Physical and mental fatigue and their risk factors in people with long-COVID after hospital discharge

An Experience Sampling Method-study on sleep quality and daily activities as risk factors for physical and mental fatigue

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Abstract (English)

Background. COVID-19 has left many people with long-COVID complaints which is often characterized by enduring severe physical and mental fatigue, although limited knowledge is available concerning their course and predictors over time. **Objective.** The relationship between physical and mental fatigue, and sleep quality and daily activities as risk factors were explored over a time period of two weeks to enhance knowledge of fatigue as a long-COVID complain. **Method.** The Experience Sampling Method (ESM) was used to collect repeated momentary self-reports seven times a day concerning current fatigue levels, activities, and sleep from ten Dutch ex-hospitalized people with long-COVID (M_{age} = 59.7, 50% women; 50% overweight; 80% one or more comorbidities) for 14 consecutive days. Linear Mixed Modelling (LMM) were applied to analyse the longitudinal relationship between fatigue, their disaggregated between-person and within-person effects, sleep, and daily activities over time. **Results.** Strong associations were found between physical and mental fatigue over time (β = .61, p = <.001) significant at both the between-person level (β = .55, p = <.001) and within-person level (β = .43, p = <.001). Sleeping more hours at night was found predictive of less physical and mental fatigue the following day (β = -.35, p = .001; β = -.27, p = .008). Performing household chores was found predictive of less physical fatigue (B = -.29, p = .019) and mental fatigue (B = -.30, p = .006) two hours later whereas eating/drinking was found predictive of increased physical fatigue (B = .20, p = .049). **Conclusion.** Fatigue was found a severe and common symptom in long-COVID, although this differed per person which indicated potential different long-COVID subgroups. Physical and mental fatigue had a strong relationship with less strong between- and within-person effects. Fewer hours of sleep at night seemed to increase mental fatigue the following day which was not researched nor confirmed in other lung diseases before. Certain daily activities were associated with increased fatigue at the time they were performed but not two hours later, suggesting they might be risk factors for a certain time period only.

Abstract (Dutch)

Achtergrond. COVID-19 heeft veel mensen met long-COVID-klachten achtergelaten die vaak worden gekenmerkt door aanhoudende ernstige fysieke en mentale vermoeidheid, hoewel er beperkte kennis beschikbaar is over hun beloop en voorspellers. **Doelstelling.** De relatie tussen fysieke en mentale vermoeidheid, en slaapkwaliteit en dagelijkse activiteiten als risicofactoren werden gedurende een periode van twee weken onderzocht om de kennis van vermoeidheid als een long-COVID-klacht te vergroten. **Methode.** De Experience Sampling Method (ESM) werd toegepast om zeven keer per dag herhaalde zelfrapportages te verzamelen met betrekking tot de huidige vermoeidheidsniveaus, activiteiten, en slaap, van tien Nederlandse ex-gehospitaliseerde mensen met long-COVID ($M_{leeftijd}$ = 59,7, 50% vrouwen; 50 % overgewicht; 80% één of meer comorbiditeiten) gedurende 14 opeenvolgende dagen. Linear Mixed Modeling (LMM) werd toegepast om de longitudinale relatie tussen vermoeidheid, hun uitgesplitste tussen- en binnen-persoon effecten, slaap, en dagelijkse activiteiten over de tijd te analyseren. **Resultaten.** Er werden sterke associaties gevonden tussen fysieke en mentale vermoeidheid over de tijd (β = .61, p = <.001) significant op zowel het niveau tussen personen (β = .55, p = <.001) als binnen personen (β = .43, p = <.001). Meer uren slapen 's nachts bleek voorspellend voor minder fysieke en mentale vermoeidheid de volgende dag (β = -.35, p = .001; β = -.27, p = .008). Het uitvoeren van huishoudelijke taken bleek voorspellend te zijn voor minder fysieke vermoeidheid (B = -.29, p = .019) en mentale vermoeidheid (B = -.30, p = .006) twee uur later op dezelfde dag, terwijl eten/drinken voorspellend bleek te zijn voor toegenomen lichamelijke vermoeidheid (B = .20, p = .049). **Conclusie.** Vermoeidheid bleek een ernstig en veelvoorkomend symptoom bij long-COVID, hoewel dit per persoon verschilde wat duidde op mogelijk verschillende subgroepen. Lichamelijke en mentale vermoeidheid hadden een sterke relatie met minder sterke effecten tussen en binnen personen. Minder uren slaap 's nachts leek de volgende dag de mentale vermoeidheid te vergroten, wat niet eerder werd onderzocht of bevestigd bij andere longziekten. Bepaalde dagelijkse activiteiten waren geassocieerd met verhoogde vermoeidheid op het moment dat ze werden uitgevoerd, maar niet twee uur later, wat suggereert dat ze slechts gedurende een bepaalde periode risicofactoren zouden kunnen zijn.

Table of Content

Introduction

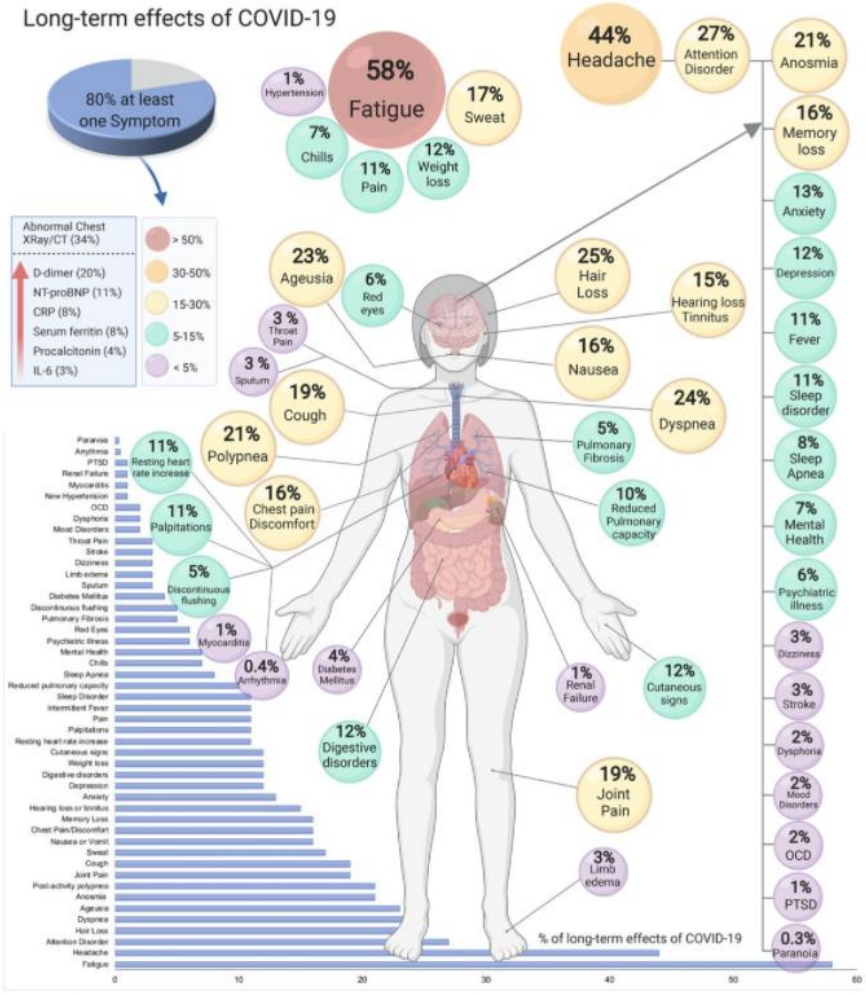
COVID-19 has spread over the world and has left millions of people with persistent so-called ‘long-COVID’ symptoms, although limited knowledge concerning these long-term effects is available. Making accurate predictions concerning the number of people who will progress to long-COVID after infection is complex due to the variation of incidence and mortality rates of COVID-19 between countries and the lack of a uniform scientifically accepted definition. What is known is that long-COVID can affect people around the whole spectrum of COVID-19 disease severity, from very mild to very severe forms (Crook et al., 2021), making the severity of infection irrelevant for the risk of developing long-COVID.

The National Institute for Health and Care Excellence (NICE) defines long-COVID as ‘‘signs and symptoms developed during or after an infection consistent with COVID-19, [that] continue for more than twelve weeks and are not explained by an alternative diagnosis’’ (NICE, 2020, p. 5). It is increasingly becoming clear that COVID-19 infection, initially expected to result in lung disease, may have long-term effects focused on other organs as well (Wild et al., 2021). A wide range of both physical and mental long-term symptoms has been reported thus far, including neurocognitive complaints (brain fog, dizziness, loss of attention), respiratory complaints (fatigue, cough, throat pain), psychological complaints (anxiety, depression, insomnia) and other manifestations such as skin rashes (Fernández-de-las-Peñas et al., 2021). In a meta-analysis by Lopez-Leon and colleagues (2020), fatigue and headache were the most reported long-COVID symptoms (See Figure 1). However, due to inconsistent definitions, patient groups, and the time range in which long-COVID symptoms are researched, it is complex to describe the nature of long-COVID. Table 1 represents this issue.

Reported risk factors for developing long-COVID are still under investigation, but there seems to be an association between long-COVID and several patient characteristics. These include having an age above 50 years, being female, and experiencing pre-existing conditions including hypertension, obesity, or psychiatric conditions (Tenforde et al., 2020). However, several cases of long-COVID have been found where people do not match these characteristics (Tenforde et al., 2020). Previous studies mainly focused on socio-demographic and biological aspects contributing to long-COVID, although research has shown that (the presence or absence of) psychological factors and behaviours can contribute to the development of conditions as well (Cohen & Herbert, 1996).

Figure 1

Reported symptoms found in the meta-analysis of Lopez-Leon and colleagues



Note. From ‘‘More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis,’’ by S. Lopez-Leon, S., T. Wegman-Ostrosky, C. Perelman, R. Sepulveda, P. A. Rebolledo, A. Cuapio, and S. Villapol, 2021, *Scientific Reports*, *11*(1), p. 9 (https://doi.org/10.1101/2021.01.27.21250617)

In terms of behaviours associated with conditions in general, it is known that certain behaviours result in increasing symptoms, and experiencing symptoms can in turn induce certain behaviours. To date, however, no studies concerning specific behaviours associated with increasing long-COVID symptoms are available. This study aims to explore this to provide fundamental knowledge on long-COVID and to provide information regarding interventions targeting potentially relevant behaviours.

Table 1

Differences in criteria for long-COVID, patient groups, and most reported symptoms

Authors	Time-range criteria for long-COVID symptoms	Patient group	Most reported symptoms
Aiyegbusi et al. (2021)	Five weeks or more	Various (hospitalized, self-reported social media users, clinic patients)	Fatigue; dyspnoea; muscle pain; joint pain; headache; cough
Huang et al. (2021)	Six months or more	Hospitalized patients	Fatigue; muscle weakness
Lopez-Leon et al. (2020)	Two weeks to three months	Various (mild, moderate, severe, hospitalized)	Fatigue; headache; attention disorder; hair loss; dyspnoea
Mandal et al. (2021)	Eight weeks or more	Hospitalized patients	Fatigue; dyspnoea; cough; depression
Sudre et al. (2021)	Four weeks or more	Self-reported app-users	Fatigue; headache; dyspnoea; anosmia

Fatigue in chronic (lung) diseases

Across the different studies so far, the most reported symptom in long-COVID seemed to be fatigue. Fatigue was found to be a severe symptom in people with long-COVID, and caused significant daily life dysfunction (Van Herck et al., 2021; Vink & Vink-Niese, 2020). However, the severity and characteristics of fatigue in long-COVID during the day and different weekdays remained unclear, even though it is known that certain daily activities resulted in increased fatigue in, among others, post-stroke patients (Lenaert et al., 2020).

