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The effect of cardiorespiratory fitness and exercise on sleep parameters in myocardial infarction patients

Master's thesis in Biology, physiology

Supervisor: Bjørn Munro Jenssen

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Abstract

Background: Regular physical exercise has been linked to various health benefits, including increased cardiorespiratory fitness (CRF), reduced risk for myocardial infarction and promoting good sleep. Adequate sleep is another vital component of a healthy lifestyle and has been linked to reduced risk for myocardial infarction. In addition, regular exercise has been suggested as a non-pharmacological treatment for poor sleep, although the mechanisms behind this are still debated. There is little reliable and available documentation regarding the effect of exercise on sleep parameters in myocardial infarction patients.

Objectives: Investigate the correlation between CRF and the sleep parameters: total sleep time (TST), sleep efficiency (SE) and sleep onset latency (SOL) in men with a history of myocardial infarction. Additionally, examine the effect of exercise compared to no exercise, exercise intensity (HI: high intensity and MI: moderate intensity) and timing of exercise (daytime and evening) on sleep parameters the following night.

Methods: 19 men with a history of myocardial infarction (58.8 ± 7.5 years) were included from the intervention group of The Norwegian Trial of Exercise After Myocardial (NorEx) in Trøndelag, Norway. Sleep parameters were monitored during the 12-week study period using a contactless sleep monitor. Exercise was monitored by continuous heart rate measurements from an activity watch, and written exercise diaries. Participants were requested to continue to exercise according to the NorEx protocol. Peak oxygen uptake (VO_{2peak}) was measured at the beginning and, after the 12 weeks, performed on a treadmill by cardiopulmonary exercise test (CPET).

Results: The mean VO_{2peak} did not statistically significantly explain the variation in mean TST, SE or SOL. Additionally, ΔVO_{2peak} was not statistically significantly associated with changes in sleep parameters over the study period. No statistically significant changes were found in TST, SE or SOL following days with and without exercise nor MI- and HI-exercise. SOL following evening exercise was statistically significantly longer compared to daytime exercise, with mean SOL of 23.2 minutes and 17.4 minutes, respectively. However, there were no statistically significant differences in TST or SE depending on the timing of exercise.

Conclusion: We found no clear relationship between CRF and sleep parameters in this group of men with a history of myocardial infarction. In addition, our findings show no sign that neither exercise nor exercise intensity substantially impacts sleep parameters the following night. However, the effect of exercise on SOL appears to be dependent on the timing of exercise, with increases in SOL after evening compared to daytime exercise. Individuals having problems falling asleep can therefore benefit from exercising earlier in the day rather than in the evening. However, no significant association was found between the timing of exercise and TST and SE.

Sammendrag

Bakgrunn: Regelmessig fysisk trening er forbundet med en rekke helsemessige fordeler, inkludert økt kardiorespiratorisk kondisjon (CRF), redusert risiko for hjerteinfarkt, i tillegg til å fremme god søvn. Tilstrekkelig søvn er en viktig del av en sunn livsstil og kan redusere risikoen for hjerteinfarkt. I tillegg har regelmessig trening blitt foreslått som en ikke-medikamentell behandling av dårlig søvn, selv om de underliggende mekanismene fortsatt er omdiskutert. Det er begrenset med tilstrekkelig og tilgjengelig dokumentasjon på effekten av trening på søvn hos hjerteinfarktpasienter.

Hensikt: Undersøke forholdet mellom CRF og søvnparameterne: total søvntid (TST), søvneffektivitet (SE) og søvnlatens (SOL) hos en gruppe menn som har hatt hjerteinfarkt. Videre undersøkes effekten av trening, treningsintensitet og tidspunkt for trening på søvnparameterne påfølgende natt.

Metode: 19 menn som har blitt behandlet for hjerteinfarkt ($58.8 \pm 7,5$ år) ble rekruttert fra intervensjonsgruppen til The Norwegian Trial of Exercise After Myocardial (NorEx) i Trøndelag, Norge. Søvnparametere ble registrert ved hjelp av en kontaktløs søvnmonitor i løpet av en studieperiode på 12 uker. Treningsdata ble registrert ved kontinuerlige målinger av hjerterytme fra en aktivitetsklokke, i tillegg til skriftlige treningsdagbøker. Deltakerne ble instruert til å fortsette å trene i henhold til NorEx-protokollen. Maksimalt oksygenopptak (VO_{2max}) ble målt ved en kardiopulmonal anstrengelsestest (CPET) på tredemølle før og etter den 12 ukers lange studieperioden.

Resultat: Det ble ikke funnet en statistisk signifikant korrelasjon mellom gjennomsnittlig VO_{2peak} og gjennomsnittlig TST, SE eller SOL. Det ble heller ikke funnet en statistisk signifikant korrelasjon mellom ΔVO_{2peak} og endring i TST, SE eller SOL over studieperioden. Videre ble det ikke observert statistisk signifikante forskjeller i TST, SE eller SOL mellom dager med og uten trening, eller netter etter trening med moderat og høy intensitet. Det ble funnet en statistisk signifikant økning i SOL etter kveldstrening sammenlignet med trening på dagtid, med en gjennomsnittlig SOL på henholdsvis 23.2 minutter og 17.4 minutter. Imidlertid ble det ikke observert statistisk signifikante forskjeller i TST eller SE mellom trening på dagtid og kveldtid.

Konklusjon: Det ser ikke ut til å være noen sterk sammenheng mellom CRF og søvnparametere i denne gruppen menn som tidligere har hatt hjerteinfarkt. I tillegg tyder funnene våre på at verken trening eller treningsintensitet i vesentlig grad påvirker søvnparametere den påfølgende natten. Effekten av trening på SOL ser imidlertid ut til å være avhengig av tidspunktet for trening, med økninger i SOL etter kveldstrening sammenlignet med trening på dagtid. Dette kan tyde på at kveldstrening ikke er optimalt for de som sliter med innsovning, og at trening på dagtid kan være fordelaktig. Imidlertid, ble det ikke funnet noen signifikant sammenheng mellom tidspunktet for trening og TST og SE.

Division of work

In writing this master thesis, we have worked closely together as a team. The data collection and statistical analysis of the data were done in collaboration. Linn had the main responsibility for the part about CRF while Ingeborg had the main responsibility for the part about the effect of exercise. However, both participated in the writing of all the sections of the thesis, ensuring a consistent and coherent overall structure. Our strong team dynamic allowed us to divide the work in a way that was efficient and effective, while also ensuring that the final product was a true reflection of our combined effort and collaboration.

Acknowledgments

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Abbreviations

AHA: American Heart Association

BMI: Body Mass Index

CPET: Cardiopulmonary Exercise Testing

CRF: Cardiorespiratory Fitness

CVD: Cardiovascular Disease

ECG: Electrocardiogram

HI: High intensity

HR: Heart Rate

HR_{peak}: Peak Heart Rate

MI: Moderate intensity

NorEx: The Norwegian Trial of Exercise After Myocardial Infarction

RER: Respiratory Exchange Ratio

RPE: Rate of perceived exertion

SD: standard deviation

SE: Sleep efficiency

SOL: Sleep onset latency

TST: Total sleep time

VO₂: Oxygen Uptake

VO_{2max}: Maximal Oxygen Uptake

VO_{2peak}: Peak Oxygen Uptake

β: Beta, Linear regression coefficient

Δ: Delta

ΔVO_{2peak}: change in Peak Oxygen Uptake

95 % CI: 95 % confidence interval

1. Introduction

Physical exercise has been extensively studied for its beneficial effects on human health, improving mental health (1–3) and immune function (4,5), in addition to reducing the risk for many lifestyle diseases, such as cardiovascular disease (CVD) (6–9). CVD includes a range of diseases affecting the heart and blood vessels, such as myocardial infarction, and is a leading cause of mortality worldwide (10,11). Myocardial infarction is caused by a decreased blood flow and oxygen to the heart which can result in cell death of cardiac tissue, and can be caused by the formation of plaques in the inner wall of an artery (12–14). In the first year after surviving a myocardial infarction, over 20% of patients experience a second event (15). Physical activity has been found to be associated with reduced risk of myocardial infarction (9,16), especially for individuals who already suffered a previous cardiac event (17). Therefore, exercise is recommended as an intervention for prevention and rehabilitation in European guidelines (18–20).

Exercise induces immediate changes in various physiological parameters such as heart rate, blood pressure, and body temperature (21,22). These changes can generate physiological responses that affect different aspects of the body, including the brain (1), cardiovascular (23,24) and musculoskeletal system (21,23). Cardiorespiratory fitness (CRF) is a measure of the ability of the body to transport and utilise oxygen during physical activity (25). CRF is influenced by various factors including, genetics, age, sex, and lifestyle factors, such as the level of physical activity (21,26,27). Studies have found regular endurance training, especially with high intensity above 85 % of peak heart rate (HR_{peak}) to be a useful exercise modality to increase CRF (28–30). Improvement in CRF can lead to adaptations such as increased stroke volume, and angiogenesis (21,23). The gold standard for measuring CRF is cardiopulmonary exercise testing (CPET) which gives a comprehensive evaluation of all systems involved in response to aerobic exercise (25,31,32). CRF can be an indicator of the level of physical fitness, and both maximal oxygen uptake (VO_{2max}) and peak oxygen uptake (VO_{2peak}) are measures of CRF (27). VO_{2max} represents the maximal amount of oxygen that can be taken up and utilised by the body during exercise, and it is achieved when no further increase in workload leads to additional increases in oxygen uptake (27,33). VO_{2peak} is the highest oxygen uptake achieved during a single exercise test, and it is often used when individuals fail to meet all the criteria for VO_{2max} (27).

Research has found CRF to be an important indicator of overall health, where low levels of CRF have been associated with a higher risk for CVD (34–37) and all-cause mortality (36–39). Additionally, it has been observed that a higher level of CRF is associated with improved sleep (40,41) and reduced symptoms of insomnia compared to individuals with lower CRF (42). The maintenance of CRF can also protect against the onset of sleep problems in middle-aged adults (43). Fernström et al. (44) observed that CRF was the strongest lifestyle predictor of CVD risk, with sleep duration following as the next most important factor.

In addition to exercise, adequate sleep is another vital component of a healthy lifestyle, playing a critical role in maintaining optimal physical (45) and cognitive function (46–49). Inadequate sleep has been linked to hypertension (50,51), obesity (51–55), diabetes (51,52) and metabolic disorders (56), all of which are risk factors for myocardial infarction (57,58). Sleep problems can significantly impact daily life, and it is

estimated that approximately 1 in 4 individuals experience poor or disturbed sleep (59,60). Exercise has been shown to have a positive effect on sleep (61–63) and has been proposed to be an important non-pharmacological treatment for poor sleep (64,65).

Sleeping is a fundamental biological process that takes up approximately one-third of our lives (66), and it is recommended that adults sleep 7-9 hours per day (67). Sleep is a natural, reversible, and recurring state of rest characterised by reduced consciousness and perceptual disengagement from the environment (68,69). This state is characterised by a series of precisely regulated physiological states, controlled by a group of brainstem nuclei projecting through the brain and spinal cord (70). Sleep facilitates restorative processes for the body, such as tissue repair and growth (68,71), regulates the immune system (72) and hormones, including those controlling hunger and metabolism (73). In addition, sleep plays a critical role in cognitive performance (46), the consolidation of memories and learning (47–49), and the development of motor skills (68,74).

