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Occupational light exposure, melatonin, and vitamin D

PhD dissertation

Stine Daugaard Pedersen

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PREFACE

This dissertation concludes the PhD project "*Occupational light exposure, melatonin and vitamin D.*" carried out at the Danish Ramazzini Centre, Department of Occupational Medicine, Aarhus University Hospital.

First of all I would like to than my supervisors Henrik A. Kolstad, Anne Helene Garde and Jens Peter Bonde for their qualified guidance, constructive criticism, and patience along the way. Special thanks to Henrik for making the project possible and always being available and committed to the project.

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Stine Daugaard Pedersen, Aarhus, August 2017

THIS DISSERTATION IS BASED ON THE FOLLOWING MANUSCRIPTS:

Paper I: Daugaard S, Garde AH, Bonde JPE, Christoffersen J, Hansen AM, Markvart J, Vistisen HT, Schlünnsen V, Kolstad HA.

Light exposure during night, outdoor and indoor work.

(Submitted to Annals of Work and Health)

Paper II: Daugaard S, Garde AH, Bonde JPE, Christoffersen J, Hansen AM, Markvart J, Vistisen HT, Schlünnsen V, Skene DJ, Kolstad HA.

Night work, light exposure and melatonin on work days and days off.

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Paper III. Daugaard S, Garde AH, Hansen AM, Markvart J, Vistisen HT, Rejnmark L, Kolstad HA.

Indoor, outdoor, and night work and blood concentrations of vitamin D and parathyroid hormone.

(Submitted to Scandinavian Journal of Work, Environment and Health)

LIST OF ABBREVIATIONS

$1,25(OH)_2D$	1,25-dihydroxy vitamin D
25OHD	25-hydroxyvitamin D
aMT6s	6-sulfatoxymelatonin
BMI	Body mass index
CI	Confidence interval
CV	Coefficient of variations
DW	Day worker
eGFR	Estimated glomerular filtration rate
IARC	International Agency for Research on Cancer
ipRGC	Intrinsically photoreceptive retinal ganglion cells
IQR	Inter quartile range
LAN	Light at night
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LOD	Lower limit of detection
Min	Minutes
NW	Night worker
OR	Odds ratio
PTH	Parathyroid hormone
SAD	Seasonal affective disorder
SD	Standard deviation
SES	Socio economic status
UVR	Ultra violet radiation
UVA	Ultra violet light A
UVB	Ultra violet light B

CONTENTS

1. INTRODUCTION

The sun and the rotation of earth create a natural 24 h light/dark cycle with high light intensities during the day, and darkness during the night, and day lengths that fluctuates by season and latitude. The invention of electric light changed this cycle. Light is now available 24/7, and the light exposure patterns of humans do not solely depend on the sun. The light provided by artificial light is sufficient to support vision, but intensities are lower than the outdoor light levels during the day and higher during the night. Furthermore the spectrum of artificial light differs from daylight's and does not contain ultraviolet radiation (UVR) (1).

Light is the main time keeper in human circadian physiology that synchronizes the biological clock with the day/night cycle (2). The discovery of intrinsically photoreceptive retinal ganglion cells (ipRGCs) and the neuronal pathways to brain areas besides the visual cortex has advanced our knowledge about the role of light in human physiology (3). Light can increase alertness, feeling of vitality and mood, delay or advance the circadian rhythm, suppress melatonin and treat jetlag, seasonal, and non-seasonal depression (4-9).

Indoor and night work is both frequent in industrialized countries. In Europe, on average 90% of the workforce work indoors (10), 20% work night shifts, and 1% have permanent night work (11, 12). Workers spent a substantial part of the waking hours at work, but little is known about light exposure during work hours, and if this impacts behavior and light exposure outside work hours. The health consequences of indoor work and low exposure to light are largely unknown. The effects of light during night work have been studies more thoroughly, but little attention has been paid to the impact of night work on 24-h light exposure.

2. AIMS

This thesis aims to describe indoor, outdoor and night workers light exposure on and off work. Furthermore to study if differences in light exposures affect melatonin production and vitamin D status.

Study I: To assess diurnal and seasonal light exposure during days with night, outdoor, and indoor work and days off to increase knowledge on light exposure to be used in studies linking light exposure to human and work related health and well-being issues.

Study II: To examine melatonin concentrations during and subsequent to night work and the mediating role of light exposure.

Study III: To examine blood concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) mong indoor, outdoor, night workers and the association with hours spent outdoors on work days and days off during summer.

3. BACKGROUND

3.1 LIGHT

Light is electromagnetic radiation erasing from the sun, fire, or electric light sources. Each light source has a different electromagnetic spectrum and color. In everyday life the word light refers to visible light that enables us to see. Sunlight reaching the surface of earth consists of ultraviolet (290-400 nm), visible (400 -700 nm) and infrared light (700 nm-1 mm). Outdoor daylight is white light defined as a broad and evenly distributed range of wavelengths (1). White light is measured in lux, this unit is weighted according to a model of the human eyes sensitivity to different wavelengths (13). In this thesis white light will be referred to as light. The intensity of daylight depends on the sun position and cloud cover. During a summer day in Denmark (55-57º N), daylight intensities can reach 100.000 lux on a clear day, 30.000 lux on a cloudy summer day, and 7.500 lux on a cloudy winter day (14). During the night, without artificial light, light levels are 1-10 lux across the year. Artificial light originates from sources such as incandescent bulbs, fluorescent tubes and LEDS. It may be monochromatic only containing one wavelength or white by mixture of different wavelengths. During day time, the indoor light is a mix of daylight from windows and artificial light.

3.2 LIGHT PERCEPTION AND NON-VISUAL EFFECTS OF LIGHT

Visible light enable humans to see the world around us, and light that reaches the retina are absorbed by three different photoreceptors. The information is transmitted to many areas of the brain. Rods and cones manly provide information to the visual cortex, but also contribute to non-visual effects. The intrinsic photosensitive retinal ganglion cells (ipRGCs) were discovered quite recently, and provide the main input to the circadian system and the non-visual effects (1). The

spectral sensitivity of ipRGCs differs from the rods and cones, and the peak sensitivity is shifted towards shorter wavelengths and blue light (15). Also, longer and higher exposure to light is needed to activate non-visual responses than to stimulate the visual system. The response to light furthermore depends on time of day.

At night white light above 80 lux and blue light at lower intensities suppresses melatonin production, and increases alertness (7, 16-19). Red light has been shown to increase alertness without suppressing melatonin (20). Light phase shift the circadian rhythm with an increasing effect the closer to biological midnight a person is exposed. Exposure to light is essential to keep humans entrained to the natural 24-h light/dark cycle, as the endogenous rhythm most commonly is a little longer than 24 hours (h) (21). Moreover light at night can hamper sleep (22), affect cortisol production (23), increase heart rate (24), and body temperature (25). The effects of light exposure during day time are far less studied. Depression and seasonal affective disorder (SAD) have been shown to respond to exposure to 2,500 lux for 60-120 minutes (min.) in the morning (4, 26). Furthermore general well-being, mood, vitality, performance, arousal, and learning abilities may be improved by increasing light intensities or exposure to blue enriched light during daytime (5, 6, 8, 9, 19, 27-31). Afternoon sleepiness also decreased after 20 min. exposure to daylight after lunch (9).

