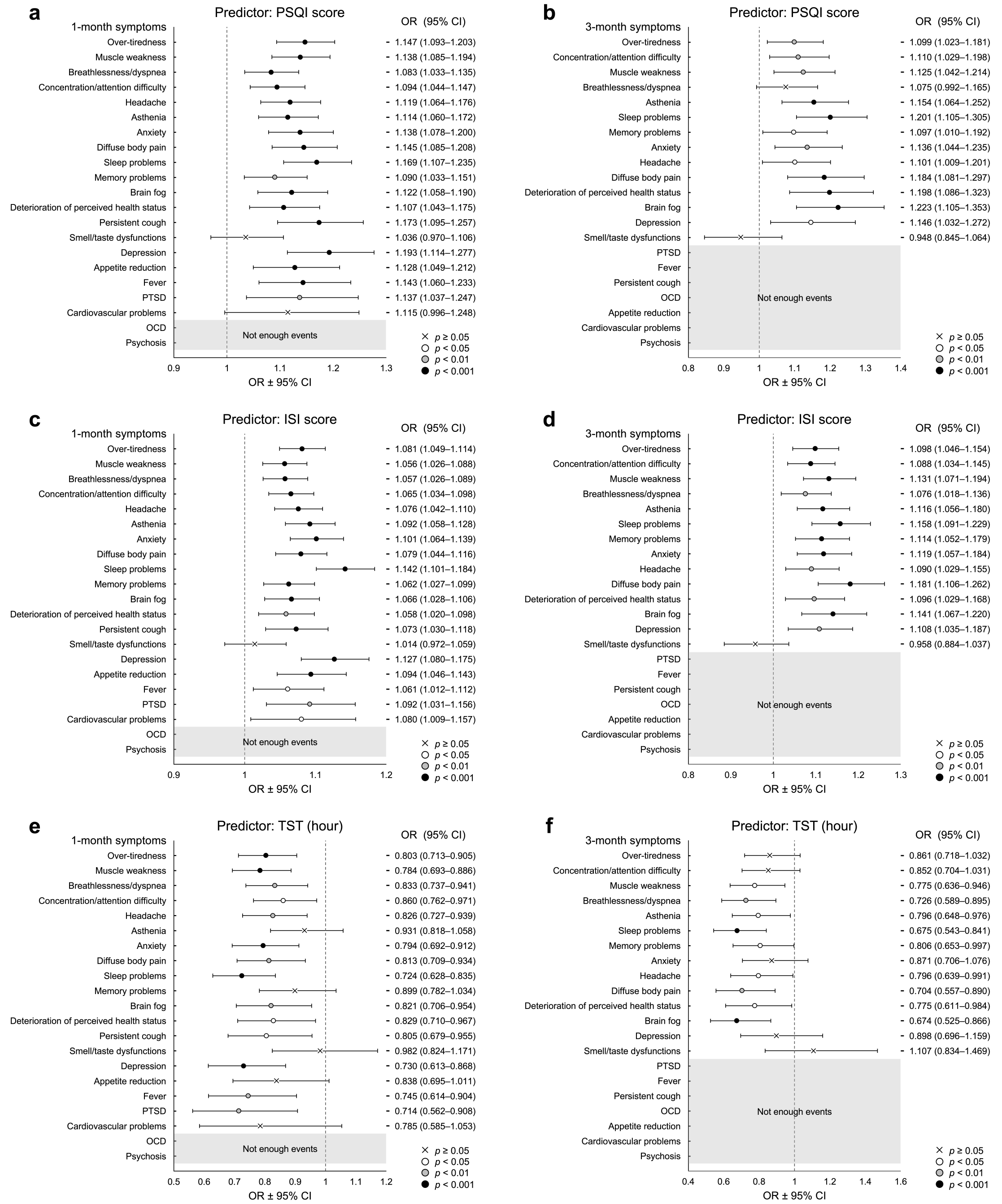

Figure 9.7. Results of logistic regressions (odd ratios and 95% confidence intervals) evaluating the predictive effect of sleep variables (PSQI score, ISI score, TST) in April 2020 on the odds of each long-term symptom one month (a, c, e) and three months after COVID-19 (b, d, f).

Notes: Long-term symptoms were ordered according to the prevalence data (top: most frequent) and represent the dependent variables. White dot indicates significance level at $p < 0.05$, grey dot at $p < 0.01$, and black dot at $p < 0.001$. “×” symbol indicates no statistically significant effect. Grey area indicates insufficient (< 5) outcome events per predictor. Each model was adjusted for age, gender, and body mass index.

Abbreviations: CI, Confidence Interval; ISI, Insomnia Severity Index; OCD, obsessive-compulsive disorder; OR, odd ratio; PSQI, Pittsburgh Sleep Quality Index; PTSD, post-traumatic stress disorder; TST, Total sleep time.