Sleep is regulated by the circadian rhythm, a biological rhythm that repeats approximately every 24 hours and is driven by an internal biological clock in the suprachiasmatic nucleus (68,70). This internal biological clock is responsible for regulating the timing of various physiological processes, including secretion of hormones, metabolism, body temperature and sleep-wake cycles (68,75–78). Light information, both the intensity and spectral content of light, is the primary synchroniser of the circadian rhythm (68,79,80). The suprachiasmatic nucleus utilises light information received from the retina to regulate the production of melatonin, a hormone that facilitates sleep (81). The suprachiasmatic nucleus sends signals to suppress melatonin production when light levels are high. In contrast, as light levels decrease, the suprachiasmatic nucleus stops inhibiting melatonin production, leading to an increase in melatonin levels, which promotes the onset of sleep (68). The regulation of the circadian rhythm is not only dependent on light but also influenced by internal factors such as genetics (82), body temperature (77), hormone secretion (68), and stress (83), as well as external factors such as exercise (84), temperature (68), and meal timing (85).

To examine the sleeping pattern of an individual, one can use both objective and subjective measures. Objective measures involve using equipment to directly or indirectly monitor and measure different physiological parameters such as brain waves, movement, muscle tone, heart rate and respiration rate (68). On the other hand, subjective measures rely on self-reported experiences of sleep and are often done by questionnaires such as the Pittsburgh Sleep Quality Index (86,87). Objective measures of sleep are generally considered more accurate than subjective measures because they can provide detailed information about the different stages of sleep and identify sleep disorders that may go unnoticed by the individual (68,75).

In the field of sleep medicine, certain parameters are often considered when examining sleeping patterns. Total sleep time (TST) is one such parameter, representing the amount of time spent asleep, excluding the time it takes to fall asleep and any time spent awake during the night (88). TST is an important sleep parameter that provides valuable information about the sleep quantity. Another commonly used parameter is sleep efficiency (SE), which refers to the time an individual spends asleep relative to the total time spent in bed. SE is expressed as a percentage and is calculated by dividing the TST by the total time spent in bed (including awakenings at night) (88). A Low SE can

indicate frequent awakenings during the night, disrupting the sleep cycle and is often used as a measure of sleep quality (89,90). Sleep onset latency (SOL) is the time it takes for an individual to transition from wakefulness to sleep (91). A long SOL can indicate difficulty falling asleep, a common symptom of insomnia (92). These parameters, among others, can be used to obtain information and understanding of the sleeping pattern of individuals and detect possible symptoms of sleep disorders (68). Figure 1 illustrates the sleep parameters TST, SE and SOL.

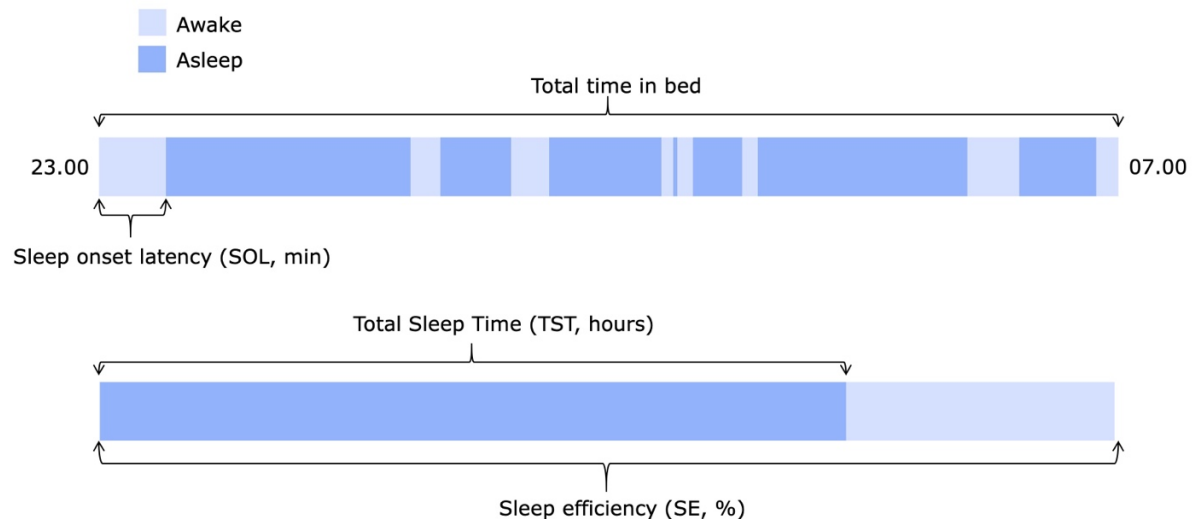


Figure 1: A graphical representation of three sleep parameters: Total sleep time (TST), sleep efficiency (SE) and sleep onset latency (SOL) over the course of a typical sleep session from 11 pm to 7 am. TST: the amount of time spent asleep, excluding the time it takes to fall asleep and any time spent awake during the night in hours. SE: TST divided by the total time spent in bed (including awakenings at night) in %. SOL: the time it takes for an individual to transition from wakefulness to sleep in minutes. Light blue represents time awake, while dark blue represents time asleep.

The prevalence of sleep problems tends to increase with age, possibly due to changes in sleeping patterns over a lifetime (68,93). As people age, they are more likely to report difficulties initiating and maintaining sleep, early morning awakening, and dissatisfaction with sleep (93). Studies have found a decrease in TST and SE (94–96) and an increase in the number of awakenings per night (68,94,97) with age. Chronic sleep deprivation has been linked to a range of negative health outcomes, including increased risk for CVD (51,98,99), diabetes (51,52), obesity (51–55) and depression (100,101), highlighting the critical role of sleep in maintaining physical and mental health.

A growing body of evidence has suggested a positive effect of exercise on sleep parameters (61–63,102–104). However, the relationship between exercise and sleep is complex and can be influenced by various factors such as time of day (105–107), duration (108,109), intensity (106,110), and modality (110,111). In addition, while short-term effects of exercise occur following a single exercise bout, regular exercise over an extended period of time can induce additional physiological changes (21). Understanding the mechanisms behind the effects of exercise on sleep parameters can provide insight into the potential for exercise to serve as a non-pharmacological treatment for sleep problems. Various pathways have been proposed to explain the relationship between exercise and sleep, yet the underlying mechanisms are still debated (63,112).

Exercise at approximately the same time of day has been shown to have circadian phase-shifting effects (84,113), helping to regulate the circadian rhythm, leading to more regular and predictable sleep-wake cycles (76,114). One proposed mechanism behind this is a change in melatonin secretion, and studies have shown that exercise can alter the timing of melatonin release (84,115). This shift can be affected by the time of day exercise is performed, and late-night exercise has been found to produce phase-delay shifts in melatonin secretion (116,117), potentially leading to delayed sleep onset.

During exercise, the core body temperature rises due to increased metabolic rate and heat production, depending on the intensity and duration of the exercise performed (21). The elevated body temperature is then followed by a subsequent decrease in body temperature during the recovery period (118,119). An important aspect of the circadian rhythm is the gradual decrease in core body temperature before bedtime, a physiological mechanism that facilitates the initiation and preservation of sleep (120,121). Changes in core body temperature during and after exercise are proposed as a factor that can impact sleep parameters, and the effect may depend on the timing and intensity of the exercise (63,112,118).

An important mechanism in the initiation of sleep is that the parasympathetic nervous system becomes more dominant while the sympathetic nervous system decreases its activity (122). This shift in the balance of the autonomic nervous system promotes relaxation and recovery (68). Exercise induces a shift towards activation of the sympathetic nervous system, increasing with exercise intensity (21). Additionally, exercise has been found to have varying effects on the autonomic nervous system balance during sleep, depending on the time when exercise is performed. Late-night exercise has been shown to increase sympathetic activity, whereas daytime exercise has been found to increase parasympathetic activity during sleep (123). Therefore, both exercise intensity and timing can impact sleep parameters by interfering with the balance of the autonomic nervous system during sleep.

Given the potential benefits of exercise on both sleep and the risk reduction of myocardial infarction, it is important to investigate the effect of exercise on sleep in this group of patients. Previous research has suggested that exercise can improve sleep parameters in healthy individuals and those with medical conditions such as insomnia (110,124). However, the relationship between exercise and sleep in myocardial infarction patients is not well understood. By gaining a better understanding of the mechanisms underlying these relationships, researchers may be able to develop more effective interventions to promote healthy sleep and reduce the incidence of myocardial infarction.

Research aims

To contribute to closing the current knowledge gap, our aim was to investigate the level of CRF and the effect of exercise on three different sleep parameters: TST, SE, and SOL in Norwegian myocardial infarction patients. Firstly, we wanted to examine if there were changes in descriptive characteristics from pre- and post-test. Secondly, we wanted to investigate the effects of CRF on sleep parameters and used VO_{2peak} as the variable to represent CRF. We tested whether individual variation in mean VO_{2peak} could explain individual variation in mean sleep parameters. In addition, we aimed to explore whether a change in VO_{2peak} from pre- to post-test (ΔVO_{2peak}) could explain changes in sleep parameters over the study period. Thirdly, we wanted to examine the effect of exercise on sleep parameters the following night by incorporating various exercise variables: exercise (yes or no), exercise intensity (high intensity (HI: > 85 % HR_{peak}) or moderate intensity (MI: 70 - 85 % HR_{peak})) and time of day (evening exercise: < 4 hours before bedtime or daytime exercise: > 4 hours before bedtime). Overall, this study aims to contribute to the understanding of the effect of exercise on sleep parameters in myocardial infarction patients.

2. Methods

2.1 Study population

The present study is a substudy of The Norwegian Trial of Physical Exercise after Myocardial Infarction (NorEx). NorEx aims to investigate the effect of 4 years of supervised physical exercise on mortality and cardiovascular morbidity in myocardial infarction patients, thereby finding evidence of the long-term effects of physical activity (125). The NorEx population consists of Norwegian men and women between 18-79 years who suffered an acute myocardial infarction (Type 1) within the period 2013-2022 and fulfilled the recruitment criteria (Table 1). Participants are randomly allocated into three groups: one intervention group and two control groups (Control group 1 and 2) with different levels of contact with study personnel, Figure 2.

Table 1: Inclusion and exclusion criteria for participating in the NorEx-study (125).