3.3 FIELD STUDIES ON LIGHT EXPOSURE DURING WORK

Previous field studies are summarized in table 1 in the appendix. Studies on indoor workers light exposure, conducted in industrialized countries at latitudes 39-51^{o}N, suggest that the average light exposure is less influenced by latitude than what could be expected. Independent of latitude the light pattern on indoor work days is markedly different from days off, and the light exposure was consequently higher on days off than on work days (5, 32-35). Median light exposure during indoor

work hours have been reported between 120-308 lux in the summer (5, 8) and about 80 lux in the winter (8). When including the hours before and after work the median light exposure during work days was 189 lux in the summer and about 83 lux in the winter (5, 8). Despite of higher median light intensities during work hours than during the entire day, exposure to light above 1000 lux primarily occurred outside work hours. Indoor workers were exposed to light above 1000 lux for approximately 15 min. during working hours in the summer (5, 36). During entire days with work, indoor workers were exposed to light above 1000 lux between 36 and 150 min. in the summer and 26 and 73 min. in the winter (5, 32, 34, 36, 37). Outdoor workers exposure to visible light has, to our knowledge, not previously been studied. During hours of outdoor work, we would expect light exposure to more or less represent day light intensities depending on shade. Night workers were on average exposed to light intensities between 60 and 73 lux during hours of night work, and 427 and 996 lux during 24-h days (38, 39). Koller et al. observed that night workers spent 13 min. above 1500 lux during a 24-h winter night work day (34). Light exposure was reported higher on days with night work than on days off, though not statistically tested (34, 35).

3.5 MELATONIN

Melatonin is a hormone primarily produced in the pineal gland (40). The function of is to synchronize the internal environment and physiological processes to the external light/dark cycle (41). The melatonin concentration exhibits a pronounced circadian rhythm with peak production during the biological night and a decline towards the morning (42). This rhythm is primarily driven by the endogenous circadian system through a poly-synaptic pathway between the pineal gland and the hypothalamic suprachiasmatic nuclei containing the master circadian clock (43). But the ambient light/dark cycle also affects the circadian rhythm, because light is a powerful regulator of the suprachiasmatic nuclei (44). Melatonin is a marker of the circadian rhythm and has been used to

study circadian rhythm in both laboratory and field studies. The melatonin profile is rather consistent within an individual (45), but inter-individual differences are substantial, mainly due to genetic influence (46). The production can be measured directly in blood (47) and saliva (48), and indirectly as the metabolite 6-sulfatoxymelatonin (aMT6) in urine (47, 49). Retinal exposure to light at night (LAN) acutely suppresses melatonin in a dose-dependent way starting at white light intensities of 80-100 lux (18, 50, 51). Melatonin have in laboratory studies shown oncostatic effects as inhibition of tumour growth, reduction of oxidative DNA damage, and change of oestrogen levels (52). It has therefore been suggested, that suppression of melatonin by light exposure during night work may be a causal element linking shift work and cancer (53).

3.5 STUDIES ON NIGHT WORK, LIGHT AND MELATONIN

Previous field studies are summarized in table 2 in the appendix. During days with night work melatonin production was lower among night workers compared to other workers working daytime only (38, 41, 54-57) except in one study (58). Studies comparing night workers melatonin production on days with night work and days without night work have mainly demonstrated lower melatonin concentrations on days with night work, though two studies concluded melatonin production did not differ (59, 60). Most studies agree that melatonin production is suppressed during night work, but the duration of this suppression is unknown. Lower melatonin production was observed among night workers during the first night sleep period after a night shift (54, 61), and during the second day off after a night shift (62) compared to day workers. However, another study demonstrated full recovery of the melatonin profile on the second day off (63). Melatonin suppression has been shown to increase by numbers of consecutive nights worked (56, 63, 64), and recovery time may depend on number of consecutive night shifts. The hangover effect and increase of suppression by nights worked in a row both indicates that other factors than ambient light

contributes to the suppression. A laboratory study of simulated night work measured melatonin suppression despite of light intensities that were to low to induce suppression (64). This emphasizes the importance of distinguishing the effect of modifiable light from other factors.

Night work has been used as a proxy of exposure to light at night, and few studies have investigated the association of objective light measurements and melatonin suppression. Night workers in the highest tertile of average light measured between 00:00-05:00 h had 37.7% lower 24-h aMT6s concentrations than day workers whereas night workers in the lowest tertile only had 27.3% lower aMT6s (38). In line with these results a correlation between median light exposure during night work and 24-h aMT6s excretion was found among 13 workers, but there was no correlation between light and aMT6s excretion during work hours (60). Grundy et al. found a slight inverse relationship between mean light exposure between 00:00 and 05:00 h and change in aMT6s production from the afternoon until the morning, but no association between mean light and peak production of melatonin (65). In conclusion, the results from field studies indicate that the effect of night work on melatonin production is transient, but the recovery period is unknown. Light at night seems to be associated with the degree of melatonin suppression, but the exact impact of light exposure has yet to be elucidated.

3.6 VITAMIN D

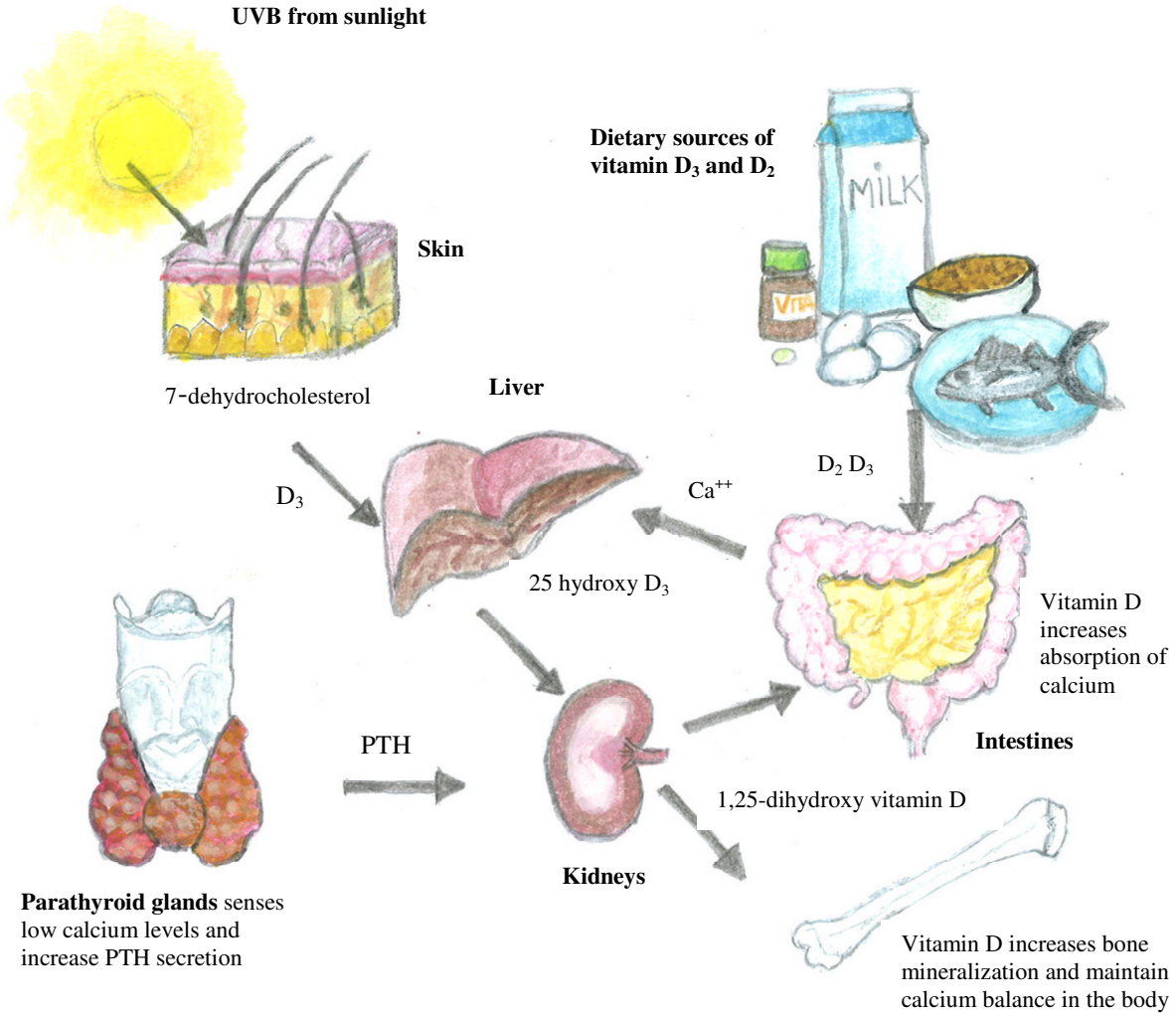
Vitamin D is a fat-soluble vitamin mainly derived from syntheses of cholecalciferol (Vitamin D_3) in the skin after exposure to ultraviolet B radiation (UVB) (280-315nm). In Denmark (latitude 55-56^{o}N) UVB is only strong enough to induce syntheses from March till September (66). Another source of vitamin D is cod-liver oil, vitamin D supplements and the diet, where important sources are mushrooms and fatty fish (67). In some countries food fortification is another source, but this is