Fatigue can generally be differentiated in physical and mental fatigue. Physical fatigue takes into account muscular exhaustion and impaired physical performance, and mental fatigue considers mental tiredness, loss of attention, concentration, or motivation (Lewko et al., 2009). The relationship between the two types of fatigue is complex and can differ among clinical and non-clinical populations and even among different lung diseases. For instance, in non-clinical populations, physical fatigue seemed to induce mental fatigue (Xing et al., 2020) and mental fatigue seemed to induce physical fatigue (Mehta & Parasuraman, 2014). In a cross-sectional study with multiple sclerosis patients, a correlation between physical and mental fatigue was discovered, although whether one type of fatigue induced the other type remained unclear (Ford et al., 1998). In addition, COPD patients were relatively more physically fatigued and relatively less mentally fatigued (Lewko et al., 2009). Sarcoidosis patients, on the other hand, reported being relatively more mentally fatigued than being physically fatigued (Kahlmann et al., 2020).

The risk factors for physical and mental fatigue also seemed to differ among populations. For instance, in lung-disease patients and fibromyalgia patients, cognitive workload was found to increase mental but not physical fatigue (Dailey et al., 2015; Zhang et al., 2015) and in healthy people, cognitive workload was found to increase physical but not mental fatigue (Boolani & Manierre, 2019). Moreover, negative cognitions in patients with chronic fatigue, such as worry and rumination, resulted in physical fatigue (Fernie et al., 2016) whereas, in multiple sclerosis patients, somatising cognitions of fatigue were associated with increased feelings of mental fatigue (Vercoulen et al., 1996).

These studies give an impression on the ambiguous nature and the risk factors that increase physical and mental fatigue among different populations, but neither the risk factors nor the timely nature of associations with fatigue are usually considered. The longitudinal relation between physical and mental fatigue and the factors associated with both types of fatigue over time in people with long-COVID remain unclear. In addition, the variance of fatigue between people and within individuals experiencing long-COVID has not been researched at all, although between- and within-person relations can be empirically and conceptually different (Zhang & Wang, 2014). Between-person effects represent the differences between people over time. For instance, the extent to which people who exercise a lot differ in mental health from people who exercise less. Within-person effects represent differences within one person over time. For instance, the extent to which an individual is mentally healthier when this person exercises more than when this person does not (Wang & Maxwell, 2015). The current study aims to explore abovementioned aspects.

Sleep quality as a risk factor for fatigue in chronic (lung) diseases

One factor that is widely established to worsen fatigue is sleep quality (Kiliç & Parlar, 2021) and is thus important to consider when studying fatigue in people with long-COVID. Sleep quality takes into account, among others, sleep duration, sleep disturbances, and resting during the day. It is expected that when sleep quality decreases, people with long-COVID feel more fatigued during the day, as has been shown among non-clinical populations (Boolani & Manierre, 2019), COPD patients (Vanfleteren et al., 2020) and fibromyalgia patients (Nicassio et al., 2002). Nonetheless, there are studies where a direct relationship between sleep quality and fatigue in other clinical populations, such as rheumatoid arthritis patients (Mancuso et al., 2006; Minnock et al., 2015; Treharne et al., 2008) and interstitial lung-disease patients (Agarwal et al., 2009) could

not be confirmed. Although it was found that long-COVID resulted in both decreased sleep quality and fatigue (Crook et al., 2021), it is not known whether sleep quality is actually a risk factor for physical and mental fatigue over time in people with long-COVID.

Risk behaviours for fatigue in chronic (lung) diseases

What is also not studied before are risk behaviours that worsen fatigue in people with long-COVID, even though it is known that fatigue was related to specific types of behaviours in other lung diseases (Swain & Jones, 2018). Certain types of behaviours could also be a risk factor for worsening fatigue in people with long-COVID. These risk behaviours can for instance be poor coping, a lack of balancing activities and rest, little involvement in social support (Kahlmann et al., 2020), all-or-nothing patterns of behaviour (Fernie et al., 2016), and being physically inactive (Woo, 2000). For instance, fatigued patients tended to move less, making them more fatigued (Vercoulen et al., 1997). A longitudinal study by Lenaert and colleagues (2020) reported that post-stroke patients were most fatigued when resting and doing nothing as a daily activity over time. Based on that study (Lenaert et al., 2020), the current study considers the following categories as potentially relevant daily activities: doing nothing, strenuous relaxation, passive relaxation, sleeping or resting, work or school, doing household, eating or drinking, self-care, being on the go, and social interaction. To explore the potential of behavioural factors associated with increasing fatigue in people with long-COVID, focussing on daily activities can give a first insight into which aspects of daily life might increase fatigue symptoms over time. Moreover, previous studies concerning other lung diseases did not focus on the potentially risk of daily activities increasing fatigue over time, nor the timely nature of associations with fatigue. Therefore, based on the abovementioned paragraphs, the research questions of this study are:

How severe are physical fatigue and mental fatigue and how are they associated over time in Dutch people with long-COVID at least six months after hospital discharge?

Are there differences in the association between physical fatigue and mental fatigue when comparing between persons and within persons over time in Dutch people with long-COVID at least six months after hospital discharge?

To what extent is sleep quality a risk factor for increasing physical fatigue and mental fatigue over time in Dutch people with long-COVID at least six months after hospital discharge?

Which daily activities are risk factors for increasing physical fatigue and mental fatigue over time in Dutch people with long-COVID at least six months after hospital discharge?

To research this in detail over time, data based on daily life experiences are needed. Retrospective surveys focus on the attention people have paid to certain situations and whether the details of these situations were processed consciously or not (Csikszentrnihalyi, 2014). Data based on daily life experiences, on the other hand, can reflect the structure and relations of phenomena as they occur over time without having to rely on the subjective and limited capacity of human attention and memory (Csikszentrnihalyi, 2014), which may be even more reduced in people with long-COVID experiencing cognitive dysfunction.

The Experience Sampling Method (ESM) is a highly ecological valid method in which daily life experiences of phenomena occurring in small samples of individuals can be measured (Weaving et al., 2017). ESM is suitable to measure momentary behaviours, moods, physiological outcomes and other factors over longer periods of time. Short self-report measures on several occasions during everyday life are often used, whether this is done via paper or mobile devices. Measurements typically last one week up to four weeks (Hardeman et al., 2019), making it a longitudinal way to repeatedly assess daily life phenomena. Because these behaviours and symptoms are measured repeatedly at an exact time point, no recall on situations or feelings is needed, decreasing the risk of memory bias (Conner & Lehman, 2012). ESM can also provide insight into symptom variance (Fisher et al., 2018) which is needed to measure within- and between-person effects. This can provide valuable input to developing personalized real-life interventions such as Just-In-Time Adaptive Interventions (JITAIs), which can provide the right type of support, at the right time, by adapting to the changing experiences of an individual (Nahum-Shani et al., 2018).

Method

The current study concerns an exploratory ESM study design. It is a complementary study derived from an ongoing longitudinal cohort study on health after COVID-19 hospital discharge from the MST hospital in Enschede. Ex-patients were invited to fill in a baseline survey directly, three months, six months, nine months and twelve months after hospital discharge. Demographic characteristics were also measured concerning factors that potentially increase the chance of obtaining long-COVID, such as older age, a high Body Mass Index (BMI) (Tenforde et al., 2020), being female (Sudre et al., 2021), lower education level (Lees, 2021) and having comorbidities (Tenforde, 2020).

Participants

During the longitudinal cohort study, participants who stated they felt significantly worse one year after hospital discharge (n = 16) and participants who stated they felt significantly better one year after hospital discharge (n = 12) were invited to participate in interviews to gain insight into their perspective on their current health status (see Appendix A). The 16 participants who stated during the interviews that their health had deteriorated were asked to participate in the current ESM study, of which 11 enrolled. One participant did not meet the required compliance rate of 30% or more of the ESM assessments (Delespaul, 1995), and one participant dropped out after four days of assessment. The drop-out did meet the 30% total compliance rate and a sensitivity analysis showed very little difference when including and excluding this participant, thus this participant is included in the analysis. This resulted in a sample of N = 10 for the current ESM study. Every participant started with the ESM study after being interviewed, thus every participant had a different start day.

The average age of the sample was 59.7 years (SD = 7.65) whereas the range was within 48 years and 76 years. The number of female participants was equal to male participants (n = 5, 50%). Half of the sample was overweight (n = 5, 50%), the other half had a range between a healthy weight to morbidly obese. Three participants had the education level of junior general secondary education (MAVO) (n = 3, 30%), the other participants were differently educated, from lower vocational education (LTS) to university (WO). Lastly, two participants had no comorbidity (n = 2, 20%), and the remaining of the sample had one or more comorbidities (n = 8, 80%).

Materials and measures

The ESM study was conducted using the design- and application platform Ethica (Ethica Data, 2020) in the form of an application on the smartphones of the participants. On the first day, participants received an identical survey to the actual research survey to practice with the application. The actual daily survey consisted of two types: one retrospective sleep survey in the morning, provided once a day, and one survey concerning momentary behaviours and feelings, provided six times a day.

The morning survey (see Appendix B) contained six questions concerning participants' sleep quality which was assessed with the following constructs: hours of sleep, trouble with sleeping, the frequency of naps taken during the day and the hours of sleep obtained with naps (e.g. 'How many hours did you sleep last night?'). The other survey (see Appendix C) contained 21 questions concerning momentary complaints such as pain, fatigue and dyspnoea, and mood such as feeling sad, disappointed, or relaxed (e.g. 'Right now, I feel mentally tired'; 'Right now, I am experiencing a headache'; 'Right now, I feel anxious'). The questions were based on multiple validated relevant questionnaires (Brys et al., 2020; Dietvorst et al., 2021; Jean et al., 2020; Lenaert et al., 2020; Maes et al., 2015; Worm-Smeitink et al., 2021). Lastly, one question was focused on the activity a participant was involved in at the moment of assessment which could be answered by choosing one of the provided options or choosing 'Other, namely…' and filling in their answer using a text box. The answer options for activity were doing nothing, strenuous relaxation (e.g. walking), passive relaxation (e.g. reading a book), sleeping or resting, working, eating and drinking, self-care (e.g. body hygiene), on the road, and social interaction (e.g. having a conversation). All the questions could be answered using a Likert scale or the Visual Analog Scale (VAS).

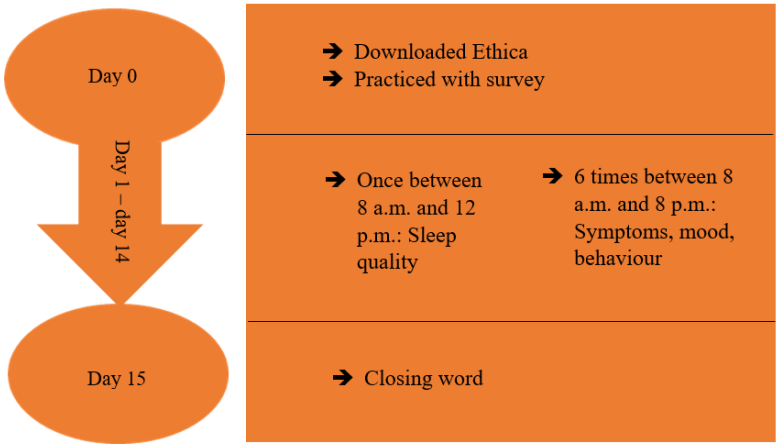
Design

Based on the guidelines of Conner and Lehman (2012), several design choices for the study were made. The current ESM study lasted for 14 consecutive days with an additional fifteenth day, since for collecting ESM data, a minimum of one week produces a representative sample and after more than 14 days of data collection, the quality of data tends to decline (Hektner et al., 2007; Stone et al., 1991). See Figure 2 for a visual overview of the duration of the study. The study was conducted using the *signal-contingent sampling strategy* where participants received unpredictable notifications at random times within equal two-hour time intervals

throughout the day. Participants received each day six unpredictable notifications for the mood and symptoms survey between 8 a.m. and 10 a.m., between 10 a.m. and 12 p.m., 12 p.m. and 2 p.m. et cetera, up until 8 p.m. According to Van Berkel et al. (2017), there is an 83% probability that people interact with the application within five minutes after notification. To reduce burden since this study dealt with ill participants, the time to fill in the mood and symptoms survey after each notification expired after fifteen minutes. The morning survey was provided once a day at 8 a.m. and was open up until 12 p.m. According to Klasnja et al. (2008), the balance between optimal results and annoyance lies between five to eight measurements a day, thus a total of seven measurements a day was seen as an optimal number of measurements.