Inclusion criteria	Exclusion criteria
Age 18-79 years when receiving study invitation	Participate in physical activity at a similar or greater level than expected from the intervention group.
Hospitalised with an acute myocardial infarction (Type I) during 2013-2022.	Participating in another study on physical exercise
Norwegian national identification number	Participate in endurance sport competitions
Speak one of the Scandinavian languages	Alcohol or drug abuse
Being able to be physically active	Cardiac conditions that may restrict moderate or high-intensity physical activity.
Signed informed consent.	Inability to comply with the study protocol due to any physical disability, somatic disease, or mental problem (i.e., dementia or serious psychiatric disease) Residing in nursing home or other institution. Participating in another research study on physical exercise. Short life expectancy due to end- stage somatic disease (i.e., advanced cancer or chronic lung disease with exacerbations)

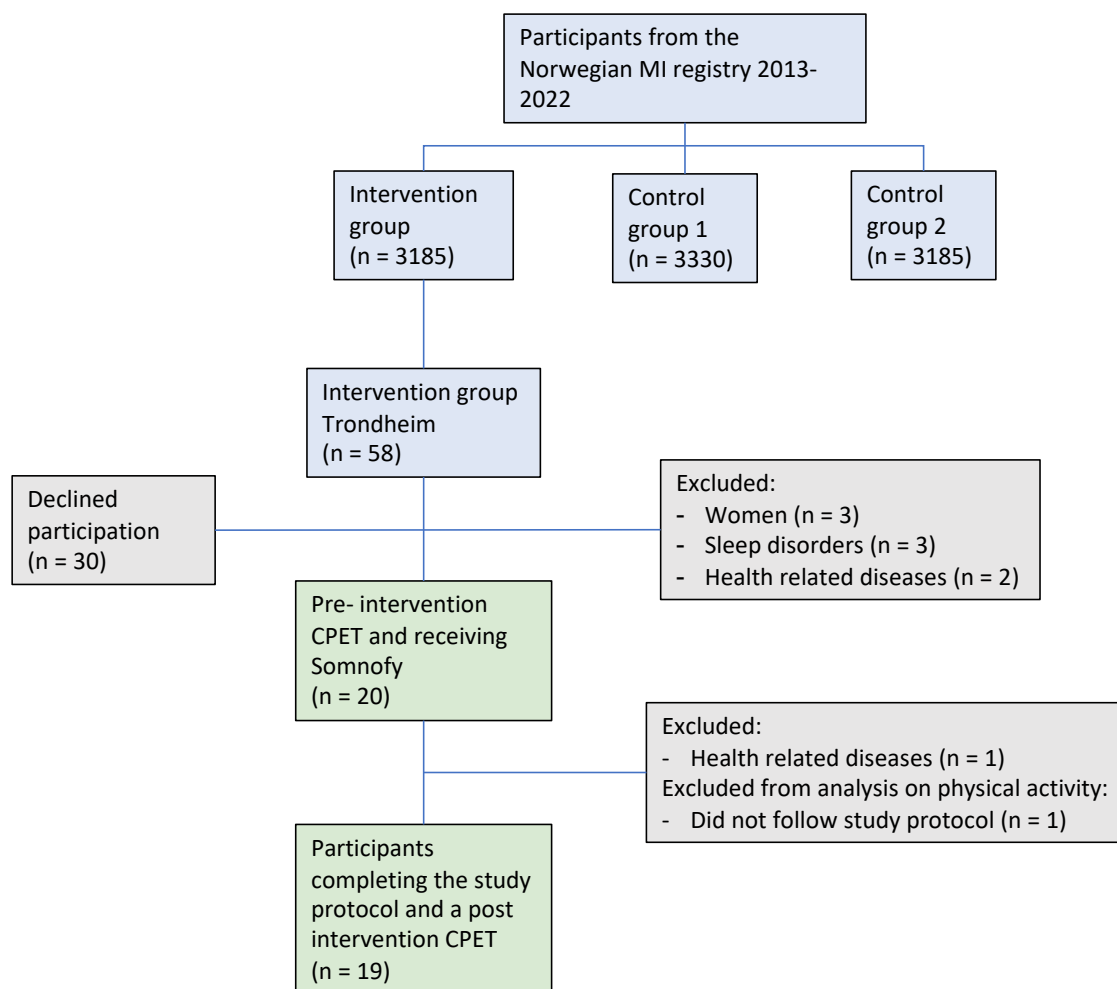


Figure 2: Flow chart illustrating the recruitment process in the NorEx-study (blue). The intervention group in Trondheim was invited to participate in our substudy. Green represents our study population after exclusion (grey).

Participants from the intervention group located in the Trondheim area ($n = 58$) were invited to participate in the substudy, and Figure 2 illustrates the recruitment of participants. 28 individuals (25 men and 3 women) showed interest in participating in the study, resulting in a response rate of 48.3%. Due to the limited sample size and uneven sex distribution, the women ($n = 3$) were not included in our study population. Moreover, participants with known sleep disorders ($n = 3$) and participants unable to follow the study protocol ($n = 2$) were excluded. Further, one participant was excluded from the data material due to the development of a severe condition. The final study population comprised 19 men between the ages of 44–72 years who completed the study protocol. One participant did not wear the Amazfit Health Watch (Model A2012. Anhui Huami Information Technology Co., Ltd., Hefei, China) or write an exercise diary, leading to missing data on exercise. The analysis with parameters from the Amazfit Health Watch or exercise diary therefore only includes 18 participants.

2.2 Study design

The study was conducted over 12 weeks from March to May 2022. At study start, the participants received and installed a Somnofy sleep monitor (VitalThings AS, Norway) to collect sleep measurements during the whole study period (see section 2.5). To evaluate submaximal and maximal levels of cardio-respiratory variables, the participants completed a treadmill walking/running CPET. The CPET was conducted once in March 2022 (hereafter termed "pre-test") and once in May 2022 (hereafter termed "post-test") (see section 2.3).

During the study period, participants were instructed to wear their Amazfit Health Watch which continuously collects data on daily exercise and heart rate (see section 2.4). Participants in the intervention group were instructed to perform 115 minutes of exercise weekly consisting of at least 20 minutes of high intensity (HI: > 85 % of HR_{peak}) and remaining minutes at moderate intensity (MI: 70-85 % of HR_{peak}) (125). The participants in this substudy were requested to continue to follow the exercise protocol and, if possible, increase the exercise dose during the study period. The participants also logged and categorised their workouts as either MI (workouts including at least 20 minutes of MI) or HI (workouts including at least 8 minutes of HI) in an exercise diary. HR_{peak} for each participant was assessed during the first CPET (see section 2.3) to ensure correct exercise intensity.

To motivate the participants to follow the exercise requirements each week, we offered group training sessions on treadmills (PPS Med 55, Woodway, Weil am Rhein, Germany) at St. Olavs hospital 2-3 times a week throughout the study period. The training protocol consisted of a 15 min individual warm-up followed by a 4 x 4 high-intensity interval session (4 min activity at 85 > % HR_{peak} , followed by 3 min of active rest at 70 % HR_{peak}). The training sessions were voluntary, and some participants chose not to attend.

2.3 Assessment of Cardiorespiratory fitness (CRF)

2.3.1 Cardiopulmonary Exercise Testing (CPET)

At pre- and post-intervention, the participants completed an individualized graded test protocol where cardio-respiratory variables were measured with CPET at the NeXt Move Core facility at St. Olavs Hospital, Emergency and Cardiothoracic Centre, Trondheim, Norway.

2.3.1.1 Measurement of descriptive variables

Before the test, body mass was measured to the nearest kilogram (kg) using a weighing scale, Model DS-102 (Arctic Heating AS, Nøtterøy, Norway). The participant's height was measured to the nearest whole centimetre with a stadiometer. An automatic blood pressure monitor (SunTech Medical, Morrisville, NC, USA) was used to measure the blood pressure once on the right overarm in an upright standing position before the warm-up and after the CPET. No CPET was performed if blood pressure values were above 200/110 mmHg in accordance with the guidelines of the American Heart Association (AHA) (126).

2.3.1.2 Electrocardiogram and heart rate measurement

To monitor the cardiac response during the CPET, an electrocardiogram (ECG) was continuously recorded using a standard 12-lead ECG (Custo Med GmbH, Ottobrunn, Germany) following the AHA guidelines for exercise testing of patients with CVD (126). During the test protocol, heart rate (HR) was measured by radio telemetry (H10, Polar, Kempele, Finland) to ensure accurate heart rate measurements. HR_{peak} was defined as the highest HR value attained during the CPET (127).

2.3.1.3 Test protocol

An ergospirometry system (Metalyzer II, Cortex Biophysik GmbH, Leipzig, Germany) was used to measure cardiorespiratory variables: oxygen uptake (VO_2 : $mL \cdot kg^{-1} \cdot min^{-1}$, $L \cdot min^{-1}$), breathing frequency (f_B : $beats \cdot min^{-1}$), peak ventilation (VE : $L \cdot min^{-1}$), expired carbon dioxide (VCO_2 : $L \cdot min^{-1}$), respiratory exchange ratio (RER) ($CO_2 \cdot VO_2^{-1}$). The participant used a size-fitted facemask (Hans Rudolph, Kansas, MO, USA) and mask harness coupled to the MetaLyzer II for gas analysis. The MetaLyzer II was calibrated each day, and after every fourth test using a standard gas calibration procedure and barometric pressure control. The two-point gas calibration consisted of two measurements, one of ambient air in the room and one including a gas mixture of 15.03% O_2 and 4.98% CO_2 in N_2 (HIQ Center, AGA HIGH Q A/S, Oslo, Norway). Ambient gas calibration was performed before every test in addition to a volume calibration of the volume transducer (Triple-V, Cortex Biophysik GmbH, Leipzig, Germany) with a calibrated 3 L syringe (Calibration Syringe 3000ml, Cortex Biophysik GmbH, Leipzig, Germany).

The participants completed a 10-minute warm-up before the test, to become familiar with the treadmill (PPS Med 55, Woodway, Weil am Rhein, Germany) and test protocol. The NorEx protocol consists of three different workloads, two submaximal and one peak (125). The workload (speed and incline) at stage 1 was determined based on the participants' self-reported fitness level, HR and rate of perceived exertion (RPE) on the Borg scale (128) during warm-up. Stage 1 lasted for three minutes until reaching stable VO_2 and HR. During stage 2, the workload was increased, either by a 2 % incline or a 1 km/h increase in speed, with stable VO_2 and HR obtained after three minutes. In stage 3 the workload was increased by either 1 $km \cdot h^{-1}$ or 2 % incline or by a combination of 0.5 $km \cdot h^{-1}$ and 1 % incline per minute. The test ended by stopping the treadmill at exhaustion (e.g., shortness of breath and leg fatigue) or earlier if any of AHA's indications for test termination were observed (126). The participants were instructed to avoid grabbing the handrails during the test if not absolutely necessary. Between each stage, the participants used Borg-scale (6-20) to determine RPE (128). The VO_{2max} was calculated as an average of the three highest 10-second measurements over a 30-second period. The criteria for reaching VO_{2max} was a plateau in VO_2 levels even with increasing workload (seen as no more than 2 $mL \cdot kg^{-1} \cdot min^{-1}$ increase in VO_2 between two 30-second epochs) combined with an RER ≥ 1.05 . Tests that did not meet these criteria were considered VO_{2peak} (125). Since 12 out of 38 tests (19 pre- and 19 post-test) did not fulfil the criteria for VO_{2max} the term VO_{2peak} was used.

2.4 Assessment of physical activity

The Amazfit Health Watch is a wearable activity tracker that collects continuous data on activity, heart rate (HR) and sleep parameters. The web portal Midong Health Platform (Anhui Huami Information Technology Co., Ltd., Hefei, China) was developed for monitoring and data storage from the Amazfit Health Watch. At the end of the study period, the pulse curves in the web portal were manually examined and compared with the exercise diary for every participant to ensure and divide the exercise sessions into categories: exercise (yes or no), exercise intensity (high intensity (HI: $> 85\% \text{HR}_{\text{peak}}$) or moderate intensity (MI: $70\text{-}85\% \text{HR}_{\text{peak}}$)) and time of day (evening exercise: < 4 hours before bedtime or daytime exercise: > 4 hours before bedtime). HR_{peak} from the CPET was used to control exercise intensities when examining the pulse curve in the web portal.

2.5 Assessment of sleep variables

2.5.1 Somnofy

Somnofy is a noncontact monitor that measures variables such as breathing frequency, sound, light and movement. The monitor uses radar technology, where pulses (IR-UWB) are emitted and then reflected by objects and returned to the device. Based on movement and respiration data, the monitor uses machine learning to categorise different stages of sleep (wake, light-, deep- and REM- sleep). In a validation study by Toften et al. (129) the Somnofy sleep monitor was compared to polysomnography, the gold standard for sleep measurements. For a comprehensive technical understanding of the sleep monitor, the validation outcomes, and limitations, see Toften et al. (129).

The participants received a Somnofy sleep monitor linked to a personal account that monitored their sleep every night over the study period. The device was installed according to the instructions given by Vital Things AS (130). The monitor was placed in the bedroom on a nightstand at chest height, pointing directly at the participant's chest, Figure 3. For the participants that shared a bed with a partner, a measurement cut-off distance was set to avoid signals from the other person during the night, Figure 3. When installed correctly, the sleep monitor automatically started and stopped a session by recognizing whether a person was in bed or not. The participants did not have access to their sleep measurements during the study period, except for the first four days, to ensure correct monitor setup.