not common in Denmark. The metabolism and actions of vitamin D and PTH are described in figure 1. Vitamin D, derived from both the diet and synthesized in the skin, is metabolized into 25OHD in the liver and further converted into 1,25-dihydroxy vitamin D ($1,25(OH)_2D$) in the kidneys. $1,25(OH)_2D$ increases the intestinal absorption of calcium and has a negative feedback on PTH secretion (68).

Serum concentrations of 25OHD are used to determine vitamin D status. The Institute of Medicine recommended in 2011 a level above 50 nmol/L to be sufficient for skeletal health (69). The same cut-off is used in present Danish guidelines (70), and this cut-off will be used in this thesis. However, it has also been suggested that sufficient vitamin D levels are only achieved at concentrations above 75-80nmol/L (67). The optimal level for non-skeletal outcomes, as e.g. autoimmune diseases or cancer has yet to be established (71). Vitamin D insufficiency is common in Denmark and the prevalence was 52% in a study on healthy adults (72).

Vitamin D is important to maintain calcium homeostasis and skeletal health (73), but the vitamin. D receptors are also expressed in various tissues not related to calcium metabolism (74). Combined with anti-proliferative and immunomodulatory effects (75, 76) this suggests pleiotropic effects of vitamin D. Low vitamin D levels have in epidemiological studies been associated with increased risk of multiple sclerosis (77), colorectal cancer (78), allergy (79), and cardiovascular disease (80, 81), but any causal relations remain to be established. Furthermore lower vitamin D levels have been suggested to be a mechanism linking shift-work and cancer (53).

Figure 1. Vitamin D and PTH metabolism (created by Lene Daugaard)



3.7 PTH

PTH is secreted from the parathyroid glands and the physiological function is to maintain a stable level of plasma calcium (82). The secretion of PTH is stimulated by low calcium and high phosphate levels, and is inhibited by high calcium and 1,25$(OH)_2$D concentrations. PTH increases the conversion of 25OHD to 1.25$(OH)_2$D, mobilizes Ca^{++} from the bones, increases the absorption of Ca^{++} in the intestines and the tubular reabsorption of Ca^{++} in the kidneys (83). PTH and 25OHD

are inversely correlated and a rise in PTH signals that vitamin D concentrations are insufficient and affect bone metabolism negatively. However, there is a large inter-individual variation of the 25OHD concentration where PTH starts to rise (84). Independent of vitamin D it has been suggested that higher levels of PTH increase overall and cardiovascular mortality (85), the risk of cardiovascular diseases (86), and risk of fracture (87).

3.8 JOB GROUP AND 25OHD AND PTH CONCENTRATION

Field studies on work and 25OHD and PTH are summarized in table 3 in the appendix. Outdoor workers had higher 25OHD concentrations and lower prevalence of vitamin D insufficiency than indoor workers (88-90), while one study did not show this association (91). The results from studies comparing rotating night workers with day workers have yielded conflicting results. Studies comparing rotating night workers and day workers reported lower 25OHD concentrations among rotating night workers (92, 93) as well as no difference (94, 95). Women working permanent night had lower 25OHD concentrations than day workers, but no difference was observed among men (96). PTH concentrations have never been compared across job groups, but both mean levels have been reported among indoor and rotating night workers and concentrations were, as expected, higher in the winter than the summer (97-99). Self-reported exposure to sunlight predicted 25OHD concentrations in some studies (96, 99), but not others (97, 100). A Danish study measured UVR doses with a UV meter during the summer, found daily UVR doses on days off were correlated with 25OHD concentrations, but daily UVR on work days were not (91).

4. Materials and methods

4.1 STUDY OVERVIEW

An overview of the materials and methods in the three studies is given in table 1. Additional information on materials and methods is available in the following sections and appended papers.

Table 1. Overview of materials and methods

	Study I	**Study II**	**Study III**
Topic	Light exposure during days off and days with indoor, outdoor and night work.	The effect of night work and light exposure on melatonin concentrations on work days and days off	25OHD and PTH concentrations among workers working indoor, outdoor and rotating or permanent night shifts in the summer season.
Design	Field study/descriptive	Follow-up study	Cross-sectional study
Population	509 workers 170 indoor workers 151 outdoor workers 188 night workers	341 workers 254 day workers 87 night workers	425 workers 162 indoor workers 112 outdoor workers 118 rotating shift workers 33 permanent night workers
Exposure	Days with indoor, outdoor and night work, and days off among indoor, outdoor and night workers	Night work Minutes above 80 lux 30 minutes prior to each saliva sample	Outdoor, rotating and permanent night work during the summer. Outdoor hours/day
Exposure assessment	Diary	Questionnaire Light measurements	Questionnaire Light measurements
Outcome	Light exposure (average light and time spent above 80, 1,000, and 2,500 lux) within six-our intervals.	Melatonin concentrations pmol/L((continuous)	25OHD (continuous) PTH (continuous) Vitamin. D insufficiency Hyperparathyroidism
Outcome assessment	Light measurements recorded by Actiwatch	Salivary melatonin measured by isotope dilution liquid chromatography-tandem mass spectrometry (LC-MS/MS)	Serum 25OHD analyzed by isotope dilution liquid chromatography-tandem mass spectrometry Plasma PTH analyzed by an automated immune analyzer
Confounders	None	Age, sex, body mass index, current smoking, diurnal preference, and use of antidepressant medication	Season, sex, age, occupation, use of vitamin D supplements, BMI smoking, fish and shell food consumption, use of sunbed, time from blood sampling ill freezing.
Main statistical analysis	Multivariate linear regression (STATA mixed procedure)	Multivariate multivariable linear regression (STATA mixed procedure) Mediation analyses	Multivariable linear and logistic regression