Figure 2

Flowchart of the study design



Procedure

The Ethical Committee of the faculty Behavioural Sciences of the University of Twente approved the study in May 2021 (request number: 210799). Data was gathered between September 1 and November 5, 2021.

The Ethica questionnaire was pilot-tested by the research team and a student with long-COVID symptoms. Practical issues such as non-visible VAS-scale lines were fixed afterwards. The participants signed informed consent before being interviewed and were asked to join the ESM study during the interview. When starting the ESM study, the participants again signed a within-app informed consent provided as default by Ethica.

Data analyses

The statistical program IBM SPSS Statistics 26 was used to analyse the data. Statistical tests were considered significant at a two-sided alpha level of .05 or lower. Based on the guideline of Cohen (1988), when the standardized beta was >.1 (.-1), this was considered a small effect, when beta was >.3 (-.3), this was considered a moderate effect, and when beta was >.5 (-.5), this was considered a strong effect.

Descriptive statistics were performed and visualisations were created to get an overall impression of the sample and the relevant variables. In addition, a time variable concerning the duration of the total fourteen days of data collection and a variable concerning the six measurements on mood and symptoms each day were created. Since the assessment period consisted of 14 consecutive days and the participants experienced symptoms, the chance of missing an assessment was increased (Myin-Germeys et al., 2018). Also, data points were not independent of each other since they were collected multiple times a day for the same individuals. These factors provided a demarcation to select Linear Mixed Models (LMM) as the appropriate statistical model for testing associations, since LMM can deal with large amounts of missing data as well as data that is not independent (Myin-Germeys et al., 2018), making LMM a suitable method to use when dealing with longitudinal and repeated data (Cnaan et al., 1997).

The first research question concerning the overall association between physical and mental fatigue was tested by transforming the variables to z-scores to obtain standardized regression coefficients. Beta estimates were computed using LMM analysis with first-order autoregressive (A1) repeated covariance type, and the overall time-points across the study were set as the repeated measures. Physical fatigue was set as the fixed covariate and mental fatigue as the dependent variable.

For the second research question, person mean scores (for between-person associations) and person mean centred scores (for within-person associations) of physical fatigue were computed to allow disaggregation of between-person and within-person associations (Curran, & Bauer, 2011) using the Aggregate function in SPSS, and were also transformed to z-scores. LMM was performed where mental fatigue was set as the dependent variable and the person mean score and person mean centred score of physical fatigue were collectively set as the fixed covariates.

For the third research question concerning whether sleep quality is a risk factor for physical and mental fatigue, hours of sleep, trouble with sleeping, frequency of naps and hours of

sleep obtained with naps were transformed to z-scores and separately set as fixed covariates in a series of LLMs, to obtain unadjusted beta estimates. Physical fatigue was set as the dependent variable, followed by mental fatigue in the next LMM. Afterwards, hours of sleep, trouble with sleeping, frequency of naps and hours of sleep obtained with naps were set as the fixed covariates at the same time to obtain adjusted beta estimates.

To analyse whether daily activities were risk factors of physical and mental fatigue, separate dummy variables of the 'context' question were made where a 0 meant no involvement in a particular daily activity, and 1 meant involvement of that activity (Caudill et al., 2013). These variables were not standardized. To obtain unadjusted beta estimates using LMMs, the daily activities were separately set as the fixed factors and physical fatigue was set as the dependent variable, and later mental fatigue was set as the dependent variable. 'Doing nothing' was set as the reference category for all activities. Lastly, another series of LMMs was conducted where one-moment lagged (T-1) scores (Jans-Beken et al., 2019) of the daily activities were separately set as the fixed factors, and physical fatigue was set as the dependent variable, followed by mental fatigue. The one-moment lagged predictions represented associations with fatigue approximately two hours later on the same day. To reduce the risk of daily activities performed at T6 (evening day one) predicting fatigue at T1 (morning day two), the first time-point each day was filtered out in the analysis.

Results

Overall, participants responded on average to 62 out of 98 prompts, reflecting a response rate of 60.8% (*SD* = 20%, range = 31%-92%). The mean physical fatigue score of the total sample during the total assessment period was 4.9 (*SD* = 1.6) and the mean mental fatigue score of the total sample during the total assessment period was 4.2 (*SD* = 1.7), with a possible score range of 1 (*not at all fatigued*) through 7 (*worst imaginable fatigue*).

Fatigue in people with long-COVID

Description of physical and mental fatigue

As can be seen in Figure 3, which visualizes individual participants' mean physical fatigue scores per time-point over all days during the assessment period, physical fatigue seemed to be fairly consistent for most participants during the day. The morning fatigue scores were quite similar to the midday and evening fatigue scores. For some participants, there were notable fluctuations in physical fatigue on a daily basis. For instance, participant 4 felt more tired between 10 a.m. and 11 a.m. than the rest of the day. Participant 5 started the day with relatively little fatigue, whereas this increased between 10 a.m. and 11 a.m. During the lunch break, this participant seemed less fatigued, and this increased as the day passed by. At the end of the working day, around 4 p.m. and 5 p.m., these fatigued feelings decreased again, ending the day with relatively little fatigue. Participants 8 and 9 seemed less fatigue in the mornings and their fatigue levels increased during the day. Overall, the variation and severity of physical fatigue differed per participant. For instance, participant 10 experienced most of the time the worst imaginable fatigue, whereas participant 9 had moments they did not experience severe fatigue.

Figure 4 represents participants' mean physical fatigue scores over all time-points during the assessment period per weekday, showing that physical fatigue seemed to differ more clearly over the different weekdays. For instance, participant 2 started the weeks on Monday with relatively severe fatigue whereas this decreased on Fridays and the weekends. On the other hand, participant 8 became more fatigued from Fridays on up until Thursdays, and this decreased considerably on Wednesdays. On Wednesdays other participants also seemed least physical fatigued, however, Wednesdays also had the lowest assessment compliance rates. This might be explained by the fact that most participants started on Thursdays and ended on Tuesdays, missing a Wednesday to answer the surveys. For participant 9, however, the weeks started with relatively little fatigue and this increased until a peak was reached on Wednesdays, which decreased again

with the lowest fatigue scores on Sundays. Saturdays and Sundays seemed for the majority of the participants a day where they were less fatigued. However, some participants who were less physical fatigued on Saturdays felt more physical fatigued on Sundays. These results might be linked to activities performed during those days which will be described later on. See Appendix D for more visualisations of physical fatigue.

Figure 3

Mean physical fatigue score per participant per time-point during the total assessment period

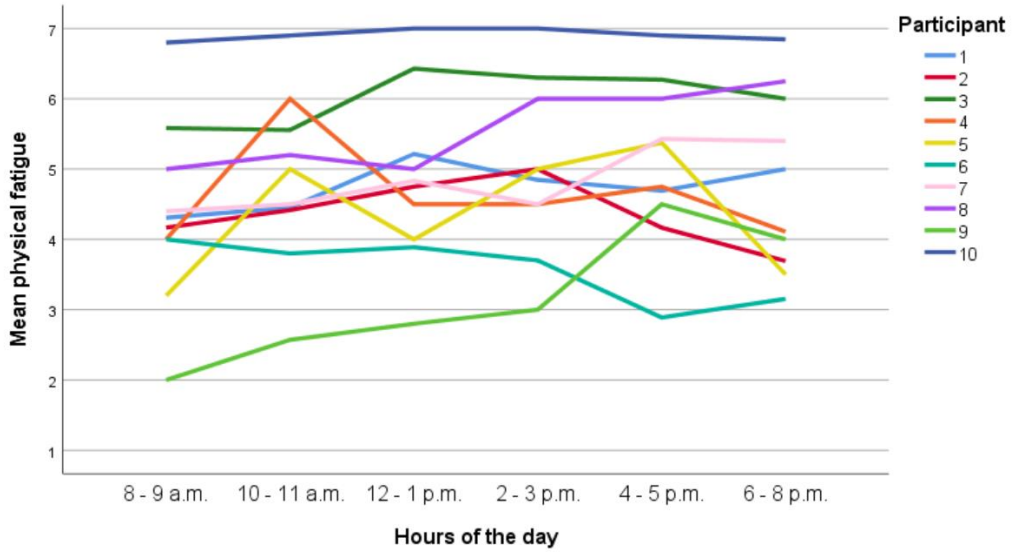
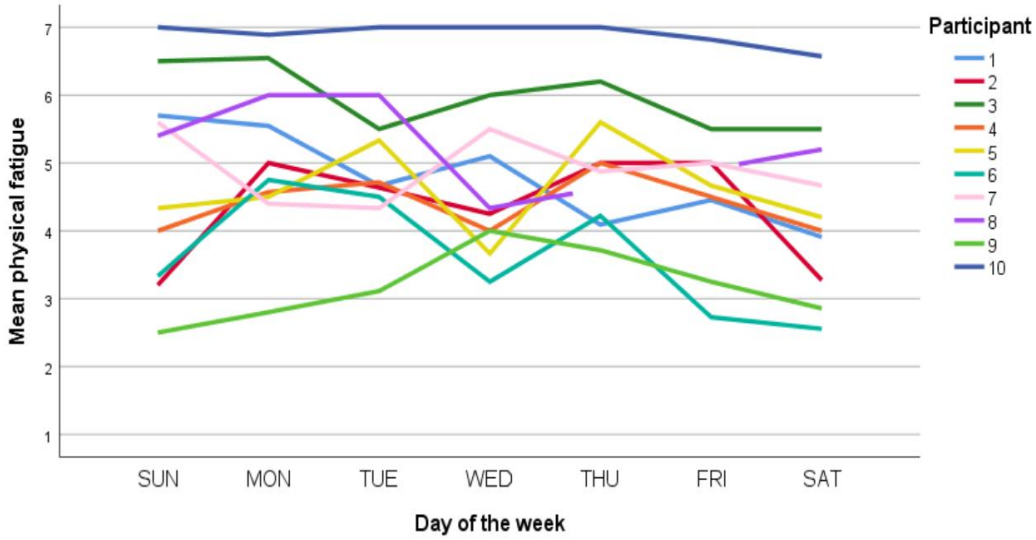


Figure 4

Mean physical fatigue score per participant per weekday during the total assessment period



When looking at the mean mental fatigue scores per different time-points, which is presented in Figure 5, it can be stated that mental fatigue also seemed fairly consistent during the day for participants 1, 2, 3, 5, 6 and 10. On the other, for participants 7, 8 and 9, from the afternoon until the evenings their mental fatigue scores seemed to increase which also seemed to happen with their physical fatigue. Overall, similar to physical fatigue, the variation and severity of mental fatigue differed per participant. For instance, participants 9 and 10 experienced most of the time very severe mental fatigue, whereas participant 4 had moments with no mental fatigue.