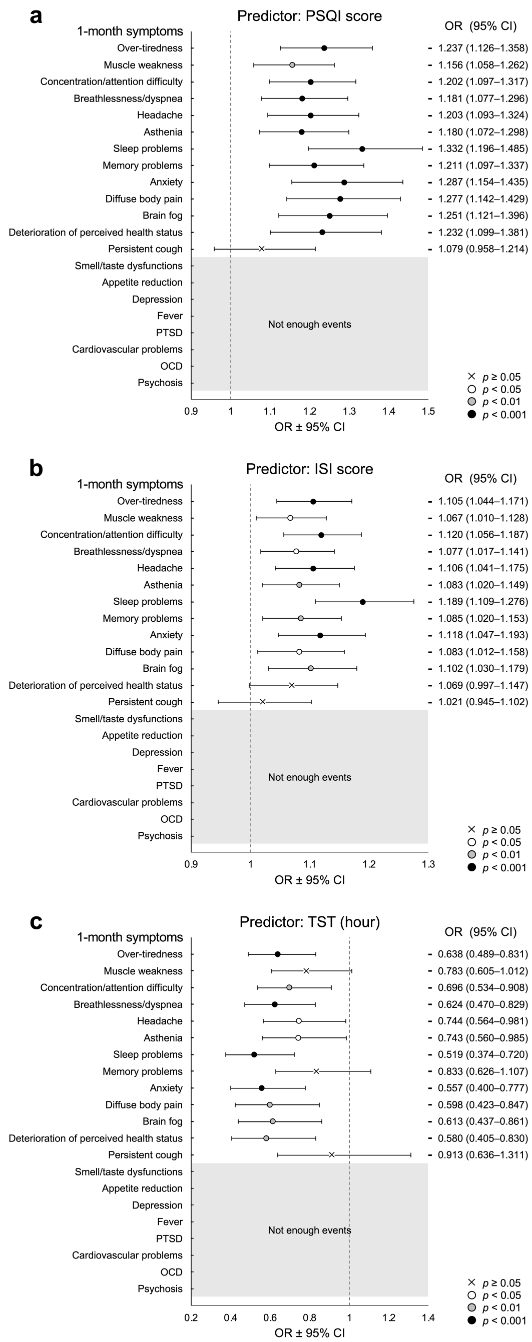

Figure 9.8. Results of logistic regressions (odd ratios and 95% confidence intervals) evaluating the predictive effect of sleep variables [PSQI score (a), ISI score (b), TST (c)] in December 2020 on the odds of each long-term symptom one month after COVID-19.

Notes: Long-term symptoms were ordered according to the prevalence data (top: most frequent) and represent the dependent variables. White dot indicates significance level at $p < 0.05$, grey dot at $p < 0.01$, and black dot at $p < 0.001$. "×" symbol indicates no statistically significant effect. Grey area indicates insufficient (< 5) outcome events per predictor. Each model was adjusted for age, gender, and body mass index.

Abbreviations: CI, Confidence Interval; ISI, Insomnia Severity Index; OCD, Obsessive-compulsive disorder; OR, Odd ratio; PSQI, Pittsburgh Sleep Quality Index; PTSD, Post-traumatic stress disorder; TST, Total sleep time.

9.4.5 *Association between pre-infection sleep and recovery time after COVID-19*

Binomial logistic regression showed that poor sleep quality, more severe insomnia symptoms, and shorter sleep duration in April 2020 predicted longer recovery time to return to the pre-infection daily functioning level after COVID-19 (Figure 9.9). A one-unit increase in PSQI and ISI scores, and a one-hour reduction of sleep duration were prospectively associated with higher odds of recovery in more than four weeks by 13.1%, 9.3%, and 16.8%, and after twelve weeks by 21.3%, 12.0%, and 25.3%, respectively. Adjusting for COVID-19 severity and the time distance between April 2020 assessment and the virus infection confirmed the above results. Finally, logistic regressions using sleep variables collected in December 2020 as predictors confirmed the significant association of recovery in more than four weeks with PSQI [OR (95% CI) = 1.138 (1.043–1.241), p = 0.004] and ISI score [OR (95% CI) = 1.077 (1.018–1.138), p = 0.009]. No association was detected for sleep duration [OR (95% CI) = 0.854 (0.664–1.098), p = 0.217].

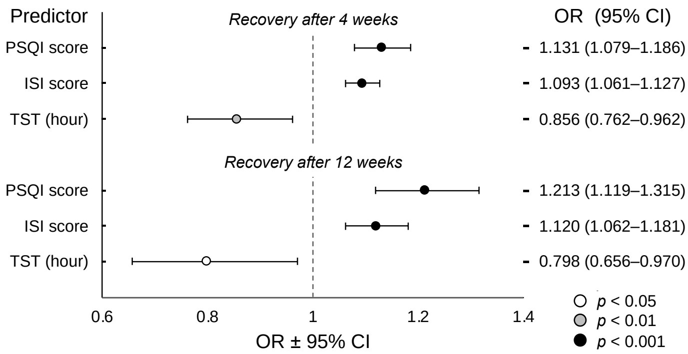

Figure 9.9. Results of logistic regressions (odd ratios and 95% confidence intervals) evaluating the predictive effect of sleep variables (PSQI score, ISI score, TST) in April 2020 on the odds of returning to the pre-infection daily functioning level after 4 and 12 weeks.

Notes: Self-reported recovery after 4 and 12 weeks was evaluated on 713 and 333 subjects, respectively. White dot indicates significance level at $p < 0.05$, grey dot at $p < 0.01$, and black dot at $p < 0.001$. Each model was adjusted for age, gender, and body mass index.

Abbreviations: CI, Confidence Interval; ISI, Insomnia Severity Index; OR, Odd ratio; PSQI, Pittsburgh Sleep Quality Index; TST, Total sleep time.

9.5 Discussion

Since the beginning of the pandemic, millions of people worldwide have reported signs and symptoms that continue or develop after COVID-19, affecting their ability to resume normal life and giving rise to serious public health concerns (The Lancet, 2021).

To the best of our knowledge, this study is the first to find a prospective association between pre-infection sleep disturbances and the occurrence of long-term symptoms after COVID-19. We highlighted significant dose-dependent relationships between previous sleep quality, insomnia severity, and sleep duration and the number of symptoms experienced at one and three months from the reported positive swab for SARS-CoV-2. Moreover, our study showed that lower sleep quality, more severe insomnia, and shorter sleep time lead to higher odds of experiencing a broad spectrum of clinical manifestations one and three months after COVID-19. Finally, we found that previous sleep problems are related to longer recovery times for returning to the self-perceived pre-infection daily functioning.

Our results were consistent with a recent study on a sample of female nurses that found an association between short sleep duration collected in 2017 and the occurrence of post-COVID-19 conditions (S. Wang, Li, et al., 2023).