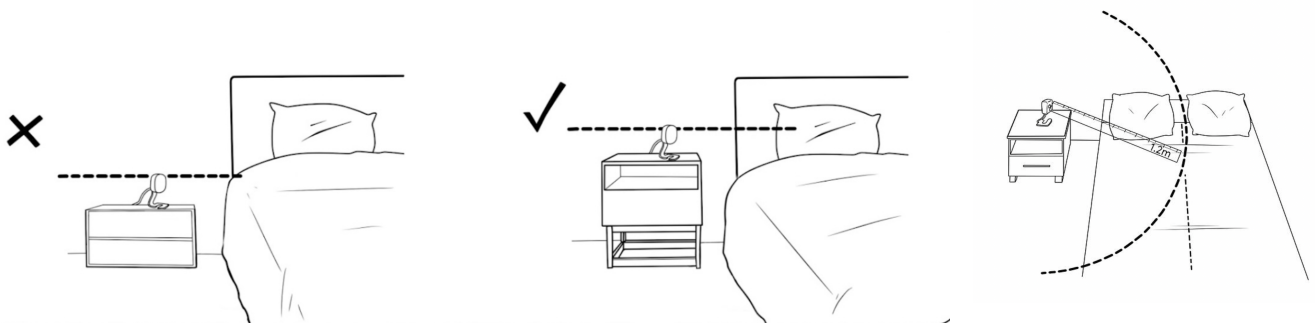


Figure 3: Installation of Somnofy in the bedroom and example of cut-off distance. From “Installasjon” by VitalThing AS (2022) (<https://kb.somnofy.com/no-no/installasjon>) (130).

The following sleep parameters were obtained from the Somnofy sleep monitor: TST (sec), SE (%) and SOL (sec). Somnofy automatically stored all the data from each sleep session. After the study period, VitalThings AS combined and exported the data set. A total number of 1438 sessions were recorded throughout the study period. The following exclusion criteria were established after consulting with an expert in VitalThings AS: 1) daytime sleep or naps ($n = 16$), 2) epoch count < 2 hours ($n = 40$), 3) time asleep < 2.5 hours ($n = 44$) and 4) poor signal quality ($n = 47$) to ensure high data quality. Poor signal quality can result from sensor blockage, signals collected from pets or other instruments such as fans and suboptimal monitor set-up. The analysis included 1291 sessions, giving a 90% compliance with the data collection.

2.6 Allometric scaling

The absolute level of VO_{2peak} ($L \cdot \text{min}^{-1}$) is influenced by body mass and increases with heavier individuals (131). To adjust for body size differences, VO_{2peak} is commonly expressed as $\text{mL} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ by dividing body mass in kg. However, VO_{2peak} ($L \cdot \text{min}^{-1}$) scales exponentially rather than proportionally with body mass (131,132) and research suggests that it increases more closely with body mass raised to the power of 0.75 (133). Scaling VO_{2peak} to the power of 0.75 adjusts for this non-linear relationship and provides a better estimate of the metabolic rate across different body sizes. Therefore, it is recommended to use allometric scaling when comparing VO_{2peak} between individuals.

In this study, VO_{2peak} was expressed as $\text{mL} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$ when comparing pre-test and post-test VO_{2peak} within individuals because body mass did not change significantly during the study period. However, when comparing among individuals, appropriate allometric scaling was applied, and body mass was raised to the power of 0.75 and VO_{2peak} was expressed as $\text{mL} \cdot \text{kg}^{-0.75} \cdot \text{min}^{-1}$. This method makes the results more intelligible and avoids the potential for bias towards either lighter or heavier individuals.

2.7 Statistical analyses

The statistical analyses were performed with R version 4.1.2 (134). Linear models were performed with the `lm` function, and used when all observations were independent. Diagnostic plots (residuals vs fitted, QQ-plot, and Cook's distance) were used to assess whether the other assumptions of linear models were sufficiently met (linearity, normally distributed residuals, and constant variance of residuals (homoscedasticity)). Sleep parameters were measured repeatedly within individuals, and such data are not independent. Hence, linear mixed-effects models were applied using the `lme4` (135) and `nlme` package (136) to analyse the effect of exercise on sleep parameters the following night. All linear mixed-effects models were fitted with individual ID as random factor (random intercept). Parameter estimates were obtained with the `summary` function, and 95 % confidence intervals (95 % CI) were obtained with the `confint` and `intervals` functions. For all tests, a significance level of $p < 0.05$ was used. The package `ggplot2` (137) was used to make scatterplots and boxplots. The boxplot shows the median and the first and third quartile in the data set, along with whiskers (minimum within first quartile $-1.5 \times$ interquartile distance and maximum within third quartile $+1.5 \times$ interquartile distance) and outliers (data outside whiskers). Results are presented as mean \pm standard deviation (SD) if not otherwise stated.

The data were analysed in three sets of analyses: 1) pre- and post-tests of descriptive characteristics, 2) sleep and CRF and 3) sleep and exercise.

1) Paired t-tests were used to compare individual descriptive characteristics between pre- and post-test: body mass (kg), BMI ($\text{kg}\cdot\text{h}^{-2}$), VO_2 ($\text{L}\cdot\text{min}^{-1}$), $\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), $\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-0.75}\cdot\text{min}^{-1}$), HR_{peak} ($\text{beats}\cdot\text{min}^{-1}$), RER ($\text{CO}_2\cdot\text{VO}_2^{-1}$), RPE (Borg), treadmill incline (%), treadmill speed ($\text{km}\cdot\text{h}^{-1}$).

2) For analysing how $\text{VO}_{2\text{peak}}$ potentially affected sleep, the three sleep parameters TST, SE and SOL were used as response variables and $\text{VO}_{2\text{peak}}$ as the predictor variable in separate models for each dependent variable. Two different approaches were used. In the first approach, the means were calculated for each individual for all sleep parameters and $\text{VO}_{2\text{peak}}$ (mean $\text{VO}_{2\text{peak}}$, mean TST, mean SE and mean SOL). The mean of each sleep parameter for each participant was used in the analysis since the sleep parameters did not change statistically significantly through the study period ($p > 0.470$) (see Appendix for calculations, Table A1). Since the sleep parameters were measured every night during the study period and $\text{VO}_{2\text{peak}}$ only twice (pre and post) for each individual, calculating means provided an independent and balanced data set. Although the sleep parameters nor $\text{VO}_{2\text{peak}}$ changed for the entire population over the study period, there was substantial individual variation, with some individuals increasing and some decreasing their sleep parameters or $\text{VO}_{2\text{peak}}$. In the second approach, we therefore investigated whether any individual change in the sleep parameters over the study period was related to a change in $\text{VO}_{2\text{peak}}$ from the pre- to post-test ($\Delta\text{VO}_{2\text{peak}}$). Changes in sleep parameters were calculated as the linear regression coefficient (β) for each sleep parameter for each participant using the sleep parameters: TST, SE or SOL as response variable and days from study start as the predictor variable. $\Delta\text{VO}_{2\text{peak}}$ was calculated as $\text{post } \text{VO}_{2\text{peak}} - \text{pre } \text{VO}_{2\text{peak}}$. Finally, linear models were used to test whether $\Delta\text{VO}_{2\text{peak}}$ affected change in sleep parameters. Changes in sleep parameters were response variables, and $\Delta\text{VO}_{2\text{peak}}$ was the predictor variable, in separate models for each of TST,

SE and SOL. Age did not significantly predict VO_{2peak} ($p > 0.05$) and was not added as a covariate in any of the models (see Appendix for calculations, Table A2).

3) Linear mixed-effects models were used to analyse the effect of exercise on sleep parameters the following night. We analysed three response variables, TST, SE and SOL, and in relation to three exercise parameters as predictor variables, in 9 separate models. The exercise parameters were: 1) exercise (binary variable: yes or no), 2) exercise intensity (binary variable: HI: $> 85\% HR_{peak}$ or MI: $70-85\% HR_{peak}$), and 3) the time of day when exercise was performed (binary variable: evening exercise: > 4 hours before bedtime or daytime exercise: < 4 hours before bedtime). All these exercise and sleep parameters were obtained on a daily basis, i.e., from the same day and following night.

2.8 Ethical Statement

The NorEx project has received approval from the Regional Committee for Medical Research Ethics (REK 2019/797), the Norwegian Data Inspectorate, and the National Directorate of Health. NorEx is registered on ClinicalTrials.gov (NCT04617639).

3. Results

3.1 Pre- and post-tests of descriptive characteristics

The following descriptive characteristics: body mass (kg), BMI ($\text{kg}\cdot\text{h}^{-2}$), VO_2 ($\text{L}\cdot\text{min}^{-1}$), $\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), $\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-0.75}\cdot\text{min}^{-1}$), HR_{peak} ($\text{beats}\cdot\text{min}^{-1}$), RER ($\text{CO}_2\cdot\text{VO}_2^{-1}$), RPE (Borg), treadmill incline (%) and treadmill speed ($\text{km}\cdot\text{h}^{-1}$) for the 19 participants at pre- and post-test are presented in Table 2. The study population consisted of only men. There was no statistically significant change ($p > 0.05$) in any of the descriptive characteristics from pre- to post-test, Table 2.

Table 2: Means (with ± 1 SD) for descriptive characteristics of the participants ($n = 19$, all adult males) at the pre- and post-test. Paired t-tests showed no statistically significant change ($p > 0.05$) for any of the descriptive characteristics from pre- to post-test. $\text{VO}_{2\text{peak}}$: Peak oxygen uptake, BMI: Body mass index, HR_{peak} : Peak heart rate, RER: Rate of perceived exertion, RPE: Rate of perceived exertion.

	Pre-test	Post-test
Age (years)	58.8 \pm 7.5	
(min-max)	(44 – 72)	
Height (cm)	180 \pm 7	
Body mass (kg)	97 \pm 15	97 \pm 15
BMI ($\text{kg}\cdot\text{h}^{-2}$)	29.8 \pm 3.9	29.9 \pm 3.9
$\text{VO}_{2\text{peak}}$ ($\text{L}\cdot\text{min}^{-1}$)	3.54 \pm 0.59	3.49 \pm 0.62
$\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	37.0 \pm 7.3	36.4 \pm 6.8
$\text{VO}_{2\text{peak}}$ ($\text{mL}\cdot\text{kg}^{-0.75}\cdot\text{min}^{-1}$)	115.5 \pm 20.4	113.6 \pm 19.4
HR_{peak} ($\text{beats}\cdot\text{min}^{-1}$)	166 \pm 8	168 \pm 8
RER ($\text{CO}_2\cdot\text{VO}_2^{-1}$)	1.06 \pm 0.07	1.08 \pm 0.06
RPE (Borg)	18 \pm 1	19 \pm 1
Treadmill incline (%)	10.8 \pm 4.5	11.0 \pm 4.7
Treadmill speed ($\text{km}\cdot\text{h}^{-1}$)	7.4 \pm 2.0	7.5 \pm 2.1

One participant did not wear the Amazfit Health Watch or write an exercise diary, leading to missing data on exercise. Therefore, the analysis regarding exercise only includes 18 participants. During the study period, the participants ($n = 18$) had a mean of 2.8 ± 1.0 training sessions per week, where 1.1 ± 0.8 was MI-exercise sessions and 1.6 ± 0.6 was HI-exercise sessions.

On group level, the study population ($n = 19$) showed no significant change in VO_{2peak} during the study period ($p > 0.05$) with a change of $-0.7 \pm 3.1 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ from pre- to post- test. However, 10 out of 19 individuals changed their VO_{2peak} by more than $2.0 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, see Figure 4.