Figure 5

Mean mental fatigue score per participant per time-point during the total assessment period

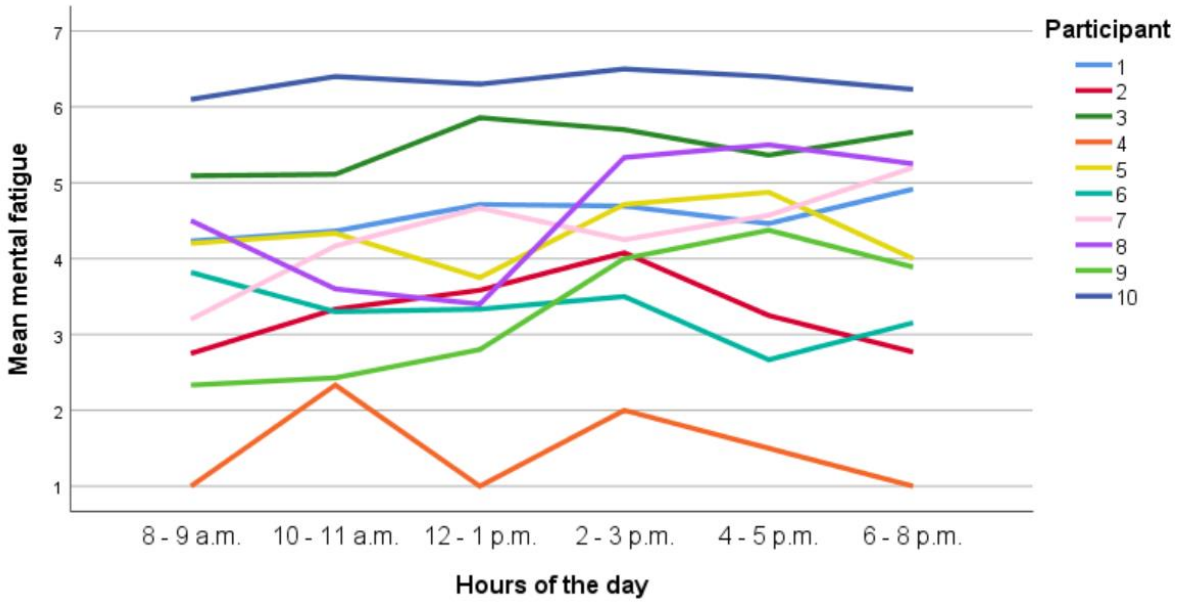
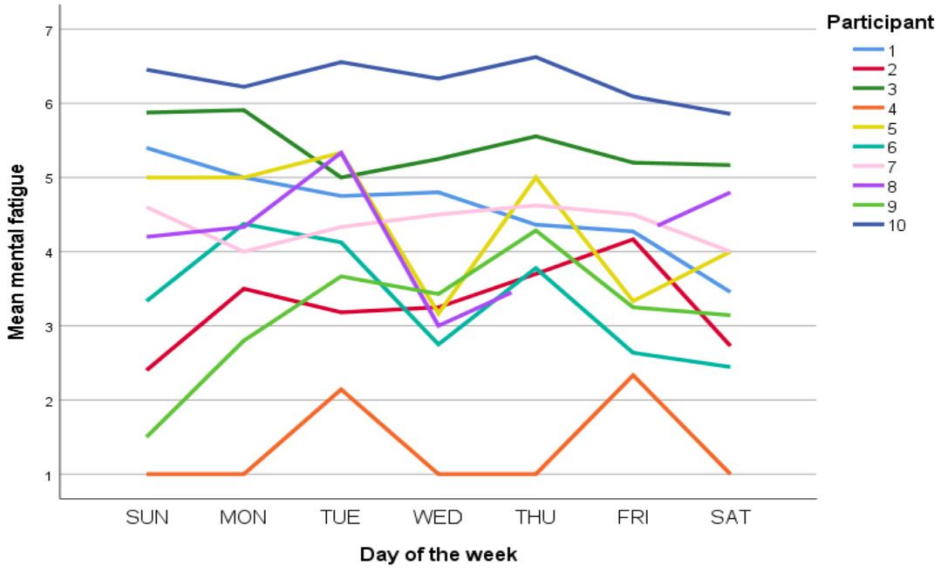


Figure 6 represents the mean score of mental fatigue per weekday during the assessment period, showing that there was a somewhat discrepancy between the days participants felt more and less mentally fatigued. On Mondays, Tuesdays and Thursdays mental fatigue seemed to increase whereas on Fridays, Saturdays and Sundays it seemed to decrease. This might be connected to their activities performed on those days. On Wednesdays, participants seemed less mentally fatigued, however, as stated before, Wednesdays had less frequent assessment points. For participant 1, mental fatigue seemed to decrease more every day, as was the same with their physical fatigue score. For participant 9, mental fatigue increased up until Thursday and decreased the days after, whereas their physical fatigue started to decrease a day earlier, on

Wednesday. Overall, when comparing the mental fatigue scores with the physical fatigue scores, it can be seen that most of the participants who experienced high physical fatigue also experienced high mental fatigue, except for participant 4. See Appendix E for more visualisations of mental fatigue.

Figure 6

Mean mental fatigue score per participant per weekday during the total assessment period



Association between physical fatigue and mental fatigue across all time-points

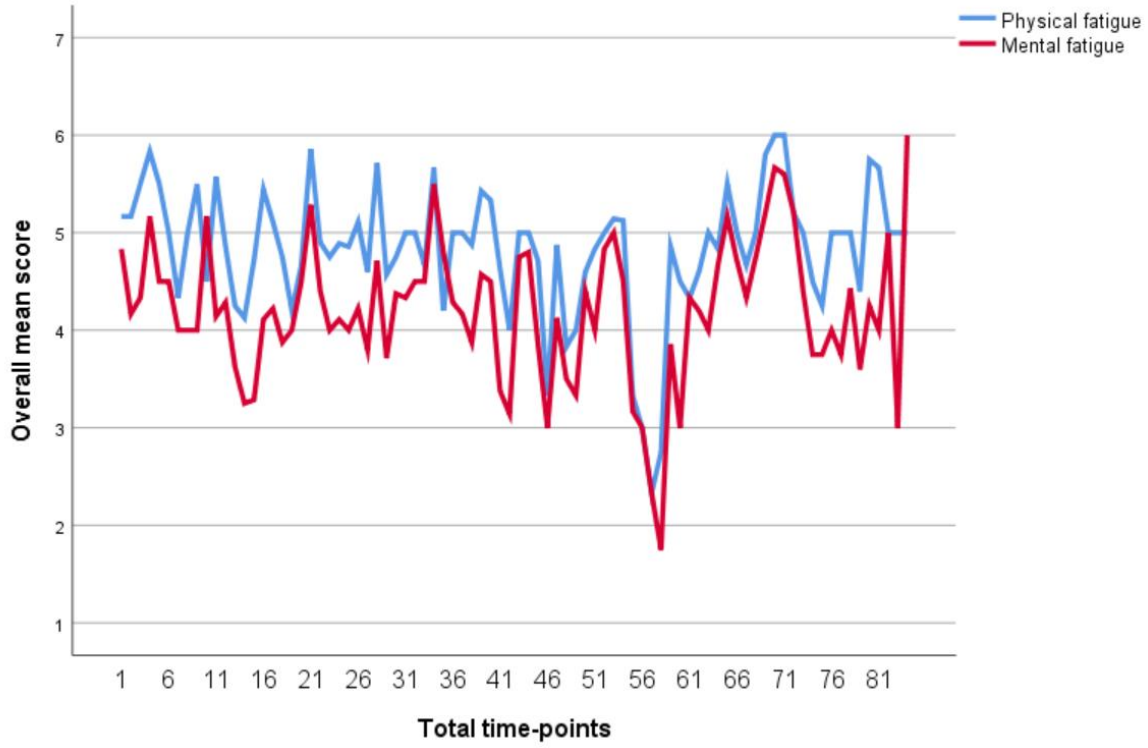
For an overall momentary association covering all time-points, LMM analysis revealed that physical fatigue was significant and strongly positive associated with mental fatigue (β = .61, *SE* = .03, *p* = <.001) at the same time-point. Figure 7 visualizes this clear association at the group level over time.

Between-person and within-person effects of fatigue

Slightly different associations for fatigue between persons and within persons were found. Overall, a significant and strongly positive association was found between persons (β = .55, *SE* = .06, *p* = <.001). When a participant was more physically fatigued than another participant on average, they experienced more mental fatigue than the other participant. A significant but moderately positive within-person association was observed (β = .43, *SE* = .02, *p* = <.001). When a participant was more physical fatigued than usual, they felt more mentally fatigued.

Figure 7

Mean physical and mental fatigue score of the sample during the total assessment period



Note. Answer range counts from 1 – not at all fatigued to 7 – worst imaginable fatigue.

Sleep quality and physical fatigue and mental fatigue in people with long-COVID

Description of sleep quality

Most of the time, participants slept between six and eight hours a night (Appendix F). During the total assessment period, most nights were concerned with a little bit of trouble with sleeping (Appendix G). Whether participants did or did not nap during the total assessment period was almost equal (Appendix H). Most of the times participants had napped, they took one nap per day (Appendix I) which usually lasted one to two hours (Appendix J).

Predictive value of sleep quality on fatigue the following day

Since sleep quality was measured retrospectively and fatigue was measured real-time, LMM were applied to explore the predictive value of hours of sleep, trouble with sleeping, frequency of naps and hours of naps on physical and mental fatigue. For physical fatigue, the unadjusted beta's showed that hours of sleep (β = -.27, *SE* = .06, *p* = <.001) was significantly but

weak negatively associated with physical fatigue. Also, trouble with sleeping (β = .20, *SE* = .06, *p* = .002) was significantly but weakly positive associated with physical fatigue. Frequency of naps (β = .01, *SE* = .09, *p* = .992) and hours of naps (β = -.15, *SE* = .09, *p* = .098) were not found significantly associated with physical fatigue. When controlling for the different sleep constructs, only hours of sleep remained significantly predictive (β = -.35, *SE* = .10, *p* = .001). More hours of sleep at night decreased physical fatigue the following day.

For mental fatigue, the unadjusted beta's showed that hours of sleep was significant but weak negatively associated with mental fatigue (β = -.15, *SE* = .07, *p* = .026). Trouble with sleeping (β = .05, *SE* = .07, *p* = .459), frequency of naps (β = -.00, *SE* = .07, *p* = .967) and hours of naps (β = -.10, *SE* = .08, *p* = .239) were not found significant. When controlling for the different sleep constructs, hours of sleep remained significant (β = -.27, *SE* = .10, *p* = .008). More hours of sleep at night decreased mental fatigue the following day.

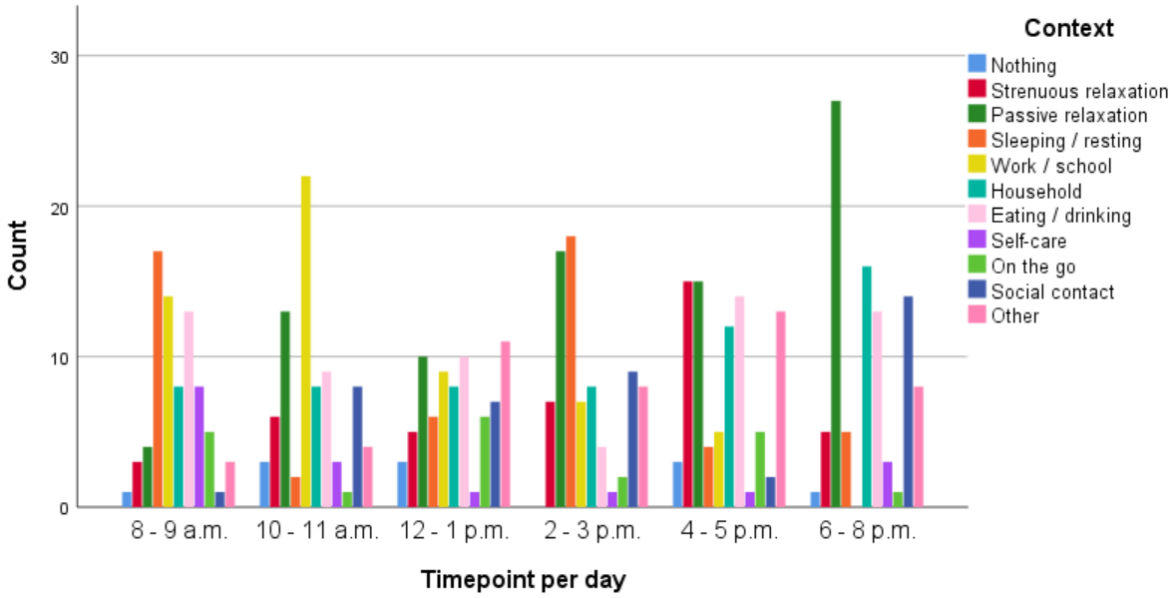
Daily activities and physical fatigue and mental fatigue in people with long-COVID

Description of daily activities

During the total assessment period, the mean scores of the sample showed that passive relaxation, for instance reading a book or watching television, was the most common daily activity performed (17.4%), followed by eating or drinking (12.7%), doing household (12.1%), working (11.5%), sleeping or resting (10.5%), other (9.5%), strenuous relaxation such as walking or exercising (8.3%), being social (8.3%), on the go (4.0%), self-care (3.4%) and doing nothing (2.2%). Figure 8 represents the activities of the sample per time point over the total assessment period. Between 8 a.m. and 11 a.m. participants were mostly working and after these time-points, the amount of spending time on working seemed to decrease. Also, self-care activities (e.g. taking medication) was highest in the mornings. In the evenings, passive relaxation, doing household and having social contacts were increasing. Figure 9 represents the performed daily activities per day of the week, showing that participants worked mostly on Mondays and Tuesdays. Being on the go most frequently happened on Fridays, and doing household was an activity that was mainly performed on Saturdays. Having social contacts and strenuous relaxation, such as going for a walk, was mostly represented on Sundays. Passive relaxation, such as reading a book, was mostly represented on Saturdays, Sundays and Mondays. Sleeping and resting was something participants seemed to fairly equally do every day, as was the same for eating and drinking and self-care.