4.2 GENERAL METHODS APPLIED IN ALL STUDIES

Study setup

All studies in the thesis are based on the "Luxar study", a field study carried out in March 2012 until May 2013. Participants were recruited through employers, advertisements, and through the homepage of the National Research Centre for the Working Environment, with the aim of recruiting equal numbers of indoor day workers, outdoor day workers, and night workers participating throughout the year. The study period lasted seven days and started at different days of the week and at different times of the day depending on participants' work schedules. On the first day a research assistant met the participants at their place of work, and instructed in the use of the Phillips Actiwatch Spectrum (Actiwatch) and handed out a questionnaire, a diary, equipment for saliva sampling (a subset of participants), and if the participants agreed, a blood sample was drawn. A subset of participants was instructed to collect up to seven saliva samples at a work day (day or night) and a day off. All participants completed a questionnaire on background characteristics (e.g. age, sex, working hours, smoking and medication). They further completed a work diary each evening and a sleep diary each morning. Light levels were continuously recorded with a Philips Respironics Actiwatch Spectrum (Actiwatch), that participants were instructed to wear at any time except during showers, swimming etc. While sleeping, the Actiwatch should be removed from the arm and kept next to the bed with the front pointing upwards to measure ambient light, except for two nights where it should be worn on the wrist to measure the sleep. At day seven, the Actiwatch, the diary, the questionnaire, and saliva samples were collected by a member of staff.

Participants

555 participants were recruited for the study. Criterions for being included in the Luxar population were questionnaire information, valid light measurements and diary information on work and sleep from at least one work day. In total 535 participants met these criteria. Of these 459 had blood samples drawn and 404 collected saliva samples.

Light measurements

The Actiwatches Spectrum was worn on the upper arm to comply with working regulations during the day and to best possibly represent retinal light exposure. Light and actigraphy (movement counts) were recorded with 1 minute epochs. The Actiwatch sensor measures light in three wavelength bands red, blue, and green. The white light (lux) output was derived from the light received by these bands. Light measurements were synchronized with diary information on the start and end of sleep and work. After data collection was completed, the light sensor outputs from the Actiwatches were calibrated as described by Markvart et al. (101). Actiwatch calibration was done using a side-by-side calibration method under overcast sky conditions. The white light output was furthermore calibrated against a cosine corrected photometer with a spectral sensitivity that closely relates to the luminosity function V(λ) established by the Commission Internationale de l'Éclairage (CIE). Inclusion of light measurements differed between studies and will be described below.

Questionnaire and diary

The questionnaire contained questions on socio-demographic factors, professional history, dietary factors, and psychological health. Information retrieved for each study will be described below. The diary contained information on bedtime, wake time, start and end of work hours and days off during

all study days. For each hour a day, the participants reported if the Actiwatch was removed for more than 20 min./h and if more than 20 min./h was spend outdoors.

4.3 STUDY I

Design

Study I was a field study.

Population

The exposure in this study was defined by diary information on indoor, outdoor, and night work. We defined a day with ≥120 min. work between 00:00 h and 05:00 h as a day with night work. A day with outdoor work was defined as a day with ≥120 min. of outdoor work. A work day not fulfilling these criteria was defined as a day of indoor work. Days with no recorded work were classified as days off. Three job groups were defined; indoor, outdoor, and night workers. Workers with ≥1 day of night work were classified as night workers, workers with no days of night work and ≥1 day of outdoor work as outdoor workers and workers with no days of night or outdoor work as indoor workers. Participants (n=26) with incomplete information to classify them as night, outdoor or indoor workers were excluded, and the study population comprised 509 participants of whom 484 had valid light measurements from workdays and 485 from days off. We only included indoor work days for indoor workers (N=693 days, 169 workers), outdoor work days for outdoor workers (N=351 days, 134 workers), and night work days for night workers (N=181 days, 181 workers) and days off (N=1,174 days, 485 workers).

Light measurements from 504 participants were included for analyses of time spent above three light intensities according to criteria described in the section "*light assessment"* below. Women comprised 72.2% of the population and the mean age of all participants was 42.2 years. Indoor workers included teachers, hospital employees, child care worker, factory workers, mechanics,

gardeners, residential social workers, craftsmen, and work environment inspectors. Outdoor workers included child care worker, gardeners, craftsmen, teachers, work environment inspectors, physiotherapists, and residential social workers. Night workers included hospital employees, factory workers, and residential social workers.

Questionnaire

At study start, participants filled in a questionnaire that included information on occupation and working hours.

Light assessment

In total, 4,222,732 min. of light measurements were collected from days off and days with indoor, outdoor, and night work. Measurements from workers without information on job group (outdoor, indoor, night work) were omitted (286,703). Likewise, data were omitted when the Actiwatch was reported to be worn on the wrist during sleep (1,007,316 min), not worn when awake (212,081 min), and if no physical activity was recorded for 20 min. by actigraphy (209,997 min). In total, 2,506,635 min. corresponding to 41,777 h with light measurements from 2,638 days were used for analyses of mean light intensity. On average, 15 hrs. and 45 min. of light measurements were available per day. Data were also analyzed according to minutes spent above three light intensities: 80, 1,000 and 2,500 lux. For these analyses we required ≥ 90% valid light measurements within four six-hour intervals according to criteria specified later. In total, 1,573,729 min. of light measurements from 4,461 six-hour intervals, and 2,290 days were included for 504 workers.

Statistical analyses

To depict individual light exposure across the day, we smoothed the graphs by a moving window that was the mean of each worker's light intensities of the last 20 min. The arithmetic mean of these smoothed light intensities were plotted for indoor, outdoor and night workers by time of the day on work days, days off and all days and stratified by season.

Data were also (not being averaged) presented as arithmetic means, medians, 10th percentiles, and 90th percentiles computed across six-hour intervals (00:00-05:59h (night), 06:00-11:59 (morning), 12:00-17:59 (afternoon) and 18:00-23.59 (evening). We presented these results separately for work days and days off and stratified by season (summer, winter as defined by standard time and daylight saving time) as these are significant predictors of light exposure caused by the rotation of earth.Within each of the strata, we also tabulated time spent (min.) above 80, 1,000 and 2,500 lux to represent thresholds for melatonin suppression and induction of alertness (7, 18), outdoor vs. indoor stay during daytime and comparison with previous literature (5, 30, 32, 33, 36, 102, 103), and light therapy for depression (4).

To investigate the lower limit of detection (LOD), the Actiwatches were placed in complete darkness for four sessions of eight hours. The highest measured intensity was 1.20 lux, corresponding to light intensities between 0 and 1.20 lux. We used the exact value of all measurements instead of assigning new values to measurements below a certain LOD criteria in order to keep as much exposure information as possible in the data (104). Light measurements with 0 lux were replaced by 0.001 lux (1.0% of light measurements included in analyses) and six-hour intervals with 0 min. above the thresholds were replaced by 1 min. before log transformation (1.0% of six-hour periods).