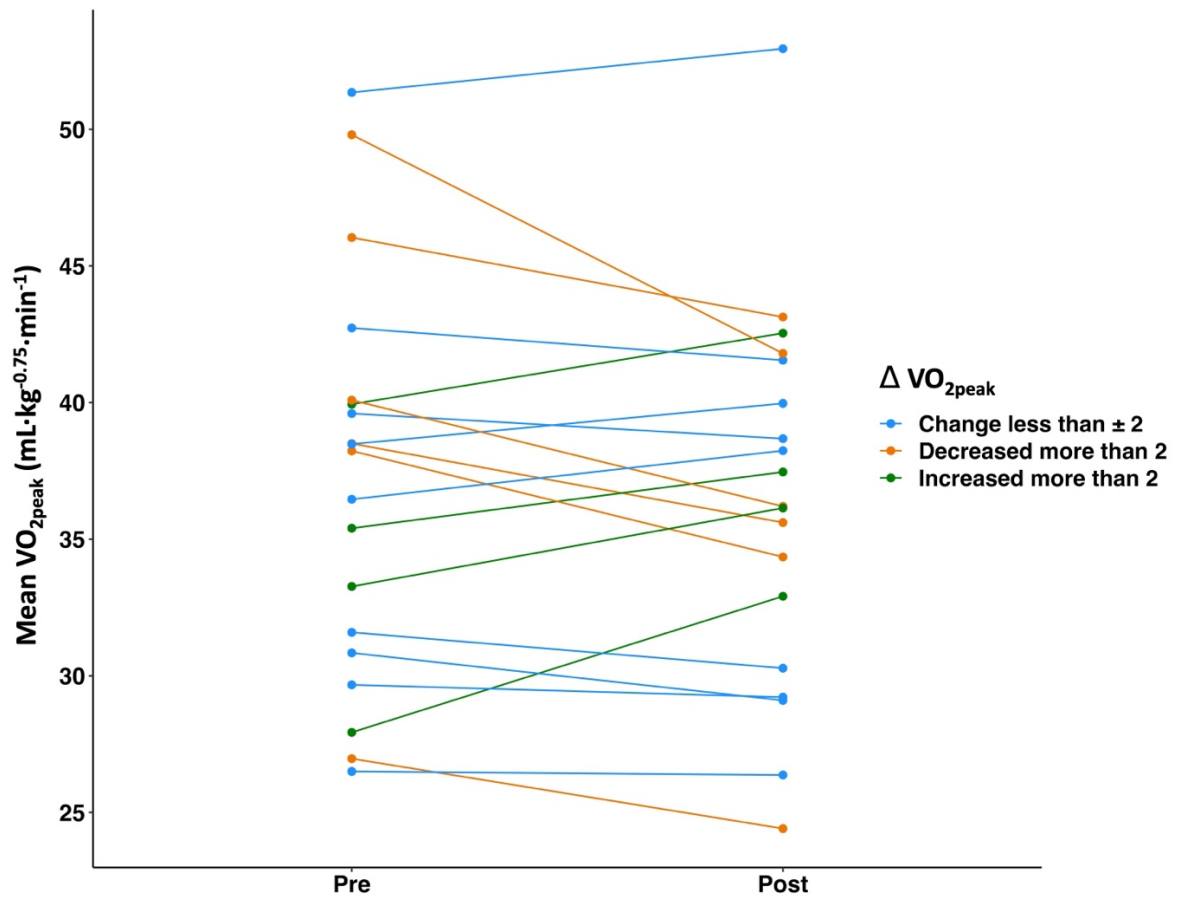


Figure 4: Change in VO_{2peak} $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ from pre- to post-test for each participant in the study population ($n = 19$). Changes in VO_{2peak} are represented in different colours; blue: changes less than $\pm 2.0 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, orange: decreased more than $2.0 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, green: increased more than $2.0 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.

3.2 Sleep and CRF

The study population had a mean TST of 6.0 ± 0.8 hours, SE of $80.4 \pm 6.9 \%$, and SOL of 19.7 ± 11.8 minutes per night. During the study period, there were no significant changes in TST ($p > 0.470$), SE ($p > 0.079$) or SOL ($p > 0.803$) for the study population (Table A1, Appendix). However, there was individual variation, with both positive and negative slopes for TST, SE or SOL during the study period, as illustrated for TST see Figure A1 in Appendix. In addition to analysing the mean sleep in relation to mean VO_{2peak} , we therefore also analysed change in sleep parameters in relation to ΔVO_{2peak} . The individual changes in TST, SE and SOL over the course of the study period were further used to investigate if ΔVO_{2peak} were associated with changes in sleep parameters.

The result from the linear models demonstrated that mean VO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$) (mean of the pre- and post-test measurements) did not statistically significantly explain the individual variation in mean TST, mean SE or mean SOL (Table 3). The mean TST increased 0.004 hours per one $mL \cdot kg^{-0.75} \cdot min^{-1}$ increase in mean VO_{2peak} , but this was not statistically significant ($p = 0.666$, Table 3), as illustrated in Figure 5. There was a negative, but non-significant, relationship between mean SE and mean VO_{2peak} with a decrease of 0.08 % per one $mL \cdot kg^{-0.75} \cdot min^{-1}$ increase in mean VO_{2peak} ($p = 0.325$, Table 3). Mean SOL increased with 0.10 minutes per one $mL \cdot kg^{-0.75} \cdot min^{-1}$ increase in mean VO_{2peak} , but this was not statistically significant ($p = 0.519$, Table 3).

The ΔVO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$) from pre- to post-test was not statistically associated with changes in any of the three sleep parameters during the study period. TST ($p = 0.611$, Table 4), SE ($p = 0.382$, Table 4) or SOL ($p = 0.278$, Table 4) during the study period among individuals. There was a positive, but non-significant relationship between the change in TST and ΔVO_{2peak} ($p = 0.611$, Table 4), as illustrated in Figure 5. The change in SE and ΔVO_{2peak} was positively correlated, while the change in SOL and ΔVO_{2peak} was negatively correlated, but neither correlation was statistically significant (SE: $p = 0.382$; SOL: $p = 0.278$, Table 4).

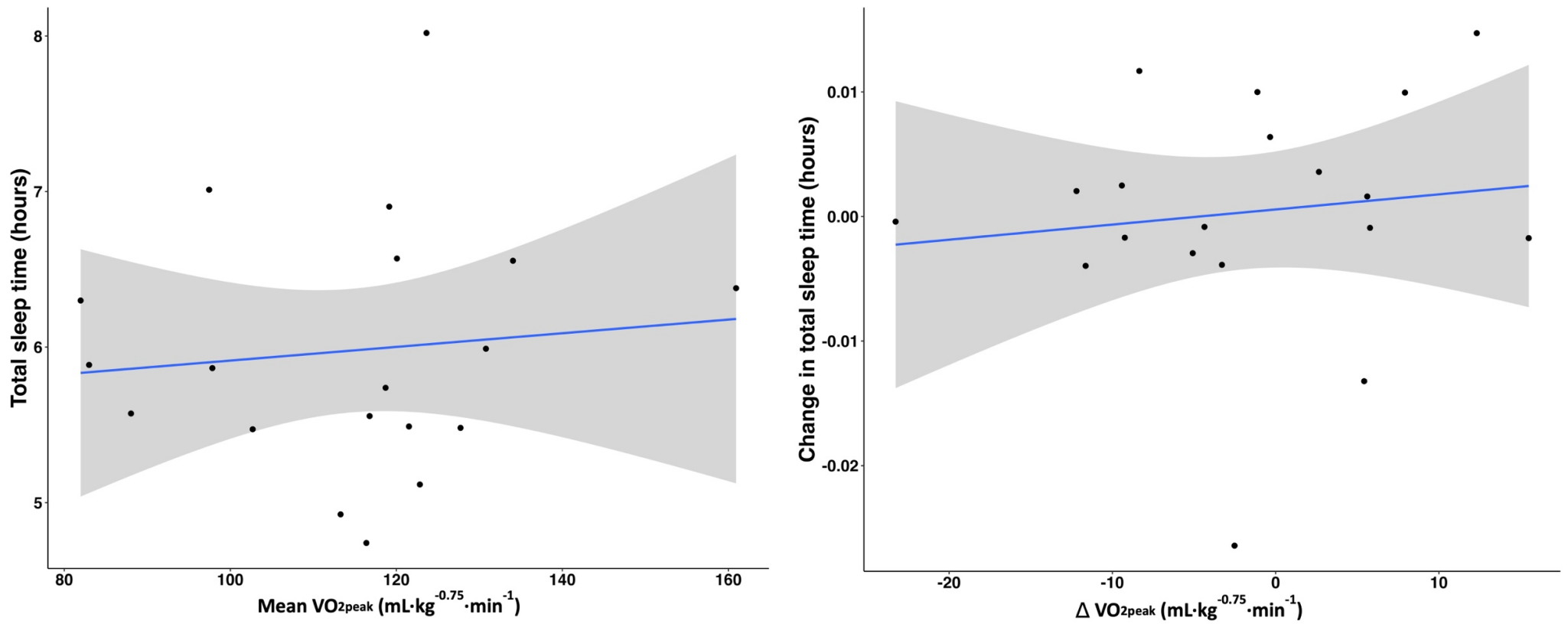


Figure 5: Linear regression of mean total sleep time (TST) on mean VO_{2peak} (left) and of change in TST on ΔVO_{2peak} (right). The slopes of the regression lines were not significantly different from zero as illustrated with the 95 % confidence intervals for the regression lines (grey). The analysis included 19 men.

Table 3: Estimates and test-statistics from the linear models analysing the relationship between: mean total sleep time and mean VO_{2peak} ; mean sleep efficiency and mean VO_{2peak} ; and mean sleep onset latency and mean VO_{2peak} . The estimate for mean VO_{2peak} represents the slope (β) of the linear regression line. The analyses included data from 19 men. 95% CI: 95% confidence interval, n: sample size

	Mean total sleep time (hours) (n = 19)			Mean sleep efficiency (%) (n = 19)			Mean sleep onset latency (min) (n = 19)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	5.47	3.02, 7.93	< 0.001	90.07	69.98, 110.15	< 0.001	8.38	-27.39, 44.15	0.630
Mean VO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$)	0.004	-0.017, 0.026	0.666	-0.08	0.26, 0.09	0.325	0.10	-0.21, 0.41	0.510

Table 4: Estimates and test-statistics from the linear models analysing the relationship between: the slope of the change in total sleep time and ΔVO_{2peak} ; the slope of the change in sleep efficiency and ΔVO_{2peak} ; and the slope of the change in sleep onset latency and ΔVO_{2peak} . Intercept represents the change in sleep parameters if no change in ΔVO_{2peak} . The estimate for ΔVO_{2peak} represents the slope (β) of the linear regression line; change in sleep parameters per day per 1 ml change in VO_{2peak} . The analyses include data from 19 men. 95% CI: 95% confidence interval, n: sample size

	Change in total sleep time (hours) (n = 19)			Change in sleep efficiency (%) (n = 19)			Change in sleep onset latency (min) (n = 19)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	0.001	-0.004, 0.005	0.802	0.02	-0.005, 0.049	0.103	0.008	-0.036, 0.052	0.691
ΔVO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$)	0.0001	-0.001, 0.001	0.611	0.001	-0.002, 0.004	0.382	-0.002	-0.007, 0.002	0.278

3.3 Sleep and exercise

The linear mixed-effect models showed no statistically significant difference for any of the sleep parameters: TST ($p = 0.187$, Table 5), SE ($p = 0.390$, Table 5) or SOL ($p = 0.616$, Table 5) between nights following days with or without exercise. The mean TST was 5.9 hours following exercise days and 6.0 hours following days without exercise. Mean SE was 80.7 % following exercise days and 80.2 % following days without exercise. Additionally, SOL following exercise days was 18.9 minutes compared to 18.3 minutes following days without exercise.