Figure 8

Count of daily activities of the sample group per time-point during the total assessment period



Association between daily activities and fatigue across all time-points

When using unadjusted, unstandardized beta's and setting 'doing nothing' as the reference category (Table 2), a significant positive association between strenuous relaxation and physical fatigue (B = 0.45, SE = .19, p = <.001) and between 'other' and physical fatigue (B = 0.23, SE = .11, p = .037) at the same moment was observed. Also, a significant negative association between social contacts and physical fatigue (B = -0.33, SE = .11, p = .003) at the same moment was observed. The other daily activities were not associated with more or less physical fatigue compared to doing nothing.

For mental fatigue, a significant positive association between strenuous relaxation and mental fatigue (B = 0.28, SE = .10, p = .004) at the same moment was observed. Also, a significant negative association between social contacts and mental fatigue (B = -0.22, SE = .10, p = .022) at the same moment was observed. The other daily activities were not associated with more or less mental fatigue compared to doing nothing.

Figure 9

Count of daily activities of the sample group per weekday during the total assessment period

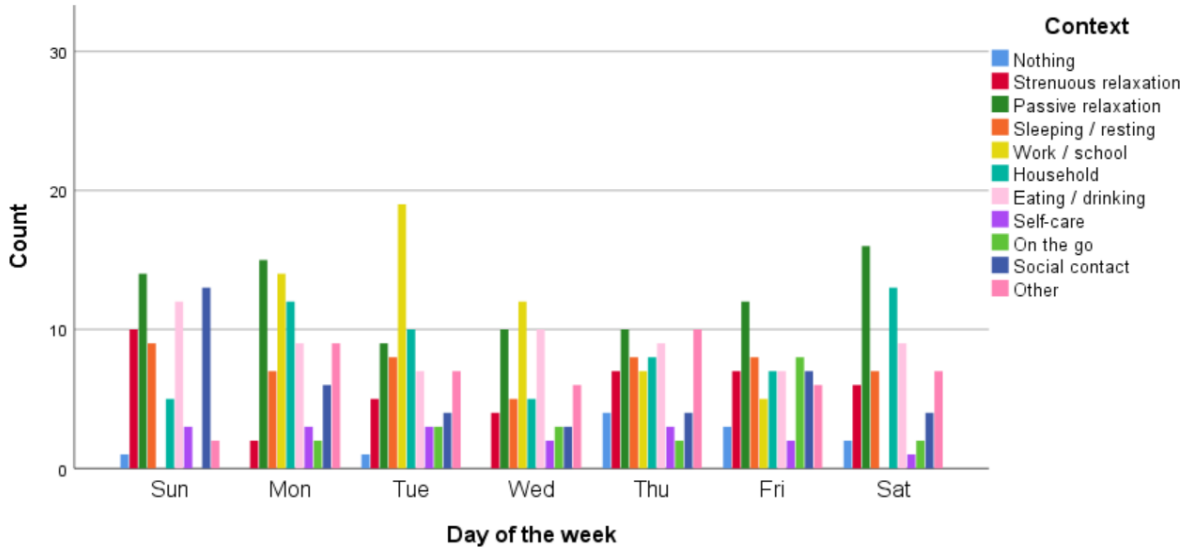


Table 2

Unadjusted and unstandardized coefficients of Linear Mixed Modelling of daily activities on fatigue across all time-points

	Physical fatigue		Mental fatigue	
Dependent variable	Unstandard. *B* estimate (SE)	*p*	Unstandard. *B* estimate (SE)	*p*
Nothing	-	-	-	-
Strenuous relaxation	**0.45 (.19)**	**<.001**	**0.28 (.10)**	**.004**
Passive relaxation	-0.10 (.08)	.183	0.00 (.07)	.942
Sleeping or resting	-0.06 (.10)	.514	0.11 (.08)	.178
Work or school	0.11 (.11)	.346	-0.00 (.10)	.965
Household	0.02 (.09)	.806	0.06 (.08)	.470
Eating or drinking	-0.13 (.08)	.127	-0.11 (.07)	.146
Self-care	0.14 (.16)	.362	0.05 (.14)	.718
On the go	-0.08 (.14)	.588	-0.22 (.12)	.072
Social contacts	**-0.33 (.11)**	**.003**	**-0.22 (.10)**	**.022**
Other	**0.23 (.11)**	**.037**	-0.00 (.10)	.947

Note. 'Doing nothing' is set as the reference category.

Predictive value of daily activities on fatigue at the next measurement

When using the performed daily activities at a prior measurement to predict fatigue at the next measurement (approximately two hours later on the same day), it can be seen that for the unadjusted and unstandardized beta's (Table 3), a significant negative association between doing

household chores and physical fatigue (B = -.29, SE = .12, p = .019) was observed. Also, a significant positive association between eating/drinking and physical fatigue was observed (B = .20, SE = .10, p = .049). Doing more household, relative to doing nothing, decreased physical fatigue. Also, eating/drinking, relative to doing nothing, increased physical fatigue. The other daily activities did not predict physical fatigue.

For mental fatigue, a significant negative association between household and mental fatigue (B = -.30, SE = .11, p = .006) was observed. Doing more household, relative to doing nothing, decreased mental fatigue. The other daily activities did not predict mental fatigue.

Table 3

Unadjusted and unstandardized coefficients of Linear Mixed Modelling of daily activities on fatigue the next measurement.

	Physical fatigue		Mental fatigue	
Dependent variable	Unstandard. *B* estimate (SE)	*p*	Unstandard. *B* estimate (SE)	*p*
Nothing	-	-	-	-
Strenuous relaxation	-0.19 (.13)	.149	-0.12 (.12)	.317
Passive relaxation	0.16 (.10)	.117	0.10 (.09)	.261
Sleeping or resting	-0.09 (.11)	.412	-0.08 (.10)	.390
Work or school	0.16 (.12)	.167	0.07 (.11)	.537
Household	**-0.29 (.12)**	**.019**	**-0.30 (.11)**	**.006**
Eating or drinking	**0.20 (.10)**	**.049**	0.00 (.09)	.973
Self-care	0.01 (.19)	.952	0.02 (.17)	.894
On the go	0.08 (.17)	.648	0.08 (.15)	.612
Social contacts	-0.11 (.15)	.455	0.08 (.13)	.522
Other	-0.11 (.13)	.407	0.09 (.11)	.412

Note. 'Doing nothing' is set as the reference category.

Discussion

The purpose of this study was to clarify the course and the interplay between physical fatigue and mental fatigue, and the between-person and within-person effects of both types of fatigue over time in people with long-COVID. Furthermore, the purpose was to understand whether sleep quality and daily activities might be risk factors for fatigue.

Descriptive results showed that fatigue was a severe and common symptom in this population of people with long-COVID, which is in line with previous studies (Aiyegbusi et al., 2021; Huang et al., 2021; Lopez-Leon et al., 2020; Mandal et al., 2021; Sudre et al., 2021; Van Herck et al., 2021; Vink & Vink-Niese, 2020). Based on the relatively high fatigue scores during the overall assessment period, the impact of fatigue during the day was visible. The severity and variability of fatigue during the day did differ among individuals, as some experienced very severe fatigue consistently during the day and others did not experience fatigue at all at some points in time.

On average, people with long-COVID seemed to experience somewhat higher levels of physical fatigue compared to mental fatigue, as was also found in COPD patients (Lewko et al., 2009). Results demonstrated a strong, but not perfect, concurrent relationship between the two types of fatigue over time. In COPD patients, sarcoidosis patients, and multiple sclerosis patients, physical fatigue and mental fatigue were considered distinct concepts but their actual relationship was not researched (Ford et al., 1998; Kahlmann et al., 2020; Lewko et al., 2009). The current study did research the relationship, and because it was found that physical and mental fatigue did not perfectly associate, it is not recommended to merge the two types and consider them as the same valid concept (Gloster et al., 2011).

To emphasize this and focus on the second research question, the results showed different between-person effects and within-person effects. Namely, it was found that someone who was more physical fatigued over time than another person would also feel more mentally fatigued than that other person. More interestingly, fatigue also showed variance within persons. Namely, it was found that when individuals felt more physically fatigued over time than they usually felt, they were likely to feel more mentally fatigued as well. Because the between-person effects and within-person effects of physical fatigue on mental fatigue were only moderately associated, the distinct nature of physical and mental fatigue was emphasized. This gives valuable input for interventions. That is, these results are in line with the idea that just-in-time adaptive

interventions (JITAIs) should adapt to the changing experiences of an individual (Nahum-Shani et al., 2018). The results of the current study indicate that focusing on decreasing one type of fatigue might decrease the other type of fatigue within an individual as well. For instance, at times an individual is indicating relatively more physical fatigued feelings than they usually feel in their daily life, interventions can recommend self-management strategies focused on decreasing physical fatigue which might decrease mental fatigue too (Ben-Zeev et al., 2014). By using preferences of the individual, a choice can be made on whether to focus primarily on the physical or mental aspect of fatigue, to make self-management techniques more tailored. Making this more specific, different intervention options could be provided for individuals to choose from such as doing mindfulness exercises or going outside for a walk, to make the intervention more feasible for different people and still tackle both types of fatigue (Yardly et al., 2015).

Concerning the third research question of whether sleep quality might be a risk factor for increasing fatigue in people with long-COVID, the current study demonstrated that sleeping more hours at night contributed to decreased physical and mental fatigue the following day. Thus, fewer hours of sleep obtained at night might be a risk factor for increasing physical and mental fatigue in people with long-COVID. These results are in line with previous studies where sleep duration was associated with physical fatigue in lung diseases such as COPD (Şahin & Dayapoğlu, 2015) and asthma (Sadeh et al., 1998). Studies on the relationship between sleep duration and mental fatigue in patients with lung-disease were not found. In the general population, the relationship between sleep duration and mental fatigue could not be confirmed (Chaiard et al., 2018; Kronholm et al., 2006). The current study, however, demonstrated that in people with long-COVID, more hours of sleep obtained at night resulted in decreased mental fatigue the following day. These results contribute to the idea by Boksem and Tops (2008) that mental fatigue as a symptom might also include biological aspects, such as sleep. Surprisingly, taking naps during the day was not associated with increased physical and mental fatigue the next day. This is unlike the study by Shackell and colleagues (2007) that demonstrated that sleeping during the day worsened feelings of fatigue the following day in COPD patients. This could not be confirmed in people with long-COVID, which was even emphasized by the results of the current study that sleeping or resting as a daily activity was not associated with increased physical or mental fatigue. These results imply that it cannot yet be advised to either take or don't take naps during the day to decrease fatigue in people with long-COVID. Also, trouble with

sleeping and the hours of naps during the day were not associated with increased physical or mental fatigue, as was also the case in rheumatoid arthritis patients (Mancuso et al., 2006; Minnock et al., 2015; Treharne et al., 2008). Thus, it cannot yet be advised for people with long-COVID to either take or don't take actions for sleep hygiene improvements, or to either increase or decrease the hours of sleep obtained with naps.