Light intensities and time spent above the thresholds showed right skewed distributions and were log transformed prior to statistical analysis. They were analysed with multivariate linear regression to estimate differences between night, outdoor and indoor workers with the latter as the reference. Analyses of light intensities were adjusted for hour of sampling within the four 6- hour strata. Analyses were carried out using the mixed procedure with an autoregressive structure. Participant was entered as an independent random variable because each participant was measured multiple times. All analyses were carried out using STATA 13.0 (StataCorp, College Station, Texas).

4.4 STUDY II

Design

Study II was a follow-up study.

Population

Saliva samples were collected by 404 participants, five were excluded due to pregnancy, and fifty-eight rotating night workers were excluded as they did not provide saliva samples during days with night work. The final study population comprised 341 participants, hereof 87 night workers, and 254 day workers. The night workers were defined as working more than three hours between 00:00 h and 05:00 h on a regular (n=19) or a rotating basis (n=68) (105). Day workers were a mix of indoor and outdoor workers, who never worked between 00:00 h-05:00 h. The night workers were hospital employees (n=75), factory workers (n=10), or residential social workers (n=2). The day workers were child care workers (n=61), hospital employees (n=56), teachers (n=47), gardeners and pavers (n=34), factory workers (n=18), craftsmen (n=13), mechanics (n=8), office workers (n=8), dentist or dental assistants (n=7), or residential social workers (n=2).

Light measurements

We included light measurements 30 min. prior to each saliva sample, as these were expected to affect melatonin concentrations (17, 106, 107). Light exposure was defined as min. above 80 lux 30 min. prior to each saliva sample (16, 18, 51). To validate light measurements, we inspected the light and actigraphy measurements and assessed if the light recordings should be included or not, if the participant did not report wearing the Actiwatch or the Actiwatch recorded no movement for 20 consecutive min. Only saliva samples with valid light measurements were included.

Questionnaire

Information on sex, age (years), pregnancy (current yes/no), occupation (current), height (centimetres), weight (current kilograms), smoker (current, former, or never), use of melatonin supplementation (yes/no), antidepressant medications (yes/no), and diurnal preference (response categories: definitely a morning person, more a morning person than an evening person, more an evening person than a morning person, definitely an evening person) was retrieved from the questionnaire.

Saliva samples

Participants were instructed to collect saliva samples on a work day and a day off. The first sample should be collected at awakening, hereafter at 07:00 h, 11:00 h, 15:00 h, 19:00 h, 23:00 h and 03:00 h if awake with a final sample just before bedtime.

Figure 2. Saliva sampling protocol

	1.sample	**2.sample**	**3.sample**	**4.sample**	**5.sample**	**6.sample**	**7.sample**
Night worker	Awakening	15.00	19.00	23.00	03.00	07.00	Bedtime
Day worker	Awakening	07.00	11.00	15.00	19.00	23.00	Bedtime

Eating was not allowed 30 min. prior to sampling. The sampling tube should contain approximately 1 ml saliva. No instructions were given on light conditions when sampling. Just after sample collection participants noted the date and exact time on a label on the saliva tube and stored the sample at 5^{o}C whenever possible until the end of the 7-day study period. Samples from day workers were classified as work day measurements if sampled within 24 h after awakening on a work day. Samples from night workers were classified as work day measurements if sampled within 24 h after the beginning of a night shift. Samples from day workers obtained within 24 h after awakening on a day off were classified as day off samples. Samples from night workers were classified as day off samples according the same criteria as the day workers but in addition requested that samples should be obtained more than 24 hh after ending a night shift. In total 3579 saliva samples were collected. We excluded 430 saliva samples from rotating night workers during days with day shift, 47 samples without valid light measurements, 45 samples from pregnant participants, 4 samples above and 14 samples below 3 standard deviations (636 nmol/L and 0.4 nmol/L) of the geometric mean of all samples according to Grubb's outlier test (108), 34 samples obtained on a day off less than 24 h after the end of a night shift, and 161 samples from night workers before the beginning of their first night shift, leaving 2842 samples for analyses.

Determination of salivary melatonin concentration

Melatonin analyses were carried out using liquid chromatography tandem mass spectrometry (LC-MS/MS) as described in Jensen et al. (48). The limit of detection (LOD) was 3.73 pmol/L, 74 samples (2%) had concentrations below LOD. For a concentration below LOD, the sample was given a random number from a normal distribution with 2/3 of the LOD as the mean. To test equivalence between analyses, reference samples at two levels (28-43 pmol/L, intra assay coefficient of variation (CV): 20%; 80-152 pmol/L, CV=13%) were analysed with every 14

samples. Westgard control charts (109) were used to document that the LC-MS/MS method remained under statistical and analytical control. Samples that failed analysis were rerun once. If the concentration was above 490 pmol/L solutions were diluted and reanalysed.

Statistics

All analyses were stratified into work days and days off. The melatonin concentration between day and night workers were compared on work days and days off work using multivariate multilevel linear regression (STATA mixed procedure) to account for the repeated measurements. For each individual we used a random intercept with a variance component covariance structure and repeated statement for the samples with an autoregressive covariance structure. Type of worker (day worker, night worker) and time of day (01:00-04:59 h, 05:00-08:59 h, 09:00-12:59 h, 13:00-16:59 h, 17:00-20:59 h, 21:00-00:59 h) were included as categorical variables. Potential confounders included were age (continuous, years), sex (male, female), body mass index (continuous), current smoking (yes, no), diurnal preference (morning type: definitely a morning person, more a morning person than an evening person; evening type: more an evening person than a morning person, definitely an evening person) and use of antidepressant medication (yes, no). To assess if light exposure 30 min. prior to saliva samples mediated the effect of night work on melatonin levels on work days, we conducted mediation analyses stratified into day (08:00-19:59 h) and night time (20:00-07:59 h). We estimated the direct, indirect (mediated by light exposure), and total effects of night work with classical path analysis methods combining the results of two regression analyses (110). Firstly, we regressed log-melatonin on night work, light exposure, and covariates. Secondly, we regressed light exposure on night work and covariates. We estimated 95% confidence intervals using 1000 bootstrap samples. The relative effects of night work (%) on melatonin were found by the exponentials.

4.4 STUDY III

Design

Study III was a cross sectional study.

Population

In total 535 participants were recruited and 459 provided blood samples. Samples of eight participants could not be measured due to insufficient blood volume. Twenty-six participants were excluded due to medical conditions or drug treatment with potential effects on calcium homeostasis and vitamin D metabolism: use of thiazide diuretics (n=10), pregnancy (n=7), suspected primary hyperparathyroidism (serum calcium and plasma PTH above normal) (n=2), anticonvulsants (n=1), systemic glucocorticoids (n=1), estimated glomerular filtration rate (eGFR) < 60 ml/min. and metastasised breast cancer (n=1). The final population comprised 425 participants with complete confounder information except for 12 participants with missing information on body mass index (BMI).

Indoor workers were defined as working daytime only and working ≤9 h outside per week during summer (June-August) (n=162). *Outdoor workers* were defined as working daytime only and outdoors >9 h/week during summer (n =112). *Night workers* were defined as working more than three hours between 00:00h and 05:00h on a permanent (n=33) or a rotating basis (n=118) (105). This classification of job groups was based on questionnaire information.

For analyses including hours spent outdoors, we only included workers who participated from April throughout September (n=227), where UVB exposure induces vitamin D production. We excluded 39 workers with missing information on either BMI, hours spent outdoors on days off or work days

leaving 186 workers (81 indoor workers, 44 outdoor workers, 46 rotating night workers, and 15 permanent night workers).