Immune dysregulation and inflammatory mechanisms may explain the association between sleep and subsequent post-COVID-19 manifestations. Consistent literature showed that sleep disturbances are associated with heightened systemic inflammation, as evidenced by increased levels of pro-inflammatory cytokines (Cho et al., 2015; Ferrie et al., 2013; Irwin et al., 2016; Mills et al., 2007; Nowakowski et al., 2018), C-reactive protein (Cho et al., 2015; Ferrie et al., 2013; Ghilotti et al., 2021; Irwin et al., 2016; Liukkonen et al., 2007), and other markers of inflammation (Irwin et al., 2006; Nowakowski et al., 2018). This evidence has been proposed to explain the documented higher risk for inflammatory diseases in people with sleep disturbances (Garbarino et al., 2021; Irwin et al., 2016). On the other hand, findings from animal (Frere et al., 2022; Rutkai et al., 2022) and human models (Crook et al., 2021; M. G. Mazza et al., 2020, 2021; Phetsouphanh et al., 2022) suggested that a possible mechanism behind the long COVID symptoms may involve an abnormal and persistent pro-inflammatory response weeks/months after infection. For example, Phetsouphanh and collaborators (2022) compared immune profiles of long COVID individuals with patients without long COVID, identifying a combination of inflammatory mediators eight months after infection as the correlate of persistent post-COVID-19 symptoms.

Another interpretation may involve the role of sleep loss as a driver of cellular stress and the consequent neuronal damage (Coulson et al., 2022) in the cognitive and neuropsychiatric manifestations of long COVID (Schilling et al., 2022).

Finally, pre-pandemic evidence suggested that insufficient sleep could impair the vaccination efficacy (Prather et al., 2021; Spiegel et al., 2002; Zimmermann & Curtis, 2019), and the importance of sleep health has also been advocated for the COVID-19 vaccination campaign (Benedict & Cedernaes, 2021; Rayatdoost et al., 2022). Since previous COVID-19 vaccination seems to reduce the risk of long COVID (Notarte et al., 2022), the link between sleep and post-COVID-19 symptoms may be mediated by the impact of sleep deficiency on the vaccination effectiveness. However, providing a clear understanding of the link between sleep and subsequent long-term symptoms after SARS-CoV-2 infection transcends the objectives and the capacity of the present investigation. Future studies should address this question to identify the potential underlying biobehavioral mechanisms of the sleep-long COVID relationship.

In a recent study, S. Wang and collaborators (2022) showed that pre-infection psychological distress was prospectively associated with the incidence of various post-COVID-19 conditions. The similarity with our findings is unsurprising considering the close relationship between sleep disturbances and short sleep duration with psychological conditions like anxiety (Alvaro et al., 2013; Cox & Olatunji, 2020), depression (Alvaro et al., 2013; Fang et al., 2019; Watson et al., 2014; Zhai et al., 2015), and stress disorders (Gardani et al., 2022; Y. Zhang et al., 2019). Furthermore, a growing body of evidence supports a causal role of sleep problems in the occurrence of mental health problems (Baglioni et al., 2011; Hertenstein et al., 2019; Pigeon et al., 2017; Zhai et al., 2015), and treating sleep disturbances seems to improve the subsequent mental health outcomes (Freeman et al., 2017; Ho et al., 2016; A. J. Scott et al., 2021). In this view, we could speculate that pre-infection sleep disturbances may get involved in the predictive role of psychological distress in the incidence of post-COVID-19 symptoms. In line with S. Wang and colleagues' study (2022), smell/taste dysfunction represented the only long-term symptom not prospectively associated with all previous sleep outcomes. However, as argued by those authors, the variability in anosmia incidence in long COVID may be explained by genetic or binding activity differences of the cell entry receptor for SARS-CoV-2 (the angiotensin-converting enzyme 2 receptor; Butowt & von Bartheld, 2021) and may be independent from inflammatory mechanisms potentially involved in the effects of distress and sleep. Further investigations should address this research question.

The present study has several strengths. The predictive effect of sleep variables was obtained by adjusting for important confounding factors (age, gender, and BMI) that were associated by previous studies with a higher risk for long COVID symptoms (Q. Huang et al., 2022; Sudre et al., 2021; Zeng et al., 2022). The main findings were also confirmed after controlling for the COVID-19 severity, which is an established predictor of long COVID conditions (Chen et al., 2022; Q. Huang et al., 2022; Taquet et al., 2021; Zeng et al., 2022), but also a documented outcome of previous sleep problems (B. Huang et al., 2020; Jones et al., 2022). Furthermore, the results were replicated in the same sample by using a different baseline assessment in December 2020. Finally, our findings were confirmed after controlling for the time interval separating the infection from the baseline/follow-up evaluation, reducing the risk for a possible recall bias due to the time elapsed between COVID-19 and the retrospective assessment. At the same time, these sensitivity analyses suggested a predictive role of sleep features even after several months from COVID-19. Nevertheless, it is worth noting that also the changes in sleep quality/quantity over time could affect the post-COVID-19 sequelae. In fact, variations in sleep variables between April and December 2020 were associated with the subsequent number of symptoms one month after infection.

Several limitations should also be acknowledged. Notwithstanding our results rely on a longitudinal data collection, the long-term symptoms after COVID-19 were retrospectively reported by participants during the last follow-up assessment (April 2022). Second, the lack of evaluation of potential pre-existing health conditions and behaviors did not allow our analyses to account for other risk factors for post-COVID-19 conditions (e.g., type 2 diabetes, asthma, smoking status, physical activity). Moreover, sleep quality, insomnia symptoms, and sleep duration were evaluated using validated self-report instruments. Future longitudinal investigations should confirm our results using objective sleep-assessment instruments (actigraphy, polysomnography) and/or a clinical evaluation of sleep disturbances.

Moreover, the absence of a control group without COVID-19 did not make it possible to evaluate if the relationship between previous sleep disturbances and some of the examined symptoms (e.g., over-tiredness, memory problems, psychiatric conditions) may be partially independent from the infection. However, logistic analyses highlighted a significant association between pre-COVID-19 sleep variables and symptoms that are not typically related to sleep problems and are specific of the long COVID syndrome (e.g., breathlessness/dyspnea, brain fog, diffuse body pain, persistent cough, appetite reduction). Sensitivity analyses supported our interpretation, showing that pre-COVID-19 sleep features also predict symptoms that were reported to occur only one month after the infection, but not three months later. Due to their transient occurrence after COVID-19, these relapsing symptoms may be unlikely interpreted as functional consequences or comorbidities of habitual poor sleep per se. Finally, our samples consisted of non-hospitalized adults and comprised a higher portion of female subjects, limiting the generalization of the results.