To answer the fourth research question, daily activities were investigated on whether they could be considered risk factors for increasing fatigue in long-COVID. Overall, the daily activities that were risk factors for physical fatigue were similar to those that were risk factors for mental fatigue, emphasizing the strong association between the two types of fatigue. Performing household chores, relative to doing nothing, seemed to decrease both physical and mental fatigue in people with long-COVID approximately two hours later. Since doing household chores might involve physical activity such as cleaning (Booth, 2000), the results of the current study are in line with previous literature where physical activity as a risk factor for fatigue in COPD- and chronic fatigue patients was studied (Vercoulen et al., 1997; Woo, 2000). It is also possible that performing household chores includes other aspects which might decrease fatigue such as being mindful (Newland & Bettencourt, 2020). Nonetheless, it can be advised to not stop performing household chores for people with long-COVID. Eating/drinking, relative to doing nothing, was found to be associated with increased physical fatigue approximately two hours later during the day. However, it remains unclear what aspects of eating/drinking might contribute to physical fatigue. For instance, poor eating habits (Odencrants et al., 2005), digestion of nutrition (Westergren, 2008), only eating at night when fatigued feelings were already increased, or even cooking a four-course dinner could have made an impact on fatigued feelings. More research is needed to understand how eating/drinking might be related to physical fatigue in people with long-COVID.

Interestingly, some daily activities were associated with fatigue at the moment they were performed, but they were not associated with fatigued feelings two hours later. For instance, strenuous relaxation such as walking seemed to increase physical and mental fatigue right after it was performed, although this was not the case two hours later anymore. The association between fatigue right after performing strenuous relaxation might be explained by the idea that physical activity increases physical fatigue, as was found in COPD patients (Waschki et al., 2012), and that physical fatigue, in turn, also could account for mental fatigue. However, it might also be the

case that the negative effects of certain daily activities are only temporary. The same applies to social contacts, which seemed to decrease physical and mental fatigue at the time it was performed but not two hours later. This might be explained by the study of Nitschke and colleagues (2021) where social connectedness was found to decrease fatigue at the moment it was performed. The current study builds upon this idea that it might be possible in people with long-COVID for having social contacts as a buffer against fatigue, but perhaps only for a limited amount of time. These suggestions require further research, for instance by performing an ESM study with an event-contingent sampling design where the assessment of social contacts includes the duration, intensity, and frequency, and is followed by assessing fatigue every ten minutes up to two hours on the same day (Conner, & Lehman, 2012).

Strength and limitations

A major strength of the study was that it was the first detailed exploration of fatigue as a symptom over time in people with long-COVID as well as related risk factors in terms of behaviours, carried out using ESM. ESM made it able to obtain rich information of which yet only fatigue, sleep, and daily activities were used in the current study, nonetheless theoretical knowledge on long-COVID is much enhanced. Furthermore, effects of physical fatigue on mental fatigue within individuals and between persons was demonstrated, which resulted in a considerably more detailed illustration of associations over time (Curran & Bauer, 2011). Since the study measured fatigue and daily activities real-time, recall bias was likely limited (Conner, & Lehman, 2012) and the ecological validity of the study was increased, making measures more representative and generalizable to the daily life of people with long-COVID (Araujo et al., 2007). Lastly, the overall compliance rates of the participants were relatively high, especially for ex-hospitalized people experiencing symptoms (Vachon et al., 2019). This resulted in a rich and detailed insight into the experiences of the participants.

A limitation of the study was that no disaggregated between-person and within-person association analyses of sleep quality and daily activities were carried out, due to the way daily activities were assessed and due to time constraints. Also, current association analyses were performed on a group level and might have levelled out the positive and negative associations within individuals, giving a distorted picture of the associations. In addition, the daily activities were operationalized by a single word (Appendix C) and therefore lacked a detailed view of what was performed during the activities. A solution for this limitation might be to create focus groups

with participants to qualitatively research the daily activities of people with long-COVID. The last limitation was a technical error from Ethica, where all participants did not receive surveys on the fourteenth day, and some also did not on the thirteenth day.

Future research

The results showed that the severity of fatigue is fairly consistent during the day for most people with long-COVID. Therefore, there does not seem to be one ideal moment to apply JITAIs. Because the severity of fatigue fluctuated during the day for some people, it might be the case that different subgroups of people with long-COVID exist (Bartley et al., 2017) and that each subgroup experiences physical and mental fatigue differently. More research is needed on this, for instance by interviewing people with long-COVID and investigating different characteristics per individual, and applying factor analyses to explore potential subgroups (Beumont et al., 1995). Afterwards, understanding why these possible subgroups experience fatigue differently needs to be researched, for instance by measuring real-time symptoms and connecting these to different patient characteristics. Lastly, it might be the case that for some of these potential subgroups JITAIs are not of additional value, and for some they are. Thus, measuring the needs, motivation, acceptability and feasibility (Michelle et al., 2019) concerning JITAIs can be done to understand the (non-)added value of the intervention perceived by the different subgroups.

In addition, the results showed that hours of sleep was associated with both physical and mental fatigue in people with long-COVID, which was also the case in COPD- and fibromyalgia patients, and non-clinical populations (Boolani & Manierre, 2019; Nicassio et al., 2002; Vanfleteren et al., 2020). The relationship between hours of sleep and fatigue could not be confirmed in patients with rheumatoid arthritis and interstitial lung-disease (Agarwal et al., 2009; Mancuso et al., 2006; Minnock et al., 2015; Treharne et al., 2008). It is important to consider how experiencing long-COVID symptoms relate to sleep quality and fatigue. What are similarities in COPD-, fibromyalgia-, non-clinical-, and long-COVID-populations that might contribute to the result that sleep quality was associated with physical and mental fatigue? For example, shortness of breath or mood might be related to the association between sleep quality and fatigue (Kapella et al., 2006), although this needs to be researched. Finding connections between other experienced symptoms (e.g. mood or pain) and fatigue needs to be researched to understand if other symptoms influence the relationship between hours of sleep and fatigue. This can be done

by measuring real-time daily mood and other symptoms in a large sample of people with long-COVID and comparing this to control groups, and/or patients with chronic (lung) diseases.

Research on the between-person effects and within-person effects of sleep quality and daily activities on physical and mental fatigue can be conducted, for instance by assessing the intensity of performed daily activities over time, which might enhance knowledge concerning at what moment daily activities become risk factors for physical and mental fatigue within individuals, to better understand if and when to intervene. In addition, ESM analyses can be performed on an individual level which can describe intra-individual changes over time, enhance insight into the associations between risk factors and physical and mental fatigue, and provide input to develop highly personalised interventions (McDonald et al., 2020).

Future research might consider including 'having contact with a health care professional' as a daily activity in people with long-COVID, since this was the most frequent given answer for the daily activity 'other' in the current study.

Conclusion

Based on the ESM results, fatigue was found a severe and common symptom in long-COVID, although this differed per person which indicated potential different long-COVID subgroups. Physical and mental fatigue had a strong relationship with less strong between- and within-person effects. Fewer hours of sleep at night seemed to increase mental fatigue the following day which was not researched nor confirmed in other lung diseases before. Certain daily activities were associated with increased fatigue at the time they were performed but not two hours later, suggesting they might be risk factors for a certain time period only.

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Appendices

Appendix A: Interview scheme

Dank u wel dat u mij wilt ontvangen [*digitaal: tijd voor mij heeft gemaakt*] en mee wilt werken aan dit onderzoek. Het doel is om meer te weten te komen over de periode na uw ziekenhuisopname vanwege COVID-19. Wij zijn benieuwd wat wij als ziekenhuis voor patiënten betekenen en hoe wij kunnen ondersteunen bij herstel van COVID. De vragen gaan over uw ziekenhuisperiode, de periode daarna, over uw huidige gezondheid en over eventuele hulp die u nodig heeft. Dit gesprek duurt ongeveer 45 minuten. Als u een vraag liever niet beantwoordt is dat geen probleem. Het gesprek is vertrouwelijk en uw naam wordt nergens vermeld. Vindt u het goed als ik dit gesprek opneem? De opname wordt alleen gebruikt om het interview uit te werken. […] Heeft u nog vragen? […]

- U bent opgenomen geweest in het MST vanwege COVID. Kunt u mij vertellen over uw tijd in het ziekenhuis? Wat heeft u meegemaakt?
    - Hoe ernstig was de ziekte? Hoe lang heeft u in het ziekenhuis gelegen? Op welke afdeling(en) bent u geweest?
- Hoe was uw gezondheid voordat u COVID-19 kreeg?
- Hoe was het om weer thuis te zijn na het ziekenhuisontslag?
- Hoe gaat het nu met u?
    - Kunt u alles doen zoals voor COVID?; Ziet u uw familie en vrienden? Hoe gaat het geestelijk met u? (Last van somberheid? Van angst?) Waar komt [beperking] door?
- Hoe gaat het nu met uw gezondheid?
    - Zijn er nog klachten waar u last van heeft? [doorvragen per klacht:]
        - [Indien relevant] waar voelt u deze?; Hoeveel last heeft u van [deze klacht] (- op schaal van 1-10)?; Hoe vaak heeft u [deze klacht]?
        - Is [deze klacht] gedurende de dag hetzelfde? En over de week?
            - [Indien nee: heeft u een idee waardoor [de klacht] verandert?
    - Zijn er klachten overgegaan? Heeft u nieuwe klachten gekregen?
    - Welke rol speelt COVID volgens u in uw gezondheid momenteel?
    - Hoelang denkt u nog last van deze COVID-klachten te houden?
- Hoe verliep/verloopt uw herstelperiode?

        - Wat heeft u geprobeerd om te herstellen? Hoe heeft dat geholpen?
    - Heeft u het gevoel uw herstel zelf in de hand te hebben? Op wat voor manier/waarom niet?
    - [Niet-hersteld] Waardoor komt het volgens u dat u nog niet herstelt bent?
- [Hersteld] Had uw herstel sneller gekund door extra hulp? Op welke manier; van wie en wanneer?
- [Niet-hersteld] Welke hulp heeft u nu nodig?; Welke hulp heeft u nodig gehad?
    - Van wie verwacht of wenst u hulp? Wanneer en waarmee?
- Is er nog iets anders wat u kwijt wilt? Iets wat nog niet besproken is?

[Aan niet-hersteld] In het interview vroeg ik hoe uw klachten continu hetzelfde zijn of over de dag veranderden. Graag willen wij onderzoeken hoe deze verandering gaat bij uw klachten. Hiervoor willen wij via uw telefoon u 5 tot 10 keer per dag een aantal hele korte vragen voorleggen. Deze vragen gaan over uw stemming en klachten op dat moment en wat u vlak voor de vragen aan het doen was. Door dat onderzoek hopen wij te kunnen achterhalen wat het beste moment is om patiënten te helpen. Zou u daar aan willen meewerken?

English translation:

Thank you for agreeing to receive me [digital: made time for me] and for participating in this research. The goal is to learn more about the period after your hospital discharge due to COVID-19. We are curious about what we as a hospital can do for patients and how we can support recovery from COVID. The questions are about your hospital discharge, the period afterwards, about your current health and about any help you may need. This conversation lasts approximately 45 minutes. If you prefer not to answer a question, that's no problem. The conversation is confidential and your name is not mentioned anywhere. Would you mind if I record this conversation? The recording is only used to elaborate the interview. […] Do you have any questions? […]

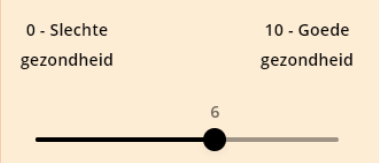
- You have been admitted to the MST because of COVID. Can you tell me about your time in the hospital? What have you been through?
    - How severe was the disease? How long have you been in hospital? Which department(s) have you been to?
- How was your health before you got COVID-19?
- What was it like to be back home after being discharged from the hospital?
- How are you doing right now?
    - Can you do everything as before COVID?; Do you see your family and friends? How are you mentally? (Suffering from sadness? From fear?) Where does [limitation] come from?
- How is your health now?
    - Do you experience any other complaints at the moment? [inquire per complaint:]
        - [If relevant] where do you feel [complaint]?; How much do you suffer from [complaint] (- on a scale of 1-10)?; How often do you have [complaint]?
        - Is [complaint] the same throughout the day? And throughout the week?
            - [If no: do you have an idea why [complaint] changes?
    - Did any complaints passed over? Did you get any new complaints?
    - What role do you think COVID plays in your health right now?
    - How long do you think you will continue to suffer from these COVID complaints?
- How was/is your recovery period?