Blood samples

Blood samples were drawn at participants' place of work, and collected in tubes without anticoagulation for serum and EDTA tubes for plasma and stored at 5^{o}C until processed to separate the serum and plasma. Most samples (n = 407) were processed within 8 hours (mean 3 hours 48 min.), 30 samples were processed 10-33 h after collection, and four samples were processed 94 h after collection because of technical problems. Samples were stored at -80^{o}C after processing.

Biochemical analyses

All biochemical analyses were carried out in September 2014. Serum levels of 25OHD (25(OH)D_2 and 25OHD_3) were analyzed by isotope dilution liquid chromatography-tandem mass spectrometry (LC MS/MS) as described by Maunsell et al. (111). Calibrators are traceable to NIST SRM 972 (Chromsystems DE). The coefficient of variation (CV) for 25OHD3 was 6.4% at level 66.1 nmol/l and 9.4% at 25.3 nmol/l. Plasma PTH was analyzed using an automated immune analyser (Cobas 6000 E; Roche Diagnostics, GmbH). The CV was 3.3% and 2.7% at PTH levels of 7.7 and 26.6 pmol/l. Standard laboratory methods were used for measurements of total calcium, creatinine, and albumin.. The estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) Study equation (112).

Light exposure assessment

The Actiwatch was worn during a 7-days study period outside clothes on the upper arm and set to one-minute sampling epochs and recorded white light (lux). Time spent outdoors was assessed as

minutes where the light intensity measured by the Actiwatch was 1000 lux or higher (102). Light measurements were considered not valid if the participants reported the Actiwatch was not worn or no physical activity was recorded by actigraphy for at least 20 minutes. We excluded days with less than 80% valid light measurements between 07:00-19:00 h.

Questionnaire

The questionnaire included information on sex, age (years), pregnancy (yes/no), current occupation, time spent outdoor work during work in spring, summer, autumn, and winter (never, 1-4 hours/week, 5-9 hours/week, 10-19 hours/week, 20-29 hours/week, 30-39 hours/week, 40+ hours/week), height (meters), weight (current kilograms), smoking (current/former/never), use of current medication (yes/no), vitamin pill use (yes/no), vitamin D supplement use (yes, 10 µg/yes, 20 µg or more/no) or cod liver oil use (yes/no), tanning bed use (weekly, monthly, never), consumption of fish and shell food (never, monthly, 1 meal/week, 2-3 meals/week,>4meals/week).

Statistical analyses

Data was presented as numbers (%), means with standard deviations (SD)**,** or medians with interquartile (25th-75th percentiles) ranges. Concentrations of 25OHD and PTH were naturally log transformed to obtain the best approximation with normal distributions. We tested the difference of 25OHD and PTH concentrations across seasons and job groups with Kruskal-Wallis test. We used multivariable linear regression to estimate the relative difference of serum 25OHD and plasma PTH concentrations between outdoor, rotating night workers and permanent night workers relative to indoor workers. Models were adjusted in two steps: model 1 included season (January-March/April-June/July-September/October-December), model 2 included in addition age (continuous), sex, socio-economic status (SES) (white collar worker/ skilled blue collar worker/unskilled blue collar

worker), current smoking (yes/no), BMI (continuous), vitamin D supplements or cod liver oil (yes/no), fish and shell food consumption (< 1 meal/week/ ≥ 1 meal/week), tanning bed use (ever/never), and time from blood sampling to storage (<24 h/≥ 24 h. These potential confounders were identified a priori based on a review of the literature (72, 87, 113-116). There was no interaction between job group and month of sampling, and thus the interaction term was not included.

We used logistic regression to estimate the odds ratio (OR) with 95% CI for vitamin D insufficiency (<50 nmol/L) and hyperparathyroidism (> 6.9 pmol/L). These analyses included the same covariates as in the linear regression models.

In linear regression analyses of the association of time spent outdoors and 25OHD concentration, we only included the 186 workers who participated from April-September. We conducted three linear regression models; (1) included job group, but not time spent outdoors, (2) included time spent outdoors, but not job groups, and (3) included both. These analyses were adjusted for month of sampling instead of season. Otherwise the covariates were the same as in the previous models. All analyses were carried out using STATA 13.0 (StataCorp, College Station, Texas).

5. RESULTS

The following section summarizes the main results of study I-III.

5.1 STUDY I

Main findings

The light patterns differed on days with indoor, outdoor and night work, whereas few differences were observed between indoor and outdoor and night workers on days off. Outdoor workers were exposed to higher median light intensities than indoor workers on work days between 06:00-11.59 in the summer (786 vs. 242 lux, *p*-value = <0.001), but not significantly in the winter (138 vs. 107 lux, *p*-value = 0.118) though median time spent above 1,000 lux was longer both summer (118 vs. 22 min., *p*-value = <0.001) and winter (33 vs. 2 min., *p*-value = <0.001). Night workers were exposed to higher median light intensities than indoor workers on work days between 00:00-05.59 in the summer (18..4 vs. 0.2 lux, *p*-value = <0.001), and the winter (22.6 vs. 0.2 lux, *p*-value = <0.001) and the median time spent above 80 lux was 14 min. in the summer and 13 min. in the winter compared to 0 min. among indoor workers (*p*-value = <0.001). During day time, night workers were exposed to lower median light intensities than indoor workers in the summer (06:00-11:59h: 53.1 lux vs. 242 lux, *p*-value = <0.001) and winter (06:00-11:59h: 19.6 lux vs. 107 lux, *p*-value = <0.001). The median time spent above 1,000 lux was also shorter during day time both summer (06:00-11:59h: 11 vs. 22 min., *p*-value = <0.001) and winter (0 vs. 2 min.utes, *p*-value = 0.004).

Table 2. Median time (minutes) spent above 1,000 lux for indoor, outdoor and night workers during work days and days off by season and, time of day.