Furthermore, there was no statistically significant difference in any of the sleep parameters TST ($p = 0.295$, Table 6), SE ($p = 0.627$, Table 6) or SOL ($p = 0.345$, Table 6) between nights following MI- and HI-exercise. The mean TST was 6.0 hours and 5.9 hours following MI- and HI-exercise respectively. Additionally, mean SE following MI-exercise was 80.7 % compared to 80.2 % following HI-exercise. Mean SOL was 17.8 minutes following MI-exercise and 19.6 minutes following HI exercise.

The timing of exercise, evening or daytime exercise significantly affected SOL the following night ($p=0.005$, Table 7, Figure 6). Mean SOL was 23.2 minutes following evening exercise compared to 17.4 minutes following daytime exercise (Table 7, Figure 6). However, exercise timing did not significantly explain the difference in mean TST ($p = 0.080$, Table 7) or mean SE ($p = 0.100$, Table 7). The mean TST and SE were 5.8 hours and 79.1 % compared to 6.0 hours and 80.9 % following evening and daytime exercise, respectively.

Table 5: Estimates and test-statistics for the linear mixed-effects models analysing: total sleep time and exercise (binary variable; yes or no); sleep efficiency and exercise (binary variable; yes or no); and sleep onset latency and exercise (binary variable; yes or no). Intercept represents the mean for the sleep parameters following exercise days. No exercise is presented as difference in mean for the sleep parameters from the intercept. 95% CI: 95% confidence interval, individual ID: the variance to individual ID as random effect.

	Total sleep time (hours)			Sleep efficiency (%)			Sleep onset latency (min)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	5.93	5.54, 6.32	< 0.001	80.67	77.41, 83.93	< 0.001	18.90	13.93, 23.88	< 0.001
No exercise	0.09	0.04, 0.23	0.187	-0.51	-1.66, 0.65	0.390	-0.58	-2.86, 1.70	0.616
Random term									
Individual ID	0.66			46.18			101.60		
Residual	1.28			92.55			362.50		
n observations	1230			1229			1230		
n individuals	18			18			18		

Table 6: Estimates and test-statistics for the linear mixed-effects models analysing: total sleep time and exercise intensity (HI: > 85 % HR_{peak} or MI: 70 – 85 % HR_{peak}); sleep efficiency and exercise intensity (HI or MI); and sleep onset latency and exercise intensity (HI or MI). Intercept represents the mean for the sleep parameters for HI-exercise. Moderate intensity is presented as the difference in mean for the sleep parameters from the intercept. 95% CI: 95% confidence interval, individual ID: the variance to individual ID as random effect.

	Total sleep time (hours)			Sleep efficiency (%)			Sleep onset latency (min)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	5.90	5.49, 6.32	< 0.001	80.24	76.84, 83.64	< 0.001	19.58	14.03, 25.13	< 0.001
Moderate intensity	0.11	-0.10, 0.32	0.295	0.48	-1.46, 2.41	0.627	-1.78	-5.48, 1.92	0.345
Random term									
Individual ID	0.72			47.26			119.4		
Residual	1.17			101.54			373.3		
n observations	508			507			508		
n individuals	18			18			18		

Table 7: Estimates and test-statistics for the linear mixed-effects models analysing: total sleep time and exercise timing (evening: < 4 hours or daytime: > 4 hours before bedtime); sleep efficiency and exercise timing (evening or daytime); and sleep onset latency and exercise timing (evening or daytime). Intercept represents the mean for the sleep parameter after daytime exercise. Evening exercise is presented as the difference in mean for the sleep parameters from the intercept. 95% CI: 95% confidence interval, individual ID: the variance to individual ID as random effect.

	Total sleep time (hours)			Sleep efficiency (%)			Sleep onset latency (min)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	5.79	5.35, 6.23	< 0.001	79.13	75.48, 82.77	< 0.001	23.15	17.02, 29.29	< 0.001
Evening exercise	0.20	-0.02, 0.43	0.080	1.77	-0.34, 3.87	0.100	-5.71	-9.72, -1.71	0.005
Random term									
Individual ID	0.71			46.13			118.30		
Residual	1.17			101.01			369.10		
n observations	507			506			507		
n individuals	18			18			18		

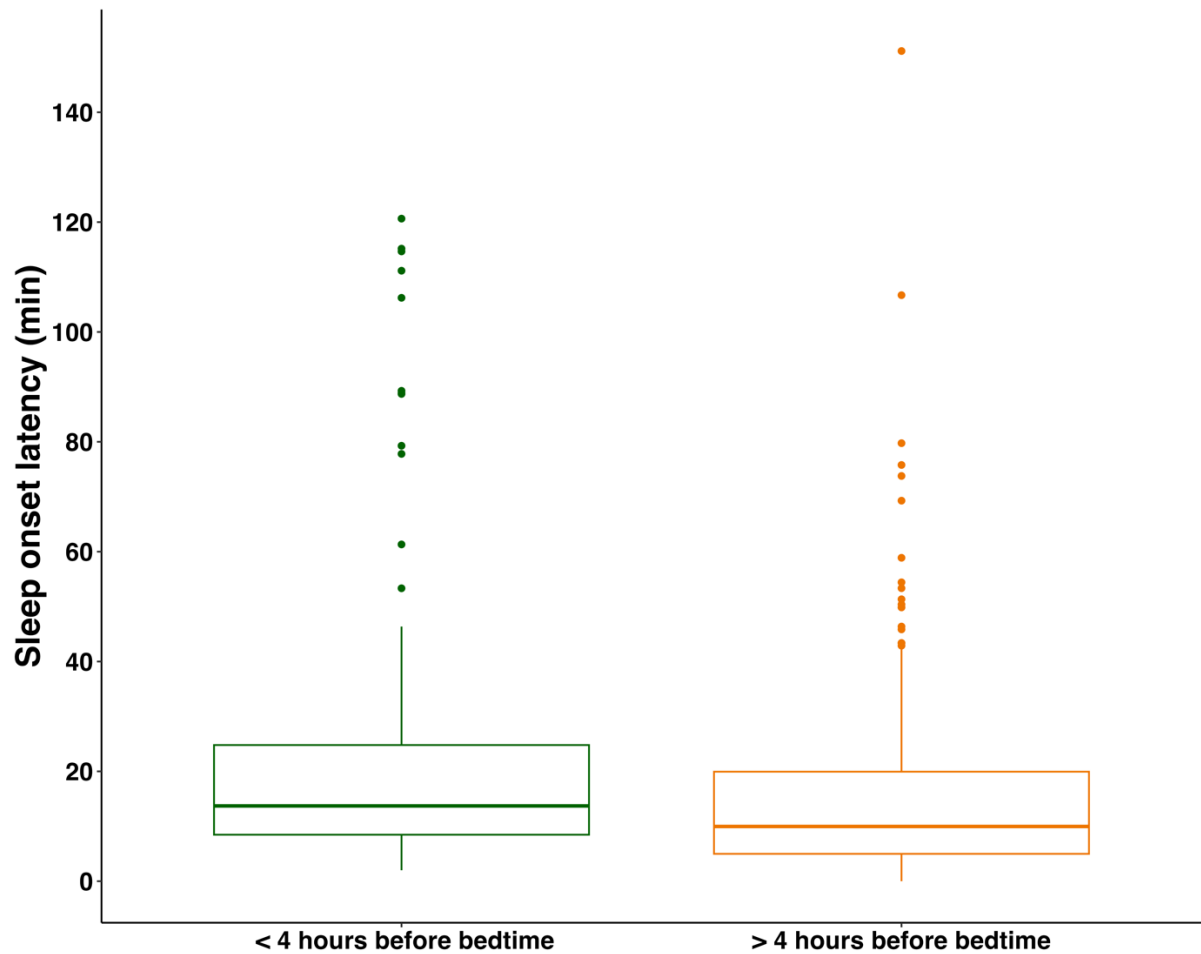


Figure 6: Boxplot showing sleep onset latency (SOL) in minutes for evening (green) and daytime exercise (orange). There is a significant difference in mean sleep onset latency between the two groups ($p = 0.005$). The analyses include 507 observations from 18 men. The boxplot shows the median and the first- and third quartile in the data set. Whiskers extend to the minimum within the first quartile minus 1.5 x interquartile distance and the maximum within the third quartile plus 1.5 x interquartile distance. Values outside the whiskers (outliers) are shown as points.

4. Discussion

During the 12-week study period, there was no change in either VO_{2peak} ($\text{mL}\cdot\text{kg}^{-0.75}\cdot\text{min}^{-1}$) or any of the sleep parameters, TST, SE and SOL, among individuals. However, individual variation was observed, with some experiencing an increase and others a decrease in sleep parameters and VO_{2peak} during the study period. Paired t-tests showed no statistically significant change in any of the descriptive characteristics: body mass, BMI, VO_2 , VO_{2peak} , HR_{peak} , RER, RPE, treadmill incline and treadmill speed from pre- to post-test.

With respect to sleep parameters, linear regression models showed that mean VO_{2peak} did not explain the variation in the mean sleep parameters, TST, SE and SOL in 19 men with a history of myocardial infarction. Neither did ΔVO_{2peak} from pre- to post-test statistically significantly explain the change in TST, SE and SOL during the study period. Linear mixed-effects models showed no statistically significant difference in TST, SE or SOL the following night between days with and without exercise or between MI- and HI-exercise sessions. Moreover, there was a statistically significant increase in SOL ($p = 0.005$) with approximately 6 minutes after evening compared to daytime exercise. However, there was no statistically significant difference in TST or SE between evening and daytime exercise.

4.1 Effects of CRF on sleep parameters

The results showed that different levels of CRF, measured as VO_{2peak} , were not statistically significantly associated with variation in sleep variables: TST, SE or SOL, in this group of myocardial infarction patients. These findings are in accordance with Paxton et al. (138), who found no association between the level of CRF and objectively measured TST and SOL comparing athletes, in both unfit and fit states, to non-athletes. In contrast, Edinger et al. (139) compared fit and unfit individuals based on their fitness level and found higher SE and shorter SOL in the fit group compared to the unfit group. However, one limitation was that the fit group engaged in regular exercise while the unfit group did not. Therefore, one can not conclude that the effect of exercise solely resulted from higher CRF levels, or from the effect of regular exercise. One mechanism by which regular exercise can impact sleep parameters is by producing phase shifts in the circadian rhythm, possibly due to changes in the timing of melatonin release (84,115). Additionally, regular exercise can improve insulin sensitivity (140), lower blood pressure (141), and promote healthy weight maintenance (21), all of which contribute to better overall health and may indirectly affect sleep parameters. In contrast to our findings, Mochón-Benguigui et al. (41) found that higher levels of CRF were associated with improved objectively measured TST and SE in sedentary middle-aged adults, suggesting that there may be an effect of CRF level on sleep parameters in sedentary individuals.