        - What have you tried to recover? How did that help?
    - Do you feel that you are in control of your recovery? In what way/why not?
    - [Non-recovered] Why do you think it is that you have not recovered yet?
- [Recovered] Could your recovery have been faster with extra help? How; from whom and when?
- [Non-recovered] What help do you need right now?; What help did you need before?
    - From whom do you expect or wish this help? When and how?
- Is there anything else you would like to say? Something that hasn't been discussed yet?

[To non-recovered] In the interview I asked how your symptoms are continuously the same or changed over the day. We would like to investigate how this change affects your complaints. To do this, we would like to ask you a number of very short questions via your telephone 5 to 10 times a day. These questions are concerning your mood and complaints and what you were doing just before the questions. Through this research, we hope to be able to find out when is the best time to help patients. Would you like to participate?

Appendix B: Morning survey

Kunt u op onderstaande lijn aangeven hoe uw **gezondheid gisteren** was? '0' betekent een slechte gezondheid, '10' betekent een goede gezondheid. Klik op onderstaande lijn om te beginnen / *Can you state **yesterdays' health status**? '0' means a bad health, '10' means a good health. Click the line below to start.*



Hoeveel **uur** heeft u vannacht geslapen? / *How much **hours** of sleep did you get last night?*

- Minder dan 4 uur / *Less than 4 hours*
- Tussen 4 en 6 uur / *Between 4 and 6 hours*
- Tussen 6 en 8 uur / *Between 6 and 8 hours*
- Tussen 8 en 10 uur / *Between 8 and 10 hours*
- Meer dan 10 uur / *More than 10 hours*

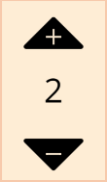
In welke mate had u **vannacht** last van problemen met slapen? / *To what extend did you experience sleep difficulties **last night**?*

- Geen last gehad / *No trouble*
- Een beetje last gehad / *A little bit of trouble*
- Redelijk last gehad / *Quite a bit of trouble*
- Behoorlijk last gehad / *A lot of trouble*
- Heel veel last gehad / *Extreme trouble*

Heeft u **gister overdag** dutjes gedaan? / *Did you take any **naps yesterday**?*

- Ja / *Yes*
- Nee / *No*

Hoeveel dutjes heeft u **gister overdag** gedaan? / *How many **naps** did you take?*



Hoeveel uur heeft u **gister overdag** geslapen? / *How much hours of naps did you take **yesterday**?*

- Minder dan een half uur / *Less than half an hour*
- Tussen een half uur en 1 uur / *Between half an hour and 1 hour*
- Tussen 1 en 2 uur / *Between 1 and 2 hours*
- Tussen 2 en 3 uur / *Between 2 and 3 hours*
- Tussen 3 en 4 uur / *Between 3 and 4 hours*
- Tussen 4 en 6 uur / *Between 4 and 6 hours*
- Meer dan 6 uur / *More than 6 hours*

Appendix C: Symptoms and complaints survey

Op dit moment voel ik mij **lichamelijk vermoeid** / *Right now, I feel **mentally tired**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **mentaal vermoeid** (bijvoorbeeld een gebrek aan energie om goed over iets na te denken, plannen te maken of creatief te zijn) / *Right now, I feel **mentally tired** (for example a lack of energy to think thoroughly, make plans or be creative)*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **kortademig** / *Right now, I feel **out of breath**.*

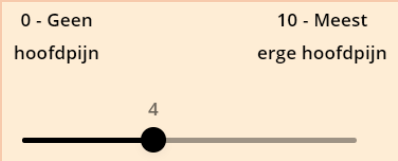
- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*

- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

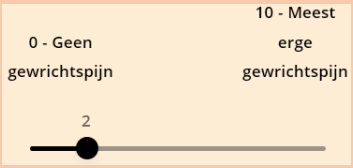
Ervaart u op dit moment pijn in uw lichaam / *Right now, do you experience any pain in your body?*

- Ja / *Yes*
- Nee / *No*

In hoeverre heeft u op dit moment **hoofdpijn**? ‘0’ betekent geen hoofdpijn, ‘10’ betekent meest erge hoofdpijn. Klik op onderstaande lijn om te beginnen / *To what extend do you experience a headache right now? ‘0’ means no headache, ‘10’ means the worst imaginable headache. Click the line below to start.*

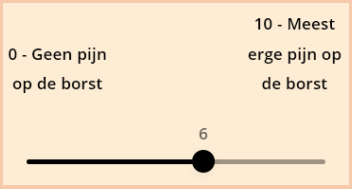


In hoeverre heeft u op dit moment **gewrichtspijn**? ‘0’ betekent geen gewrichtspijn, ‘10’ betekent meest erge gewrichtspijn. Klik op onderstaande lijn om te beginnen / *To what extend do you experience joint pain right now? ‘0’ means no joint pain, ‘10’ means the worst imaginable joint pain. Click the line below to start.*

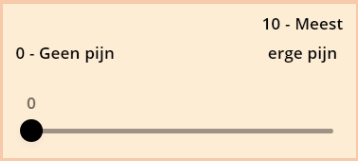


In hoeverre heeft u op dit moment **pijn op de borst**? ‘0’ betekent geen pijn op de borst, ‘10’ betekent meest erge pijn op de borst. Klik op onderstaande lijn om te beginnen / *To what*

extend do you experience chest pain right now? '0' means no chest pain, '10' means the worst imaginable chest pain. Click the line below to start.



In hoeverre heeft u op dit moment **pijn ergens anders in uw lichaam** dan aan het hoofd, aan de gewrichten en/of op de borst? '0' betekent geen pijn, '10' betekent meest erge pijn. Klik op onderstaande lijn om te beginnen / *To what extend do you experience pain elsewhere in your body right now, other than your head, joints and/or chest? '0' means no pain, '10' means the worst imaginable pain. Click the line below to start.*



Hoe gaat het met uw '**denken**' (concentratie, geheugen, aandacht) op dit moment? '0' betekent dat het denken langzaam en moeilijk gaat, '10' betekent dat het denken scherp en alert is. Klik op onderstaande lijn om te beginnen / *How is your '**thinking**' (concentration, memory, attention) right now? '0' means that your thinking goes slow and hard, '10' means that your thinking is sharp and alert. Click the line below to start.*

Op dit moment voel ik mij **angstig** / *Right now, I feel **anxious**.*

- Sterk mee oneens / *Strongly disagree*

- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **somber** / *Right now, I feel **depressed**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **verdrietig** / *Right now, I feel **sad**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **prikkelbaar** / *Right now, I feel **irritable**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*

- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **teleurgesteld** / *Right now, I feel **disappointed**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **opgewekt** / *Right now, I feel **excited**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **ontspannen** / *Right now, I feel **relaxed**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*

- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **tevreden** / *Right now, I feel **satisfied**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **dankbaar** / *Right now, I feel **thankful**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*
- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Op dit moment voel ik mij **blij** / *Right now, I feel **happy**.*

- Sterk mee oneens / *Strongly disagree*
- Oneens / *Disagree*
- Een beetje oneens / *Disagree a little bit*
- Neutraal / *Neutral*

- Een beetje eens / *Agree a little bit*
- Eens / *Agree*
- Sterk mee eens / *Strongly agree*

Vlak voor het invullen van de vragen was ik bezig met… / *Right before answering the questions I was doing…*

- Niets / *Nothing*
- Inspannend ontspannen (bijvoorbeeld wandelen, fietsen, tuinieren) / *Strenuous relaxation (for example walking, riding a bike, gardening)*
- Passief ontspannen (bijvoorbeeld televisie kijken, boek lezen) / *Passive relaxation (for example watching television, reading a book)*
- Slapen of rusten / *Sleeping or resting*
- Werk of school / *Work or school*
- Het huishouden / *Household*
- Eten en drinken / *Eating and drinking*
- Zelfzorg (bijvoorbeeld lichaamshygiëne, medicatie) / *Self-care (for example body hygiene, medication)*
- Onderweg / *On the go*
- Sociaal contact / *Social contacts*
- Iets anders, namelijk… / *Other, namely…*

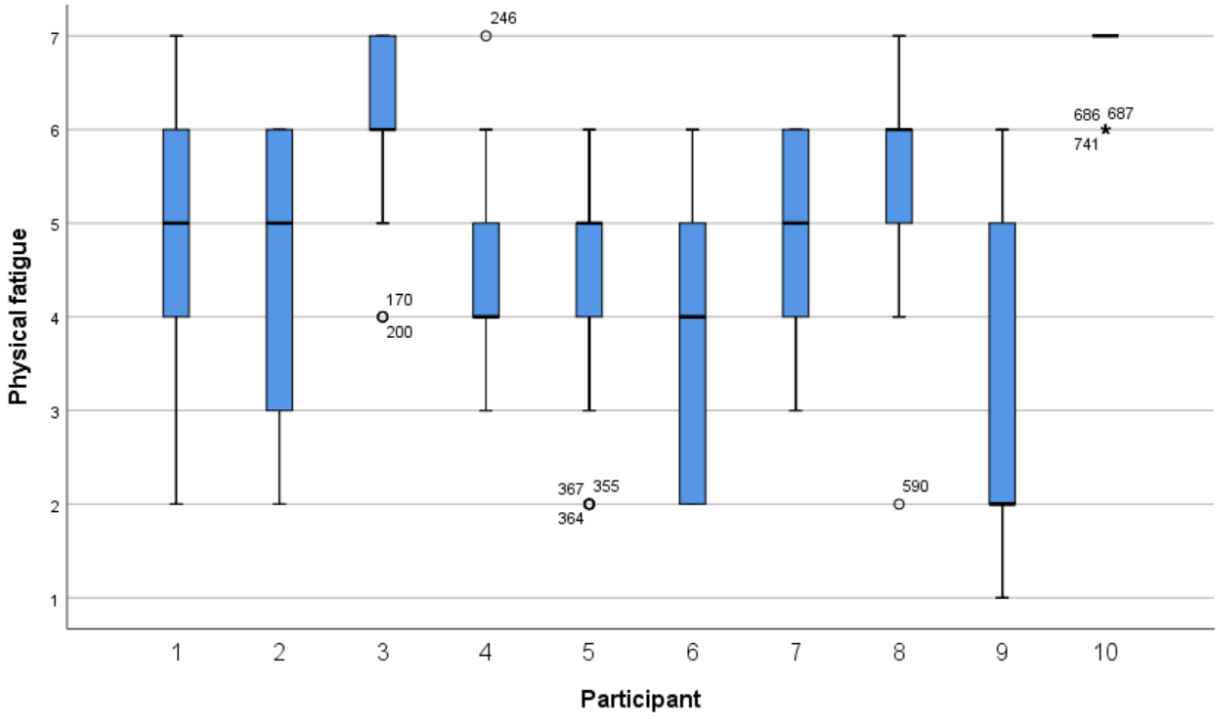
Met welke activiteit was u vlak voor het invullen van de vragen bezig? / *What where you doing before answering the survey?*

…

Appendix D: Boxplot of physical fatigue

Figure 10

Boxplot of physical fatigue during the total assessment period

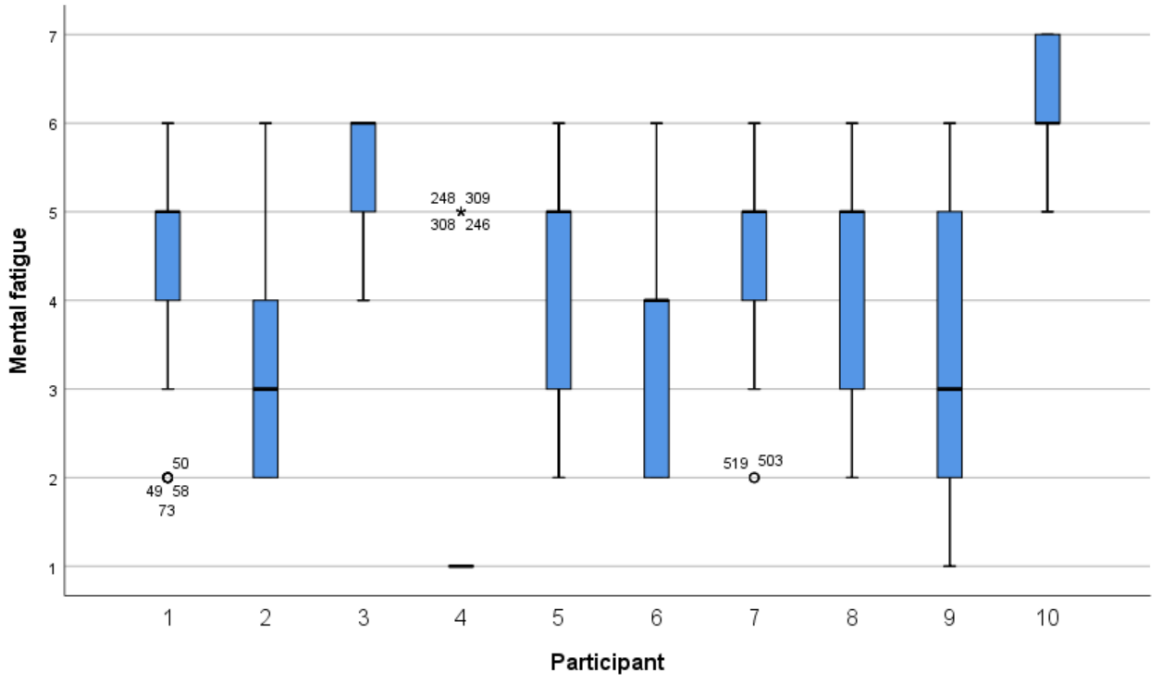


Note. Answer range counts from 1 – not at all fatigued to 7 – worst imaginable fatigue.