9.6 Conclusions

In conclusion, this study suggests that pre-existing sleep disturbances and inadequate sleep duration are associated with subsequent risk of long-term symptoms after COVID-19. Our findings could have large-scale implications considering the sleep-loss epidemic in our society (Chattu et al., 2018; S. Wang, Rossheim, et al., 2023) and the considerable rates of insomnia disorder and occasionally experienced insomnia symptoms among the adult population (10% and 20%, respectively; Morin & Jarrin, 2022). Furthermore, the present results may be even more relevant during a historical period that pervasively impacted the worldwide population's sleep. Indeed, meta-analytic studies showed that half of the people experienced subthreshold and clinically significant insomnia symptoms in the first two pandemic years (AlRasheed et al., 2022), and sleep disturbances affected four out of ten people worldwide (Jahrami et al., 2022).

Raising public awareness about healthy sleep habits may represent an effective preventive approach to mitigate the COVID-19 repercussions in the long run, with substantial indirect effects at societal level. Further research is warranted to determine whether intervention aimed at promoting sleep quality/quantity could improve the long-term consequences of COVID-19.

Chapter 10

Lessons from the COVID-19 pandemic

10.1 Sleep disturbances during the lockdown

All the contents of this Chapter refer to the chapter "Sleep patterns and sleep disturbances during the lockdown periods" in the book "COVID-19 and Sleep: A Global Outlook" (Salfi & Ferrara, 2023), reproduced with permission from *Springer Nature*.

Since the early months of the pandemic, a considerable effort by the international scientific community has been conducted to understand the consequences of the lockdown periods on human sleep. However, the restraining measures led to the closure of research laboratories worldwide, and the only way to collect data during social distancing consisted of online surveys. Despite the intrinsic limitations of self-reported questionnaires (selection and response biases), the massive literature developed during the first pandemic phase provided a crucial contribution to the advancement of knowledge about the lockdown consequences.

Italy was the first Western country to deal with the pandemic and to apply a total lockdown, and the first evidence of the effect of the self-isolation period on sleep was addressed by an Italian study (Cellini et al., 2020). Through an online survey, the authors evaluated sleep quality of 1,310 young Italian citizens, retrospectively comparing the second week of lockdown with the previous month. The investigation showed decreased sleep quality, with an increase in poor sleep rates from 40.5% to 52.4% based on PSQI (Buysse et al., 1989). In the subsequent months, the detrimental effect of the self-isolation period was systematically confirmed in Italy (Casagrande et al., 2020; Gualano et al., 2020). One of the most extensive studies (Salfi, Lauriola, et al., 2021) on 13,989 participants reported alarming rates of poor sleepers (61.1%) and people with at least subthreshold insomnia (52.8%), based on PSQI and ISI (Bastien et al., 2001), respectively. As the virus spread worldwide, the international scientific interest increased in studying the repercussion of the stay-at-home orders on sleep. Blume and colleagues (2020) showed reduced sleep quality in three European countries (Austria, Germany, and Switzerland). Increased sleep disturbances were reported in Greece (Voitsidis et al., 2020), France (Kokou-Kpolou et al., 2020), Spain (Dal Santo et al., 2021), Belgium (Cellini et al., 2021), India (Gupta et al., 2020), China (Y. Li et al., 2020; Lin et al., 2021), Brazil (Taporoski et al., 2022), USA (Mandelkorn et al., 2021), Argentina (Valiensi et al., 2022), as well as by multinational studies (Mandelkorn et al., 2021; Yuksel et al., 2021).

In response to this emergent literature, some studies summarized the results coming from all over the globe. The first systematic review and meta-analysis on this topic (Jahrami et al., 2021) was carried out on 44 papers involving a total of 54,231 participants from 13 countries. This study estimated a pooled prevalence rate of sleep problems among all populations of 35.7%. A more recent systematic review and meta-analysis (Jahrami et al., 2022), covering the first six months of the pandemic, analyzed 250 papers comprising 493,475 participants from 49 countries. This study revealed a global prevalence of sleep disturbances of 40.5%, showing that sleep disturbances were higher during lockdown (42.5%) compared to no lockdown periods (38.0%). Finally, to provide a global overview of the insomnia symptoms, a systematic review and individual participant data meta-analysis was specifically performed on research involving the ISI (AlRasheed et al., 2022). This study analyzed 48 studies from 25 countries comprising 133,006 respondents, showing that the pooled estimate of insomnia symptoms (subthreshold and clinically significant) was 52.6%. Specifically, 16.7% of the population suffered from clinically significant insomnia, of which 13.8% suffered from moderate insomnia, and 2.5% suffered from severe insomnia.

The same meta-analyses tried to clarify potential risk factors for the development of sleep disturbances. One of these studies focused on possible differences between genders, reporting similar prevalence rates of sleep problems during the lockdown periods (Alimoradi et al., 2022). Notably, this evidence was supported by other meta-analyses that confirmed the absence of a moderating role of sex in the global prevalence rates of sleep issues (Alimoradi et al., 2021; Jahrami et al., 2021, 2022) and insomnia symptoms (AlRasheed et al., 2022). These findings are inconsistent with the pre-pandemic literature as sleep problems such as insomnia were typically more common among women (B. Zhang & Wing, 2006). However, the closure of the gender gap could be specifically ascribable to the confinement situation, as shown by our longitudinal study reported in Chapter 4 that highlighted a specific gender-related time course of sleep disturbances during prolonged self-isolation (Salfi et al., 2020). Comparing the third and the seventh weeks of lockdown, men reported decreased sleep quality and exacerbated insomnia symptoms, while women relieved insomnia severity. In this scenario, the higher prevalence of moderate/severe insomnia conditions among females was no longer present with the extension of the confinement period.