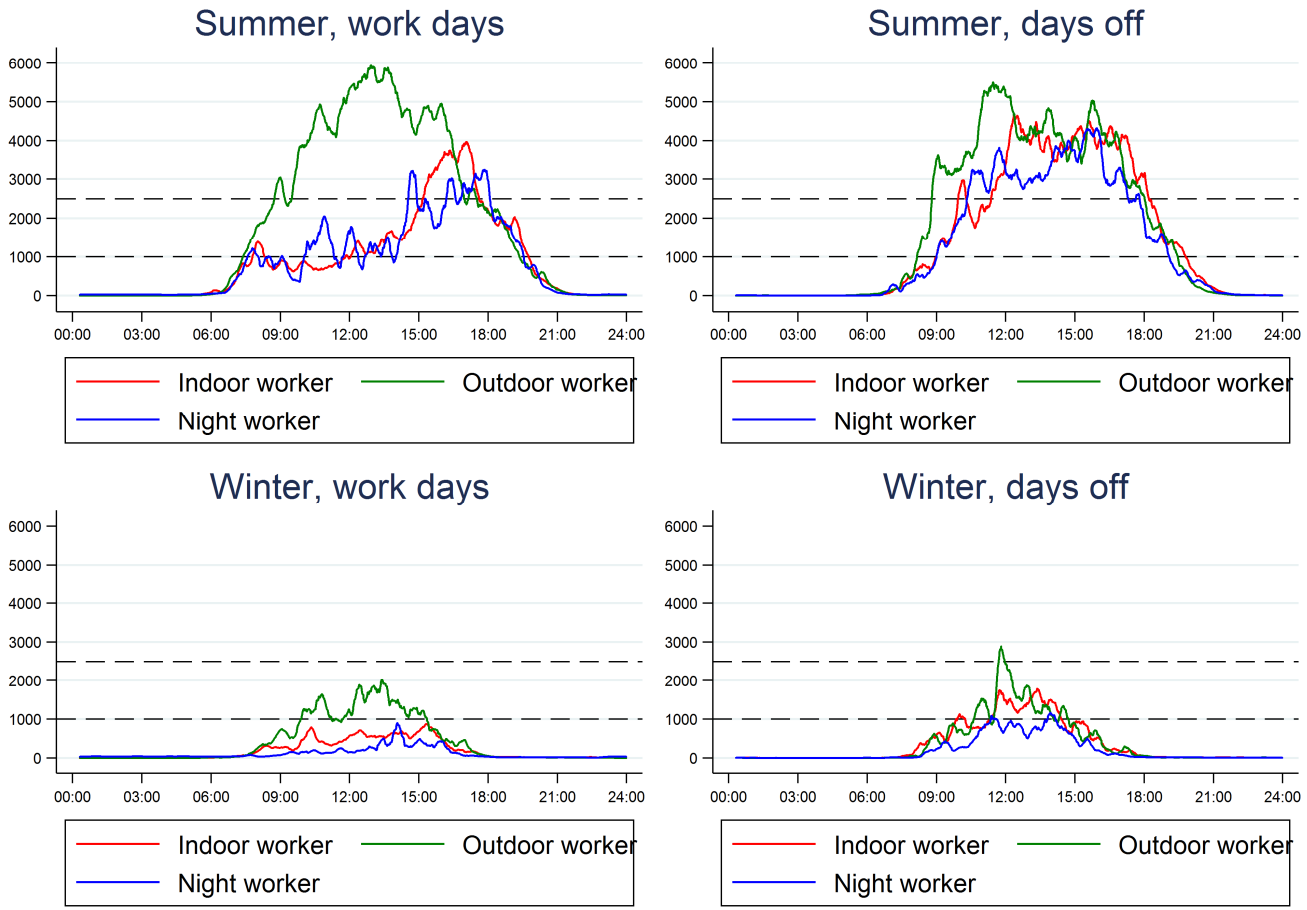
Time periods by day and season	Indoor workers		Outdoor workers				Night workers			
	6-hour periods N	Median (IQR[1])	6-hour periods N	Median (IQR[1])	% diff[2]	*p*-value[2]	6-hour periods N	Median (IQR[1])	% diff[2]	*p*-value[2]
Summer										
Work days										
00:00-05:59	78	0 (0-0)	74	0 (0-0)	-8.7	0.059	157	0 (0-0)	-8.4	0.033
06:00-11:59	196	22 (7-42)	206	118 (58-204)	401	<0.001	56	11 (0-23)	-59.3	<0.001
12:00-17:59	320	75 (37-106)	252	139 (85-196)	81.7	<0.001	48	66 (21-123)	-32.3	0.010
18:00-23:59	163	14 (0-47)	98	10 (0-34)	0,3	0.991	123	5 (0-29)	-24.2	0.274
Days off										
00:00-05:59	75	0 (0-0)	80	0 (0-0)	0.0[3]	-	60	0 (0-0)	0.0[3]	-
06:00-11:59	63	28 (15-67)	60	67 (19-110)	43.9	0.206	49	34 (15-65)	-18.3	0.490
12:00-17:59	161	98 (44-175)	140	102 (48-168)	2.9	0.847	136	89 (51-145)	2.2	0.883
18:00-23:59	108	8 (0-45)	85	6 (0-28)	-2.9	0.916	90	4 (0-19)	-26.4	0.260
Winter										
Work days										
00:00-05:59	62	0 (0-0)	28	0 (0-0)	0.0	1.000	161	0 (0-0)	3.3	0.177
06:00-11:59	129	2 (0-13)	70	33 (5-62)	300	<0.001	49	0 (0-0)	-55.0	0.004
12:00-17:59	234	11 (2-32)	88	44 (17-69)	206	<0.001	43	1 (0-24)	-56.6	0.002
18:00-23:59	102	0 (0-0)	37	0 (0-0)	-3.1	0.439	88	0 (0-0)	-3.1	0.308
Days off										
00:00-05:59	69	0 (0-0)	40	0 (0-0)	0.0[3]	-	35	0 (0-0)	0.0[3]	-
06:00-11:59	39	17 (0-39)	29	15 (2-76)	8.8	0.856	26	11 (0-25)	-20.6	0.623
12:00-17:59	125	20 (4-48)	61	21 (3-65)	-4.3	0.877	98	19 (6-42)	-7.2	0.578
18:00-23:59	65	0 (0-0)	34	0 (0-0)	0.0[3]	-	63	0 (0-0)	0.0[3]	-

[1] IQR interquartile (25^{th}–75^{th} percentile) range

[2] Values computed from a mixed linear regression analyses with indoor workers as reference group.

[3] All measurements are below 1,000 lux

Figure 3. Smoothed arithmetic mean light intensities for indoor, outdoor and night workers across the day on work days, days off and stratified by summer and winter.



5.2 Study II

Main findings

On average night workers had 16.5 % (95 % CI -30.5; -0.2 %) lower salivary melatonin concentration on days with night work than day workers. On days off there was no difference between night and day workers (table 3). On work days there was no interaction between type of work (night/day) and time of day (03:00/07:00/11:00/15:00/19:00/23:00h) and the relative difference did not differ across the day (Figure 2). The mediation analyses showed that light exposure during the night mediated a 5.9 % (95 % CI -10.2; -1.5 %) decrease in salivary melatonin concentration among night workers, whereas no mediating effect was present during daytime (table 4). The direct effects of night work were -18.3% (95 % CI -36.7; 5.4 %) during daytime and -9.6 % (95 % CI -27.0; 11.9 %) during night time.

Table 3. Crude and adjusted relative difference (%) in salivary melatonin concentration in night workers compared with

			Crude		Adjusted[1]	
	Samples N	Participants N	% difference	95 % CI	% difference	95 % CI
Work days	1541	322	-17.0	-29.1; -1.6	-16.5	-30.5 ; -0.2
Days off	1301	301	3.2	-12.8 ; 22.1	8.5	-9.3 ; 29.8

[1] Adjusted for time of day, age, sex, BMI, smoking, diurnal preference and use of antidepressant medication.

Figure 4. Estimates of geometric mean (95 % CI) of salivary melatonin concentrations for day and night workers within 4 time intervals on work days and days off. The figure shows the estimated melatonin concentrations of a worker with the following characteristics: male 40 year old, BMI=25kg/m^2, non-smoker, no antidepressant medication, and morning preference.