Changes in VO_{2peak} from pre- to post-test were not statistically significantly associated with changes in TST, SE or SOL, suggesting that changes in CRF did not affect sleep parameters in our study population. The changes in VO_{2peak} from pre- to post-test were not statistically significant among individuals, while the individual changes in VO_{2peak} ranged from -8 to +4 $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, see Figure 4. Our results indicate that the changes

in CRF may not substantially impact sleep in this group. However, the small sample size ($n = 19$) and the modest change in VO_{2peak} in either direction may not be large enough to detect any significant changes in sleep parameters, and this must be considered when interpreting our result. In line with our findings, two studies on women (142,143) and a study on older individuals with mild to moderate sleep complaints (144) found no significant effect of improved CRF on changes in objectively measured TST, SE or SOL. On the other hand, a study by Shapiro et al. (145) reported that increases in CRF were associated with longer TST, higher SE and a decrease in SOL in army recruits. However, it is important to note that the study involved military recruits, who engaged in an 18-week-long exercise regime, and the sample size was small ($n = 8$). The possible effects on sleep may come from consistent exercise stimuli rather than a response to improved CRF. While improvements in CRF can enhance oxygen utilisation and cardiovascular function (21), these mechanisms may not be the primary drivers of improved sleep with exercise. Some studies have investigated the impact of regular exercise on sleep parameters without exploring the potential effects of changes in CRF (62,102–104) and found that exercise can lead to improvements in sleep parameters. However, it can be difficult to distinguish between the effect of improved CRF and regular exercise on sleep parameters, and future studies should implement different exercise modalities that create different increases in CRF, such as high-, moderate- and low-intensity endurance exercises, yoga or resistance training.

One potential reason for why we did not observe any statistically significant relationship between CRF level or change in CRF level and sleep parameters can be the potential non-linear relationship between these parameters. Studies have found that the most significant improvements in health are observed when going from a sedentary to an active lifestyle, even with a relatively low dose of exercise, while increasing the exercise dose beyond a certain point does not result in a proportionate increase in benefits (146–149). For individuals with low initial CRF, a small increase in CRF level may therefore result in substantial improvements in sleep, but further increases may not produce the same magnitude of change. Thus, there may be a limit to the amount of improvement in sleep parameters that can be achieved through an increase in CRF. In our study, the participants had already been a part of the NorEx-study for a year and may have already reached the point where additional exercise may not result in further benefits for sleep. To explore the association between changes in CRF level and sleep parameters, it would have been ideal to examine the participants in the early stages of adopting an active lifestyle and conduct a training intervention aimed at increasing their CRF.

It is important to acknowledge that the pre- and post-test measurements may not accurately represent the CRF development of the participants due to daily variation in performance caused by illness, lack of sleep, emotional stress, fatigue, or varying levels of motivation to complete the test (21). To obtain a more comprehensive understanding of the progress in CRF, additional CPETs should have been carried out throughout the study period. Furthermore, it should be noted that 12 out of 38 tests conducted (19 pre-tests and 19 post-tests) failed to fulfil the criteria for VO_{2max} . VO_{2peak} does not represent the true VO_{2max} , as the individual may not reach their true maximum effort during the test, which can impact the accuracy of the CRF level used in the analysis.

Given the potential advantages of exercise on reducing the risk of myocardial infarction and improving sleep, it was important to investigate the effect of exercise on sleep in this study population. The findings indicate that neither the level of CRF nor any changes

in CRF level impact sleep in this cohort of 19 participants with previous myocardial infarction. However, the small sample size and the modest change in VO_{2peak} may not be large enough to detect any significant changes in sleep parameters. Furthermore, it can be challenging to distinguish between the effect of improved CRF and regular exercise on sleep parameters. To fully understand the complex association between CRF and sleep, it is essential to conduct further research using a wide range of study populations with different CRF levels and exercise interventions creating different changes in CRF.

4.2 Effects of exercise on sleep parameters the following night

No statistically significant difference was observed in TST, SE or SOL between nights following days with and without exercise in our study population. The results align with previous research that did not observe any significant alterations in objectively and subjectively measured TST, SE, and SOL on days with exercise compared to days without exercise (124,150–155). In contrast to our findings, some studies have found an increase in SE (156) and TST (157) and decreased SOL (119,158) on nights following exercise compared to no exercise in young, healthy study populations. This suggests that exercise can affect sleep parameters, especially in young, healthy populations. It should be noted that most studies exploring the impact of exercise on sleep parameters have only examined the response after one or a few exercise sessions and compared it to a single control night. The limited amount of measurements might not provide sufficient data to provide a complete understanding of the sleeping pattern of the participants. The limited number of measurements and may not offer enough data to fully comprehend the sleeping patterns of the participants. Furthermore, sleep measurements are often conducted in a laboratory may not accurately reflect the typical sleeping patterns of the participant due to an unfamiliar and uncomfortable environment, leading to altered sleep patterns (159). Future research should incorporate multiple measurements, preferably in a home-based setting, to gain a more comprehensive understanding of the relationship between exercise and sleep parameters the following night. This will help to reduce the potential influence of confounding factors and provide more robust data for analysis.

When interpreting our result, it should be noted that our study population has been engaging in regular exercise for a year. Therefore, the participants in our study might have adapted to the physical stress of exercise over time, which could have resulted in a diminished response in sleep parameters after a single bout of exercise. In addition, one limitation was that we did not ask the participants to register exercise sessions of intensities lower than 70 % of HR_{peak} , such as slow walking or resistance training. Consequently, days with lower intensity exercise were classified as days without exercise, which could be a potential confounding factor in our results, as this type of exercise may affect sleep parameters (111,160,161).

Regarding exercise intensity, our result showed no statistically significant differences in TST, SE and SOL the following night between HI- and MI-exercise. This is consistent with findings from previous research on healthy young men (105,156,162,163). It is worth noting that our study population had no sleep-related disorders or known sleep problems. As a result, the variation and changes in sleep parameters may be limited, and it can be challenging to detect. On the other hand, some studies found a relationship between exercise intensity and sleep parameters the following night (106,110,164).

Passos et al. (110) observed an increase in TST, SE and decreased SOL after MI-exercise, but found no change in these parameters after HI-exercise, resistance exercise or control in patients with chronic primary insomnia. Additionally, Ramos-campo et al. (106) studied amateur ultra-endurance runners and found a decrease in TST after HI-exercise performed in the evening compared to MI-exercise performed in the morning. Furthermore, in a study on children by Dworak et al. (164), it was reported that HI-exercise led to a significant improvement in sleep efficiency (SE) and reduction in sleep onset latency (SOL) compared to MI-exercise. These mixed results on this topic can be due to the use of different study populations, which may respond differently to exercise intensities due to sex, age, and health status.

In our study, MI was defined as exercise intensity between 70-85% HR_{peak} , while HI was defined as exercise intensity above 85% HR_{peak} . The relatively narrow range between these two exercise intensities may have limited our ability to detect differential effects on sleep parameters. Additionally, different definitions of MI- and HI-exercise have been used in various studies, which may have contributed to the divergent findings in the literature. For instance, Myllymaki et al. (162) defined MI as 60% VO_{2max} and HI as 75% VO_{2max} and found no significant difference in sleep parameters. On the other hand, Ramos-Campo et al. (106) defined MI as 60% VO_{2max} and HI as 100% VO_{2max} and observed a significant decrease in TST after HI-exercise performed in the evening compared to MI-exercise performed in the morning. It is worth noting that the definition of HI, 100% VO_{2max} , used in the study of Ramos-campo et al. (106) is of a very high intensity, near possible maximal effort equivalent to 100% of HR_{peak} (21). From these results, it appears that differences in exercise intensities may need to be sufficiently large to potentially detect any effects, however, more research is needed to confirm this.

One limitation of the present study is the use of the Amazfit Health Watch to measure heart rate during exercise, as there may be measurement errors associated with wristband heart rate monitoring, particularly at higher exercise intensities (165–167). This may have resulted in an incorrect classification of the session intensity. In addition, we did not control for the exercise modality, time of day or duration, which may influence the result. These limitations should be taken into consideration when interpreting the results of the study.

Our findings revealed a statistically significant increase in SOL of approximately 6 minutes after evening exercise compared to daytime exercise ($p = 0.005$). Although the effect size is small, it can still be significant for those struggling with falling asleep. The result aligns with a study by Soussi et al. (107), who observed an increase in SOL of approximately 8 minutes after evening exercise compared to daytime exercise. In a meta-analysis conducted by Youngsted et al. (168) on diverse study populations, it was found that exercising within certain time frames before bedtime had different effects on SOL. Exercising more than 8 hours or less than 4 hours before bedtime was associated with an increase in SOL of approximately 2 minutes compared to days without exercise, whereas exercising between 4-8 hours before bedtime was linked to a decrease in SOL of approximately 3 minutes compared to days without exercise. Contrary to our findings, some studies have reported no increase in SOL following evening exercise compared to daytime exercise (168,169). Using wristwatch actigraphy, Saidi et al. (168) found no difference in SOL between moderate exercise training in the morning versus the evening after a 12-week intervention in obese adults. However, the exercise was performed at fixed times, 9 am and 7 pm, while they did not control for the bedtime of the

participants, potentially leading to more than 4 hours between evening exercise and bedtime. Additionally, Buman et al. (169) reported no negative impact of evening exercise on sleep in adults with varying activity levels. However, their study relied on self-reported sleep measurements obtained from questionnaires, and the accuracy of these measures may have been susceptible to bias since participants were aware of the focus of the study. The inconsistent results from previous studies suggest that more research is needed to fully understand the impact of exercise timing on SOL using reliable, objective sleep measurements and carefully designed exercise protocols that consider the timing of the exercise before the usual bedtime of the participants.

Our study showed no statistically significant differences in TST and SE following evening and daytime exercise. The findings agree with Saidi et al. (168), who found no difference in TST and SE between morning and evening moderate exercise programs in obese adults. On the other hand, Souissi et al. (107) observed a reduction in both TST and SE after evening exercise as opposed to daytime exercise in young trained individuals. However, the findings of Souissi et al. (107) may have been influenced by the fixed bedtimes and the fact that exercise was carried out until exhaustion. In addition, Ramos-campo et al. (106) investigated the combined effect of intensity (MI and HI) and exercise time of day (morning and evening) and observed a higher SE for morning sessions compared to evening for both intensities. Furthermore, a higher SE was observed after evening MI-exercise compared to morning HI-exercise, highlighting the complex relationship between intensity and timing of exercise. As suggested by previous meta-analyses (170,171), the inconsistent and diverse findings across studies highlight the need for more comprehensive research that considers multiple factors such as exercise duration, intensity, modality, and time of day, while also accounting for differences between study populations.

One possible explanation for the increased SOL after evening exercise observed in our study is the influence on the circadian rhythm. Exercise can produce changes in the timing of melatonin release, which can lead to phase shifts in the circadian rhythm (84,113). A study by Yamanaka et al. (115) found that the timing of exercise created different effects on the circadian melatonin rhythm and that evening exercise generated slight phase-delay shifts in the offset of nocturnal melatonin release. This delay in melatonin release might lead to disturbances in the initiation of sleep, thereby increasing SOL. The circadian rhythm also controls the natural decrease in body temperature before sleep onset (77,120). It has been hypothesised that exercise can interfere with this rhythm by creating elevations in body temperature if performed close to bedtime (63,112), however, some studies have found no support for this hypothesis (171,172). Unfortunately, we did not measure body temperature and cannot explore the possible effect of elevated body temperature after evening exercise compared to daytime exercise. Additionally, the observed difference in SOL between daytime and evening exercise may be due to differences in light exposure. One limitation of this study is that we did not collect data on light exposure or outdoor sessions. Light exposure in the morning has been found to reset the circadian rhythm and be beneficial for sleep initiation (173,174). Some participants may have chosen to exercise outside in the morning, which could be a confounding factor as it may alter the sleep of the participant independent of the exercise performed. In addition, artificial lights late at night can interfere with the natural production of melatonin and create sleep disturbances (175,176), which could affect our results. In future research, it would be beneficial to

expand the analysis to include additional variables, such as measures of body temperature, light exposure, and melatonin.