Meta-analytic studies also confuted a possible role of age in predicting sleep problems during the first pandemic phase (Alimoradi et al., 2021, 2022; AlRasheed et al., 2022; Jahrami et al., 2022). Again, this finding was unexpected as aging is typically associated with increased sleep disturbances (J. Li et al., 2018; Patel et al., 2018). As shown in Chapter 2 and 3, the absence of moderation effects of age could be driven by a specific vulnerability to sleep problems of the youngest people (Amicucci et al., 2021) and the student population under confinement (Jahrami et al., 2022; Viselli et al., 2021).

During the first contagion wave, healthcare professionals were the frontline workers in dealing with the emergency. The increased stressful workload, accompanied by higher contagion risk and irregular work schedules, could have led them to experience acute sleep disturbances (see Chapter 1 and 6). Some meta-analyses confirmed this idea, showing that sleep problems were most prevalent in healthcare workers (Alimoradi et al., 2021; Cénat et al., 2021; Jahrami et al., 2022). However, the literature in the field is heterogenous, and some reports failed to highlight statistically significant differences (AlRasheed et al., 2022), showing only numerical higher rates of sleep disturbances in healthcare professionals compared to the general population (Alimoradi et al., 2022; Jahrami et al., 2021).

The raised sleep issues under confinement were complemented by higher levels of mental health problems and decreased psychological well-being (Rajkumar, 2020; Vindegaard & Benros, 2020). Considering the bidirectionality between sleep and mental health (Alvaro et al., 2013), psychological distress could have played a crucial role in fostering sleep disturbances during the first contagion wave of COVID-19, as highlighted in Chapter 1. A systematic review and meta-analysis of 177 papers comprising 345,270 participants from 39 countries addressed this topic, evaluating the relationship between sleep problems and psychological distress during the first months of the pandemic (Alimoradi et al., 2021). The study revealed a moderate positive association between sleep disturbances and the severity of depressive and anxiety symptoms, emphasizing the need for effective programs treating mental health to improve pandemic-related sleep problems and *vice versa*.

Overall, the literature supported the evidence of a general increase in sleep disturbances in the worldwide population due to the exceptional measures applied to contrast the virus spread. In this scenario, the concomitant psychological distress could have significantly contributed to the development and exacerbation of sleep problems.

10.2 The sleep duration paradox

Although the stressful situation of self-confinement led to increased sleep problems among the general population, several studies reported a clear dissociation between trends of quality and quantity of sleep during the lockdowns. Before the COVID-19 outbreak, modern societies were already dealing with a sleep-loss epidemic (Centers for Disease Control and Prevention, 2015). The social and technological revolutions in the most industrialized nations have been associated with a decline in sleep duration across the last decades (Bixler, 2009). In this view, the loosening of social obligations during the lockdown seemed to paradoxically unlock more time for sleep (Kantermann, 2020). One of the first studies to address this issue was by Leone and colleagues (2020), who analyzed data from 1,021 respondents that completed questionnaires before and during the home confinement period. This study showed longer sleep duration during lockdown weekdays, with only 37.3% of participants not reaching the recommended 7 hours of sleep (Hirshkowitz et al., 2015) during the quarantine compared to 60.2% during the pre-pandemic period. Consistently, a larger multinational investigation (Global Chrono Corona Survey) on 7,517 respondents from 40 countries described longer sleep duration on workdays by 26 min than before COVID-19-mandated social restrictions (Korman et al., 2020). This phenomenon was systematically reported by several studies on adult populations (Blume et al., 2020; Cellini et al., 2020; Wright et al., 2020), and similar results were reported by research focused on younger people. A study involving 17,000 school-aged children and adolescents in the UK during the first national lockdown showed that participants reported longer sleep duration than in 2019, with a maximal improvement in younger secondary school students (+45 min) (Illingworth et al., 2022). These results were objectively confirmed by research that analyzed large amounts of smartphone users' data. Robbins and co-workers (Robbins et al., 2021) examined 2.9 million nights of sleep recordings from different continents, suggesting the lockdown periods were associated with a 20-min sleep extension worldwide compared with the previous year.

Further confirmations of the lockdown-induced sleep extension came from longitudinal studies carried out during different pandemic phases, and the study described in Chapter 8 provided a compelling countercheck of the *sleep duration paradox*. Indeed, we showed that, as the COVID-19 mitigation strategies were gradually loosened, sleep disturbances improved, while sleep duration decreased (−20 min) (Salfi, Amicucci, et al., 2022). Reduced sleep times after the lockdowns were confirmed by other studies using wearable sleep/activity trackers (Massar et al., 2021) and by investigations that analyzed large datasets from thousands of smartphone users (R. K. Yuan et al., 2022).

In sum, this literature supported the idea that lockdown periods provided people worldwide increased opportunities to sleep, suggesting the existence of a societal sleep deficit during pre-pandemic times. However, it was a transitory phenomenon that tended to disappear with the gradual resolution of the emergency.

10.3 Changes in sleep schedule and social jetlag

One of the most striking consequences of the lockdown periods was a pervasive shift in sleep schedules. The international literature consistently found delayed sleep timing, perhaps because of the relaxed social time pressure under self-confinement. Our large cross-sectional study (Chapter 1) showed that 59% of the sample reported delayed bedtimes and 63% delayed wake-up times during lockdown (Salfi, Lauriola, et al., 2021). The same studies that demonstrated the sleep extension effect also shed light on when people slept during the lockdown. In a sample of young workers, Cellini and colleagues (2020) demonstrated later bedtimes (+41 min) and even later wake-up times (+73 min). Similar results were obtained by investigations on a large sample of children and adolescents (Illingworth et al., 2022), as well as among university students (Marelli et al., 2021; Wright et al., 2020). Later sleep timing than 2019 was confirmed by a global analysis of almost 65,000 users of the "*Sleep As Android*" smartphone application, with the extent of changes strictly linked with the progression of the emergency in each country (R. K. Yuan et al., 2022).