Appendix E: Boxplot of mental fatigue

Figure 11

Boxplot of mental fatigue during the total assessment period

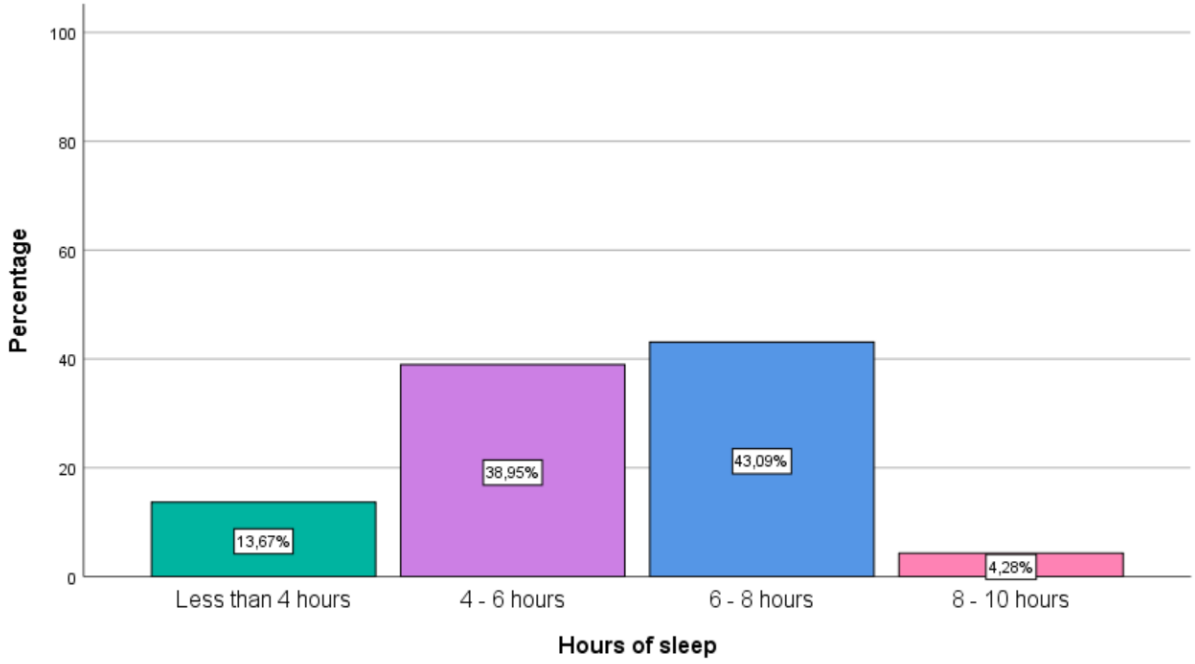


Note. Answer range counts from 1 – not at all fatigued to 7 – worst imaginable fatigue.

Appendix F: Hours of sleep

Figure 12

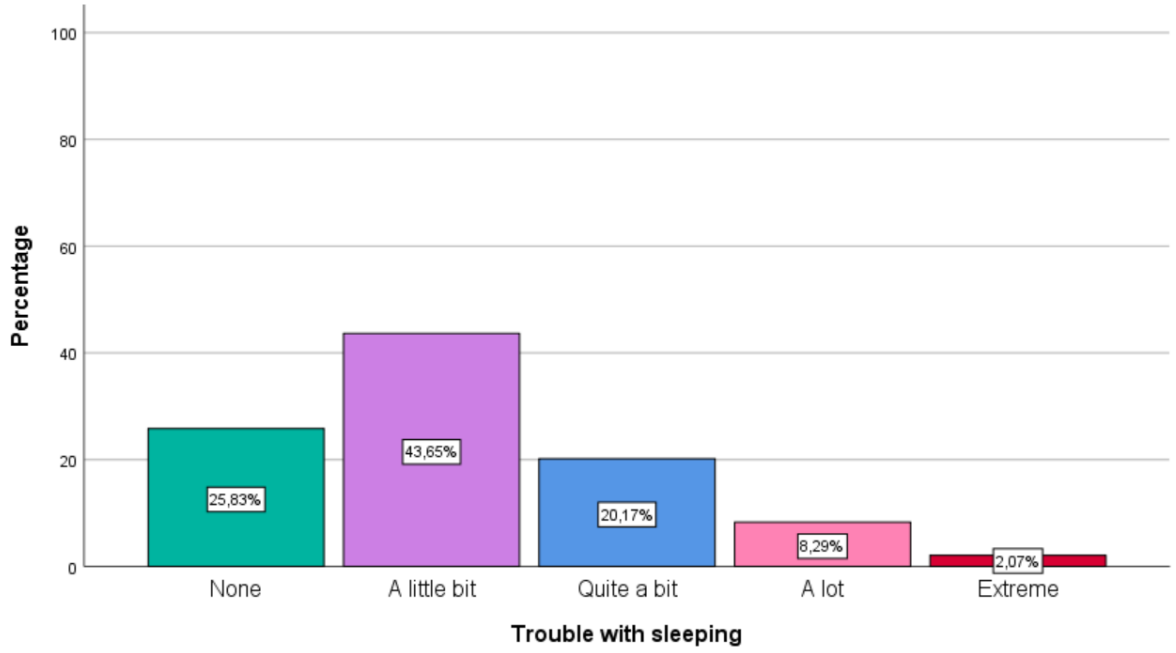
Percentage of scores on 'hours of sleep' of the sample group during the total assessment period



Appendix G: Trouble with sleeping

Figure 13

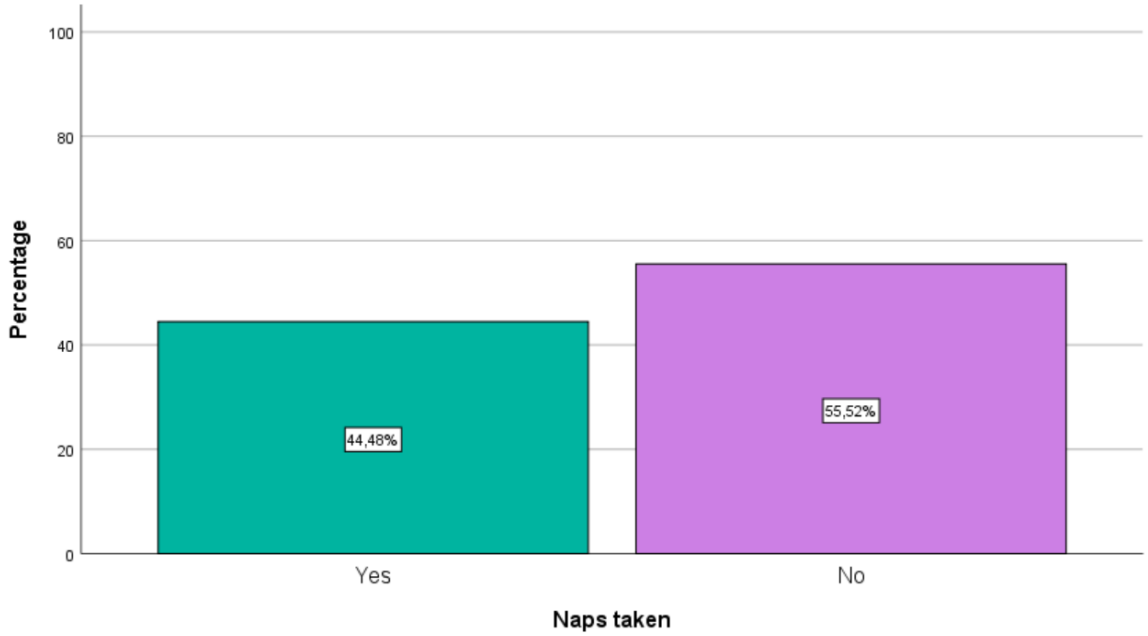
Percentage of scores on 'trouble with sleeping' of the sample group during the total assessment period



Appendix H: Naps

Figure 14

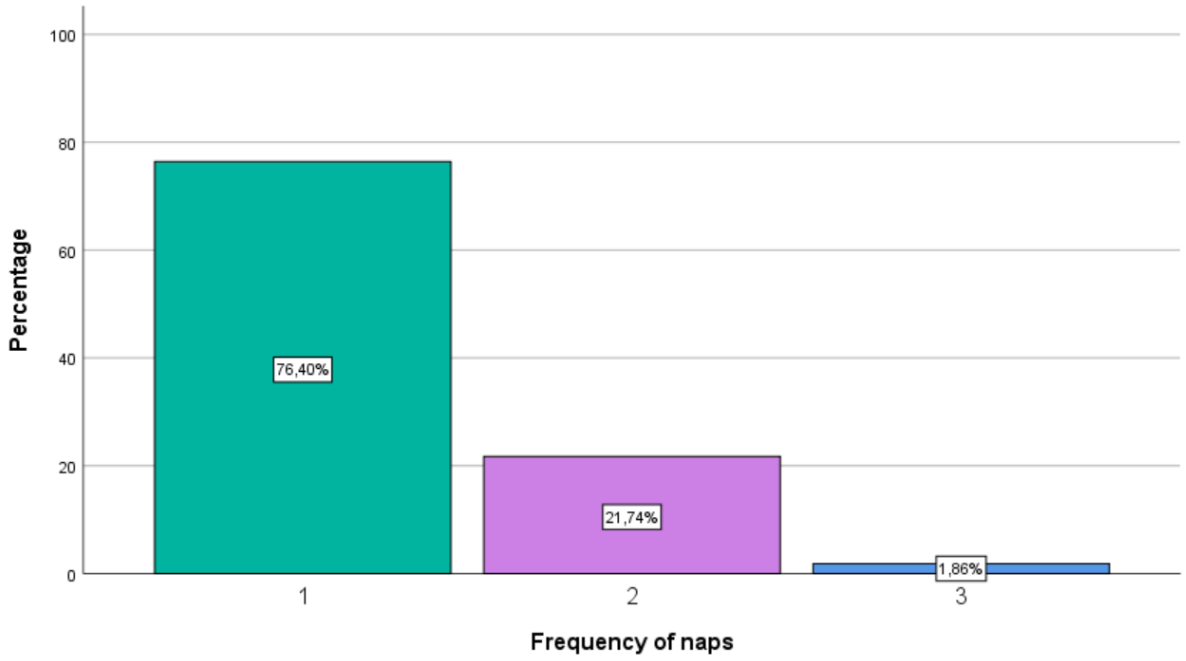
Percentage of scores on 'naps taken' of the sample group during the total assessment period



Appendix I: Frequency of naps

Figure 15

Percentage of scores on 'frequency of naps' of the sample group during the total assessment period



Appendix J: Hours of naps

Figure 16

Percentage of scores on 'hours of naps' of the sample group during the total assessment period