In our study, the participants could exercise and go to bed when they wanted, in contrast to other studies which have used fixed exercise and bedtime schedules (105,107,156). Fixed schedules may disrupt the natural sleep-wake cycles dependent on chronotype and other individual preferences, which may impact the results. The chronotype of an individual is typically referred to as the preference for scheduling daily activities during morning or evening hours (177). Individuals with a "morning" chronotype usually experience peak alertness and productivity in the morning and may feel more inclined to sleep earlier in the evening. In contrast, individuals with an "evening" chronotype tend to experience peak alertness and productivity in the evening and may stay up later (178). Vitale et al. (179) studied the effect of evening exercise based on the chronotype of the individuals. They observed that individuals with the morning chronotype had reduced sleep quality after an evening session, whereas no changes in sleep parameters were observed in individuals with the evening chronotype. The regular exercise regime of the participants who chose to exercise late at night in our study might have aligned with their chronotype, potentially minimising the effects of evening exercise on sleep parameters. Therefore, our results may not fully capture the effects of evening exercise on sleep parameters for individuals who do not typically exercise late at night or have a different chronotype.

As done in previous studies (155,164,169,180), we chose 4 hours before bedtime as the threshold for evening exercise. However, we did not control for the individual differences in when exercise was performed within this time frame. If exercise disrupts the natural decline in body temperature, the current 4-hour cut-off may not be sufficient to observe the impact of evening exercise on sleep parameters. Previous research has indicated that the increase in body temperature due to exercise returns close to baseline levels within 45-90 minutes after the end of exercise (118,172). Future studies should investigate the impact of exercise on sleep parameters at different time intervals before bedtime, while taking into account individual differences in chronotype.

Our result on the effect of different exercise variables on TST, SE and SOL the following night produced mixed results in our population of 19 men with a history of myocardial infarction. We found that SOL was significantly longer after evening exercise compared to daytime exercise, suggesting that the timing of exercise can influence sleep initiation. However, no difference in TST and SE was observed following evening compared to daytime exercise, implying that the timing of exercise may not be the most important factor for overall sleep. Additionally, there was no change in TST, SE and SOL following days with and without exercise or MI- and HI-exercise. However, we did not collect data on chronotype, lower intensity exercise, exercise duration and modality, and these could be confounding factors which could have impacted our result. Hence, the absence of significant differences in sleep parameters and exercise could be due to the complex interplay of these different factors. Despite the lack of observable changes in sleep parameters after exercise compared to no exercise it is important to recognize that regular exercise is still linked to various long-term health benefits. Therefore, the participants should continue to prioritise exercise as an important aspect of a healthy lifestyle, and potentially reducing the risk for a new cardiac event.

4.3 Strengths and limitations

It is important to note that our results are based on a specific study population consisting of only men with a history of myocardial infarction taking part in the NorEx study. In our study, the participants served as their own control, and this design allowed for a within-subject comparison that controlled for individual differences. We were unable to experimentally manipulate the exercise volume and the CRF of the participants due to the NorEx-study protocol, and we did not have data on the participant in a sedentary state. As such, the NorEx-study protocol functioned as an observational study design for our study. An experimental study could have provided stronger tests of causal relationships and specific questions. Additionally, it was not possible to include a non-training control condition of matched subjects. The small sample size of this study ($n = 19$) may have limited the statistical power to detect significant effects, and further research with a larger sample size is needed to confirm these findings. Moreover, there may have been a selection bias as the participants who agreed to participate may have differed from those who declined. This could affect the generalizability of our results, as individuals who are more interested in exercise or improving their sleep may be overrepresented in our sample. Furthermore, all the participants in our study were men with a history of myocardial infarction, and our findings cannot be transferred to women, younger individuals, and individuals with other medical conditions.

The Somnofy sleep monitor has some limitations in measuring different sleep parameters. A validation study by Toften et al. (129) reported that the Somnofy sleep monitor showed high accuracy in detecting TST and SE in healthy adults compared to polysomnography. However, the monitor showed less agreement with polysomnography in measuring SOL (129). In addition, the Somnofy sleep monitor is validated on a healthy population of primarily young adults, which can have different sleep patterns than our study population of older adults. Our result showed substantial variations in all the sleep parameters, possibly due to measurement error from the Somnofy sleep monitor. Poor signal quality can result from sensor blockage or signals collected from a partner or pets. It is important to consider these limitations when interpreting the results.

The quality and duration of sleep on a given night could significantly influence the quality and duration of sleep on the subsequent night (181), which could potentially impact the findings in this study. Additionally, daytime naps can be associated with impaired sleep and lead to difficulties falling asleep at night (182,183). Unfortunately, we did not collect data on daytime napping, which could impact our findings. Furthermore, incorporating a subjective measure of sleep could have provided valuable information and a more comprehensive understanding of the sleep of the participants. In addition, the variation in seasonal light exposure in the northern hemisphere can impact the circadian rhythm and potentially affect sleeping patterns (184). Although this may be a confounding variable, we found no statistically significant changes in sleep parameters during the study period (Table A1, Appendix).

The strengths of our study lie in the objective, continuous measurements of sleep parameters by the Somnofy sleep monitor over the course of 12 weeks. Additionally, we collected a large amount of exercise data, which allowed us to assess the effects of days with and without exercise, the intensity of exercise and exercise timing in the same

individual on sleep parameters the following night. Moreover, we used CPET to evaluate VO_{2peak} , which gives an accurate representation of the CRF level of the participant compared to estimating CRF from submaximal testing.

Conclusion

Based on the results of this 12-week study, there appears to be no relationship between the level of CRF and variation in TST, SE or SOL in this group of men with a history of myocardial infarction. In addition, the findings suggest that changes in CRF do not result in changes in sleep parameters. The observed individual variations indicate that factors other than CRF level may be influencing sleep parameters in these participants. Furthermore, our findings suggest that neither exercise nor exercise intensity substantially impacts sleep parameters the following night. The results showed a statistically significant increase in SOL after evening compared to daytime exercise, whereas no statistically significant differences were observed in TST or SE. These results suggest that the timing of exercise could play an important role in the initiation of sleep, and individuals who experience difficulty in falling asleep may benefit from exercising earlier in the day rather than in the evening. It should be noted that this study had a limited sample size and future research with larger sample sizes is needed to detect statistical power and to improve the generalizability of the findings to other study populations. In addition, future research should investigate the combined effect of various factors, such as exercise timing, intensity, modality, and duration, to gain a more comprehensive understanding of their complex interplay and their impact on sleep parameters.

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Appendix

There was no statistically significant change observed in any of these sleep parameters over the course of the study ($p > 0.05$), as shown in Table A1. Figure A1 illustrate the change in TST from days from study start.

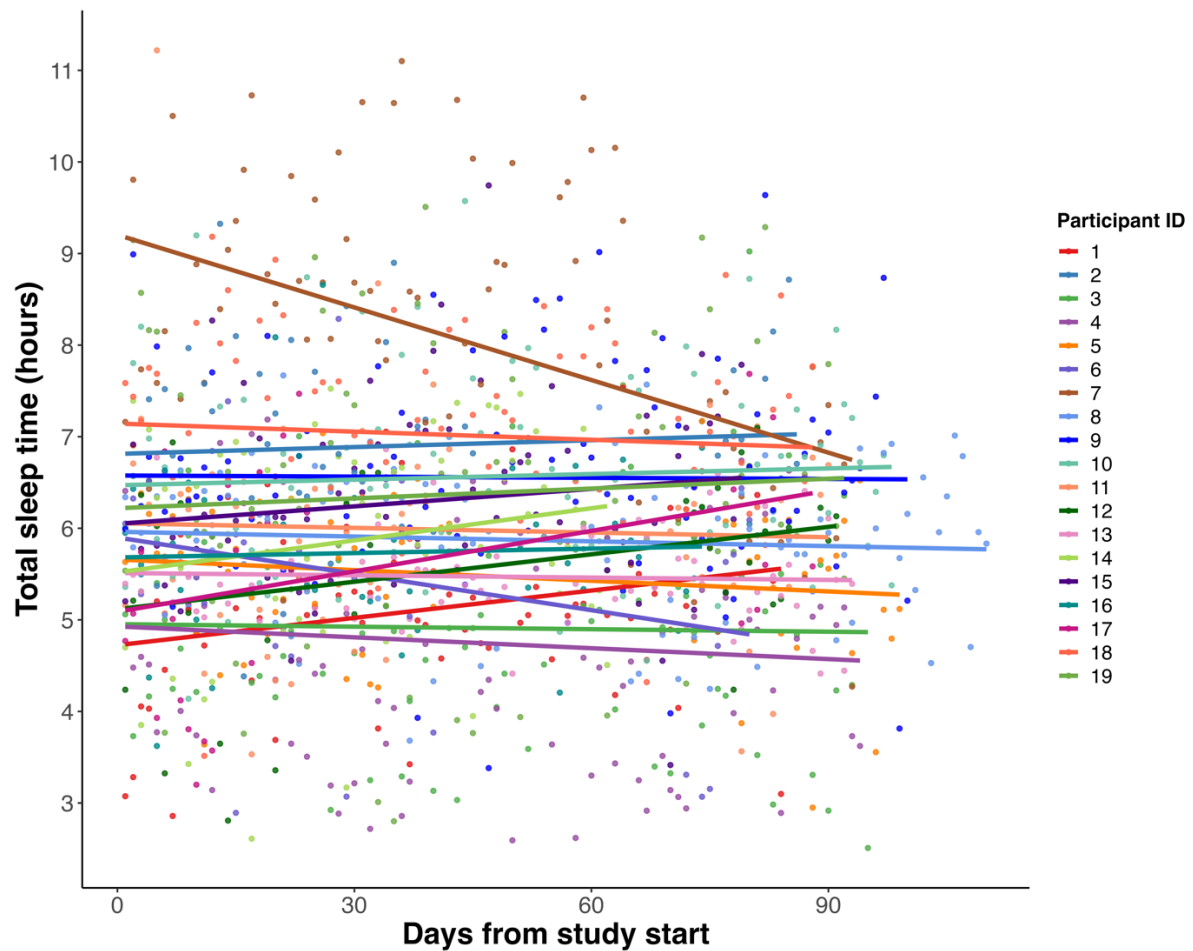


Figure A1: Total sleep time (TST, hours) for all participants ($n = 19$) at days from study start. Each participant is presented as an individual colour with each night presented as a point with a corresponding linear regression line.

Age does not statically significantly predict VO_{2peak} ($p > 0.274$, Table A2)

Table A1: Estimates and test-statistics for the linear mixed-effects model analysing: total sleep time and day from study start; sleep efficiency and day from study start; and sleep onset latency and day from study start. The estimate days from study start represents the slope (β) of the linear regression line. 95% CI: 95% confidence interval

	Total sleep time (hours)			Sleep efficiency (%)			Sleep onset latency (min)		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Intercept	6.01	5.64, 6.39	<0.001	79.85	76.73, 82.96	<0.001	18.54	13.69, 23.38	<0.001
Days from study start	-0.001	-0.003, 0.001	0.470	0.02	-0.002, 0.036	0.079	0.005	-0.034, 0.043	0.803
Random term									
Individual ID	0.6316			43.23			96.43		
Residual	1.2874			92.41			382.84		
n observations	1291			1290			1291		
n Individuals	19			19			19		

Table A2: Estimates and test-statistics for the linear model analysing mean VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) in relation to age of the participants. The estimate for age represents the slope (β) of the linear regression line; change in mean VO_{2peak} per year. The analyses include data from 19 men. 95% CI: 95% confidence interval.

	Estimate	95% CI	p-value
Intercept	154.66	79.28, 230.04	< 0.001
Age	- 0.68	-1.95, 0.59	0.274



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