During home confinement, people interrupted their daily social activity, and millions of workers and schoolers began to work from home with more flexibility in working hours. In this view, the lockdown represented a unique opportunity to reduce the discrepancy between the social/working clocks and the endogenous sleep-wake rhythm (*social jetlag*) (Wittmann et al., 2006). Several studies demonstrated that the changes in sleep schedule were significantly different between weekdays and weekends, and the most evident variations were found on weekdays (Blume et al., 2020; Korman et al., 2020; Leone et al., 2020; Wright et al., 2020). A large international study collecting data from 40 countries showed delayed mid-sleep time on workdays and free days by 50 and 22 min, respectively (Korman et al., 2020). These outcomes were objectively confirmed by analyzing nocturnal sleep patterns of ~113,000 sleep tracker users from 20 countries (Ong et al., 2021). This study found later midsleep times particularly on weekdays, whose extent was greater with increasing stringency of confinement measures. Based on this evidence, the current literature is consistent in indicating that the lockdown periods led to better regularity of sleep timing worldwide, alleviating the social jetlag phenomenon (Blume et al., 2020; Korman et al., 2020; Leone et al., 2020; Wright et al., 2020).

The confirmation of the lockdown-related delay of sleep times and reduced social jetlag also came from studies evaluating people longitudinally after lifting the stay-at-home orders. The study described in Chapter 6 showed that the participants went to sleep 36 min earlier and woke up 56 min earlier during a subsequent period of lighter restraining measures compared to the first lockdown (Salfi, D'Atri, et al., 2021). Moreover, a study using wearable sleep trackers showed an immediate increase in social jetlag as a consequence of the cessation of the isolation measures (Massar et al., 2021).

In conclusion, studies across multiple societies and different population groups showed a substantial shift to later sleep schedules during the lockdown, and the effect was more prominent on weekdays. This effect temporarily allowed people to comply with their circadian rhythms, leading to a transitory reduction of social jetlag.

10.4 The chronotype matter

The lifted societal demands under home confinement led to a worldwide reduction in social jetlag (Blume et al., 2020; Korman et al., 2020; Leone et al., 2020; Wright et al., 2020). This phenomenon is intrinsically linked with the circadian typology concept, with evening-types experiencing the most pronounced misalignment between social and biological clocks in modern society (Roenneberg et al., 2019). In this view, the lockdown periods could have unevenly affected the sleep patterns of different chronotypes.

The first to address this topic was the study described in Chapter 1. We found a higher prevalence of delayed bedtime (75.3%) and wake-up time (77.1%) in ET compared with MT people (44.3% and 49,8%, respectively). In stark contrast with pre-pandemic literature (Adan et al., 2012), ET slept longer than MT. However, a higher rate of ET respondents reported a negative impact of the confinement measures on sleep than the MT group (69.0% vs. 50.4%), and eveningness was associated with lower sleep quality and more severe insomnia symptoms (Salfi, Lauriola, et al., 2021). The vulnerability of late chronotypes during the lockdown periods was subsequently confirmed by a multinational investigation of 19,267 adults from 15 countries (Merikanto et al., 2022). The authors showed specific delayed sleep timing and increased sleep duration in the ET group under confinement compared with a retrospective pre-lockdown assessment. This effect led to the disappearance of the well-known differences in sleep duration between chronotypes. On the other hand, the same study highlighted that sleep problems (e.g., insomnia symptoms, nightmares, and daytime sleepiness) primarily increased among evening-types. A specific benefit on sleep duration of *night owls* was confirmed by another investigation on 610 US adults (Bottary et al., 2022) that found a stronger lockdown-related decrease in social sleep restriction (the difference between weekend and weekday sleep duration) among the ET population. Remarkably, the only investigation providing an objective sleep evaluation reported similar results (Pépin et al., 2021). Using data from 599 adults collected by a commercial EEG wearable headband, the authors compared confinement and the pre-lockdown period, demonstrating a larger shift to later sleep timing among the ET people, and no difference in sleep duration. Furthermore, eveningness preference was associated with a higher increase in REM sleep as a consequence of the longer sleep duration. Remarkably, looking at subsequent pandemic phases, the study described in Chapter 8 showed that the time course of sleep duration variations differed between chronotypes. We found that the gradual loosening of restraining measures led ET people to sleep less and less than morning-types across the subsequent two years from lockdown (Salfi, Amicucci, et al., 2022).

Overall, the literature described distinct changes in sleep patterns according to circadian typology. The lockdown period allowed ET people to sleep longer and more aligned with their endogenous clock (decreased social jetlag), suggesting a pre-existing sleep deficit in this population and greater susceptibility to pandemic-related societal changes. Meanwhile, these benefits were over-weighted by a concomitant worsening of sleep disturbances. On the other hand, the MT population was characterized by a more stable sleep schedule, with morningness suggested as a protective factor against the development of sleep disturbances during home confinement.

10.5 The impact of working/schooling adjustments

The societal changes imposed by the COVID-19 outbreak radically disrupted the labor market worldwide. Millions of people suspended their work, while most of the general population began working from home for the first time (Brynjolfsson et al., 2020; Eurofound, 2020). Home working removed the need to commute to the workplace and could be characterized by higher flexibility of working schedules. This situation drastically affected the daily routine as well as the sleep rhythms of workers, giving rise to an unprecedented natural experiment to understand how sleep changes when work hours and work environments change.

In one study, Leone and colleagues (2020) analyzed a subgroup of their sample that reported working from home, compared with people continuing to reach the workplace during the stay-at-home orders. The authors showed a specific benefit of working from home, as this condition was associated with longer sleep time, reduced social jetlag, and delayed sleep timing compared to the pre-pandemic assessment. Moreover, the study found an increased prevalence of remote workers reaching the minimum recommended 7 hours of sleep on weekdays during the lockdown (from 39% to 65%). In contrast, this prevalence was stable among those who continued to work outside (from 27% to 32%). Our investigation (Chapter 1) provided similar results as we demonstrated better sleep quality, lower insomnia severity, longer sleep duration (+27 min), and later bedtime and wake-up time among 3,536 adults working from home compared with 1,675 respondents who reached the workplace (Salfi, Lauriola, et al., 2021). Raman and Coogan (Raman & Coogan, 2021) confirmed these findings in a group of 797 Irish adults, showing that remote working during restrictions led to a more delayed midsleep time, longer workday sleep duration, and a more marked reduction of social jetlag than "essential" workers who continued to attend their workplace. However, the benefits of remote working may not have involved all circadian typologies in the same way, considering that the effect of working schedules on sleep quality and duration seems to depend on individual chronotypes (Juda et al., 2013; Vetter et al., 2015). In line with this idea, the results reported in Chapter 7 demonstrated that the effects of the working adjustments due to the COVID-19 outbreak were not generalizable to the whole population, highlighting better sleep quality, reduced insomnia symptoms, and longer sleep duration specifically among the *night owls* (Salfi, D'Atri, et al., 2022).

Another main consequence of the confinement measures was a pervasive upheaval in the school community. In-presence lessons were suspended, and remote learning became the norm for millions of students. Although homeschooling continued to be characterized by fixed schedules, removing morning commutes could have facilitated young people to follow their endogenous circadian rhythm, typically oriented to the eveningness (Roenneberg et al., 2019), with possible implications for their sleep health. This idea finds its roots in a large body of evidence demonstrating the beneficial effects of later school start time on the younger population' sleep (e.g., Alfonsi et al., 2020).

A Brazilian longitudinal study addressed this topic, comparing sleep measures collected during the lockdown with measures collected one year before among a sample of 259 high school adolescents (Santos & Louzada, 2022). The authors found that students during remote classes slept later, spent more time in bed (+152 min), and reported lower daily sleepiness compared to the pre-pandemic assessment. Moreover, the nap habits decreased during the lockdown as a consequence of increased sleep duration at nighttime. Consistently, another longitudinal study on 94 high school students showed substantially delayed sleep schedules during the pandemic. Moreover, participants who slept less than 7.4 hours before the COVID-19 outbreak reported longer sleep duration (+30 min) and improved sleep quality during school closures (Genta et al., 2021). Notably, similar findings were obtained by a study that evaluated sleep patterns using wrist actigraphy and sleep diaries, confirming later bedtime and wake-up time, longer sleep duration (+22 min) and lower sleepiness during school days from home (Stone et al., 2021).

In conclusion, working and schooling adjustments due to the COVID-19 outbreak compromised the role of one of the crucial *social zeitgebers*, leading to a general delay in sleep schedules. However, this scenario allowed both workers and students to sleep longer and better, suggesting a detrimental effect of working/schooling obligations in pre-pandemic times, particularly among the so-called *night owls*.

10.6 The role of daylight exposure

The sun's daily cycle substantially affects the circadian clock, sleep, and alertness. Ambient light is the most important *zeitgeber* and plays a crucial role in human physiology, entraining the circadian cycle to local time (Blume et al., 2019). Moreover, environmental light is intimately involved in the daily regulation of melatonin, a key sleep-promoting pineal gland hormone (Brown, 1994). High-intensity daylight exposure is beneficial for sleep, and some studies showed that low light level could impact sleep quality (Boubekri et al., 2014; Figueiro et al., 2017), lead to shorter sleep duration (Boubekri et al., 2014), cause longer sleep-onset latency (Figueiro et al., 2017), and interfere with sleep architecture (Wams et al., 2017).

During lockdown periods, the freedom of movement was substantially reduced as people were allowed to leave their homes for limited purposes, e.g., shopping for basic necessities and reaching the workplace. Consequently, one of the main implications of the stay-at-home orders was a large-scale reduction of daylight exposure. This situation could have interfered with sleep health and the circadian clock, and international agencies immediately recommended ensuring adequate daylight exposure during self-isolation (Altena et al., 2020; Morin et al., 2020). However, under strict confinement, many citizens could have hardly followed the advice, especially those living in homes with limited outside areas and small windows. Despite the significance of this topic, few studies were performed in this field. Blume and colleagues (2020) addressed this issue by surveying 435 adults and retrospectively comparing the lockdown scenario with a pre-confinement period. Their study showed decreased sleep quality under quarantine, but higher levels of daylight exposure buffered the sleep quality impairment and were associated with longer sleep time. An online survey performed during New Zealand's 2020 lockdown on 723 adults confirmed these results, reporting that people spent 1 hour less per day under the open sky. The reduced daylight exposure predicted worsened sleep quality compared with a pre-pandemic assessment (Gibson et al., 2022). Similar findings were obtained by the Global Chrono Corona Survey (Korman et al., 2022). The authors demonstrated a 1-hour median decrease in outdoor light exposure among 7,517 respondents during social restrictions. This variation was significantly associated with reduced sleep quality compared to the pre-lockdown period.

Besides sunlight, artificial light also plays a role in regulating sleep rhythms, with positive effects of high levels of office lights in the morning (Figueiro et al., 2017). However, indoor home light levels are generally lower than those for commercial office or school spaces, and some evidence suggested that staying in a bright room indoors may counteract sleep disturbances and sleep-related impairments under confinement (Figueiro et al., 2021).

In sum, the literature consistently demonstrated that reduced daylight exposure due to home confinement was an important contributory factor in explaining the raised sleep disturbances worldwide. Spending more time outdoors, when possible, represented an effective strategy to mitigate the detrimental effects of home confinement.

10.7 The screen time effect

The imposition of social distancing measures and the limitations of outdoor activities during the lockdowns had an inevitable consequence around the world: the massive use of digital devices. Self-confined people substantially increased the time spent on social networks and video calling to compensate for the limited face-to-face interactions. The world population began to spend more and more time facing a television or using the internet to occupy their growing free time and fight boredom. Furthermore, hundreds of millions of people began to work or attend school from home, leading to an unprecedented daily use of computers and tablets. All these factors led to a worldwide increase in screen time. A systematic review and meta-analysis of 89 studies (Trott et al., 2022) tried to summarize this phenomenon, indicating that the total screen time and leisure screen time (non-work/non-academic) of the adult population increased by 1 hour/day and 0.7 hour/day during the pandemic, respectively.

Notwithstanding that the use of computers, smartphones, tablets, and televisions may have helped to deal with the stressful confinement situation, the pre-pandemic literature consistently described a negative impact of evening screen exposure on sleep health. Several studies showed alerting effects of lights emitted by modern electronic devices by dampening melatonin release (Cajochen et al., 2011; A. Green et al., 2017).

The study described in Chapter 5 was the first to address a possible impact of the increased evening screen exposure during the lockdown on sleep, showing that the variations of screen habits before bedtime played a critical role in the time course of sleep problems under self-isolation (Salfi, Amicucci, et al., 2021). Our study demonstrated that increased screen time led to lower sleep quality, more severe insomnia symptoms, shorter sleep duration, prolonged sleep onset latency, and delayed bedtime and get up time. On the other hand, people who decreased their exposure to electronic devices reported the opposite pattern of outcomes. In line with these results, a recent systematic review confirmed the detrimental role of screen exposure on sleep duration and quality during the COVID-19 pandemic (Drumheller & Fan, 2022). Notably, the pandemic-related upsurge in screen time was reported in all age groups (Trott et al., 2022), and some studies confirmed the association between overuse of electronic devices and sleep problems also in the younger population (Bruni et al., 2021).

Another way that evening exposure to electronic devices could have impaired sleep is by the arousing and exciting effects of some screen-mediated contents (Higuchi et al., 2005). During the initial phase of the emergency, media have played an essential role in advising people about adequate prevention behaviors. However, a constant overexposure to ever-changing news and the overload of information consisting of potentially traumatic content and dramatic news may have contributed to deteriorating sleep by fueling anxiety and distress (J. Gao et al., 2020). In this view, an online survey of 1,005 adults representative of the

French population found that overexposure to media content about COVID-19 emergency was linked with more severe sleep problems, daytime impairment, and/or sleeping pill use during the self-isolation situation (Léger et al., 2020).
Overall, the current literature supported the assumption that the large-scale increased screen time during the social distancing period negatively impacted general population’s sleep health, also affecting their sleep schedule. The light *per se* and the COVID-19-related contents could have interfered with sleep patterns, simultaneously intervening in physiological and cognitive mechanisms of arousal.

10.8 The sleep-immunity interaction in the context of COVID-19

Good sleep is essential for the proper functioning of the immune system. Evidence from human studies indicated that sleep deprivation impacted immune-cell number, function, and cytokine production (Bryant et al., 2004). Consistently, short sleep duration and poor sleep efficiency have been associated with increased susceptibility to infectious illness and having a more challenging time fighting off infections (S. Cohen et al., 2009; Prather et al., 2015; D. E. Wang et al., 2016).
These results were confirmed by recent studies addressing the role of previous sleep on SARS-CoV-2 infection and COVID-19 course. A multicenter, retrospective cohort study including 164 infected and 188 uninfected Chinese adults showed that reduced sleep in the week before COVID-19 was associated with higher illness severity (B. Huang et al., 2020). This finding was later confirmed by a larger investigation utilizing 20 years of registry data and follow-up of over 500,000 people from the UK Biobank and FinnGen (Jones et al., 2022). In the study, Mendelian randomization suggested that insomnia is a causal risk factor for COVID-19 infection, hospitalization, and death from COVID-19.

Moreover, Vargas and colleagues (2023) analyzed a sample of 149 COVID-19 survivors demonstrating that those who reported insomnia in the two years before infection were more likely to report a longer symptom duration (24.8 sick days) than no insomniac group (16.1 sick days).

Beyond the acute illness phase, COVID-19 is characterized by a wide range of long-term symptoms (long COVID), whose incidence has been ascribable to an aberrant and persistent pro-inflammatory response on a systemic level after several months from infection (Crook et al., 2021; Phetsouphanh et al., 2022). The results described in Chapter 9 suggested to extending the role of pre-infection sleep to the occurrence of long COVID symptoms (Salfi, Amicucci, et al., 2023). Our study showed a predictive effect of previous sleep disturbances and short sleep duration in predisposing people to experience long-term manifestations after COVID-19. This hypothesis has been supported by another prospective investigation showing that sleeping less than 7 hours or more than 9 hours per night in 2017 was associated with increased risk for post-COVID-19 conditions compared with people who slept 7–9 hours (S. Wang, Li, et al., 2023).

On the other hand, consistent pre-pandemic literature suggested that insufficient sleep could impair the vaccination (Prather et al., 2021; Spiegel et al., 2002; Zimmermann & Curtis, 2019). These studies led to hypothesize that an adequate sleep amount and quality may promote the vaccination efficacy against SARS-CoV-2 (Benedict & Cedernaes, 2021; Rayatdoost et al., 2022). To date, only one study addressed this topic showing on a sample of 544 adults that insomnia was associated with lower antibody levels against COVID-19 three weeks after Pfizer–BioNTech vaccine inoculation (Athanasiou et al., 2023).

Further investigation is warranted, considering that the vaccination implications may not be limited to the odds of infection or illness severity. Consistently, a recent meta-analysis of six studies involving over 17 million individuals indicated that vaccination before SARS-CoV-2 infection led to lower risks of long-

COVID, with higher efficacy for two doses than one (Notarte et al., 2022). In this view, the sleep-vaccine efficacy interaction may also be relevant when examining the long-term COVID-19 sequelae.

In conclusion, a growing body of evidence supports the notion that good sleep is crucial for effectively dealing with SARS-CoV-2 infection. The benefits may also extend to the long COVID condition, although future studies should confirm the preliminary results clarifying the biobehavioral mechanisms involved. Finally, sleep could prove to be important in promoting the efficacy of vaccinations against SARS-CoV-2. However, this idea, which finds its roots in the pre-pandemic literature, has been scarcely addressed in the context of COVID-19.

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