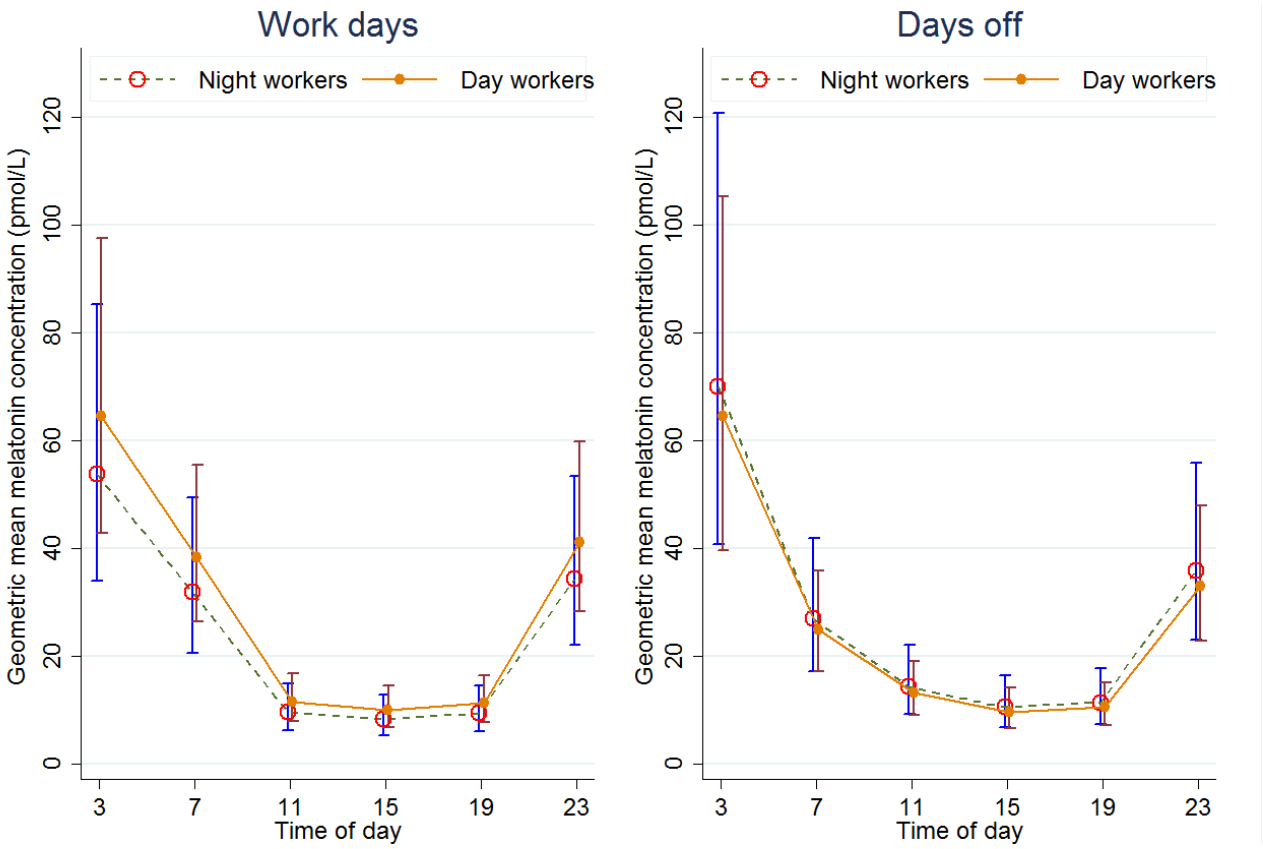


Table 4. Adjusted[1] total, direct, and indirect effects of light exposure[2] on the association of night work with salivary melatonin concentration by time of the day. Results from 87 night workers and 254 day workers followed for 24 hours since starting on the work shift.

	Samples N	Total effect		Direct effect		Indirect effect	
		% difference	95 % CI	% difference	95 % CI	% difference	95 % CI
Night 20:00 h – 07:59	726	-15.0	-31.4 ; 5.2	-9.6	-27.0 ; 11.9	-5.9	-10.2 ; -1.5
Day 08:00 – 19:59	791	-16.2	-34.6 ; 7.5	-18.3	-36.7 ; 5.4	3.0	-2.8 ; 9.1

[1] Adjusted for time of day, age, sex, BMI, smoking, diurnal preference and use of antidepressant medication.
[2] Light exposure is the duration of measurements above 80 lux 30 minutes prior to each saliva sample.

5.3 Study III

Permanent night workers had 24.6 % (95 % CI 11.1; 36.1%) lower 25OHD, and 14.2 % (95 % CI-0.2; 30.6 %) higher PTH concentrations than indoor workers. Outdoor workers tended to have lower PTH concentrations (7.3 %: (95 % CI: -0.7; 14.7 %) than indoor workers, but 25OHD concentrations were similar. Rotating night workers PTH and 25OHD concentrations did not differ from indoor workers (Figure 5). Permanent night workers had 4.16 (95 % CI 1.29; 13.33) times higher odds of having vitamin D insufficiency than indoor workers and 2.20 (0.60; 8.06) times higher odds of hyperparathyroidism (not significant). Outdoor workers had three fold lower (OR=0.29; 95 % CI 0.08; 1.04) odds of hyperparathyroidism (not significant). The odds of vitamin D insufficiency were similar among indoor, outdoor and rotating night workers (Figure 6). In main analyses, there was no interaction between job group and season of blood sampling.

Figure 5. Relative differences (%) in serum 25OHD and plasma PTH concentrations between indoor (n=162), outdoor (n=112), rotating night (118), and permanent night workers (n=33)

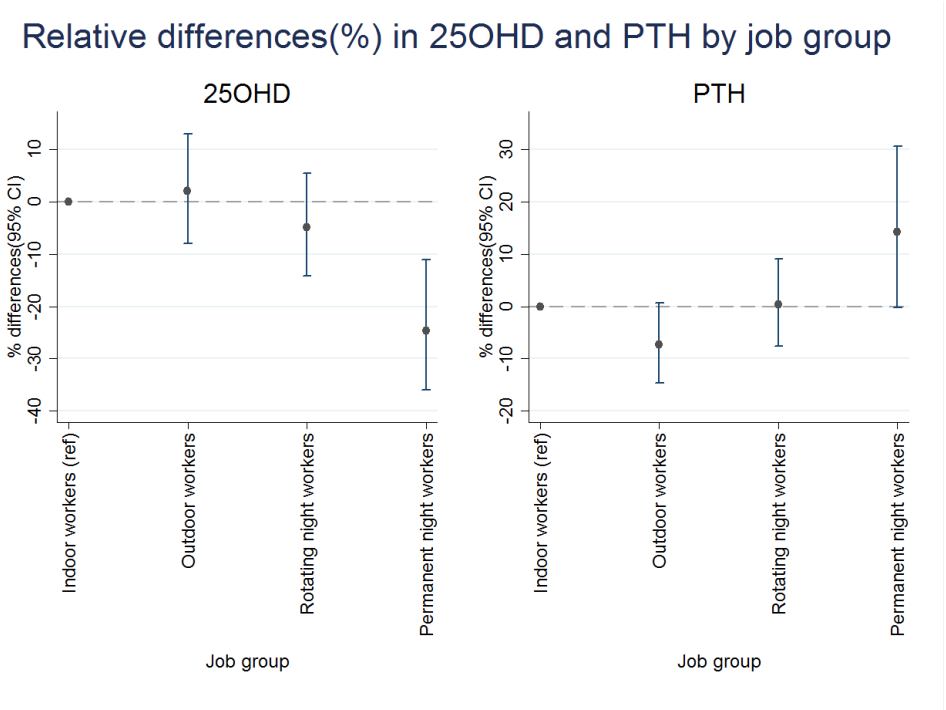
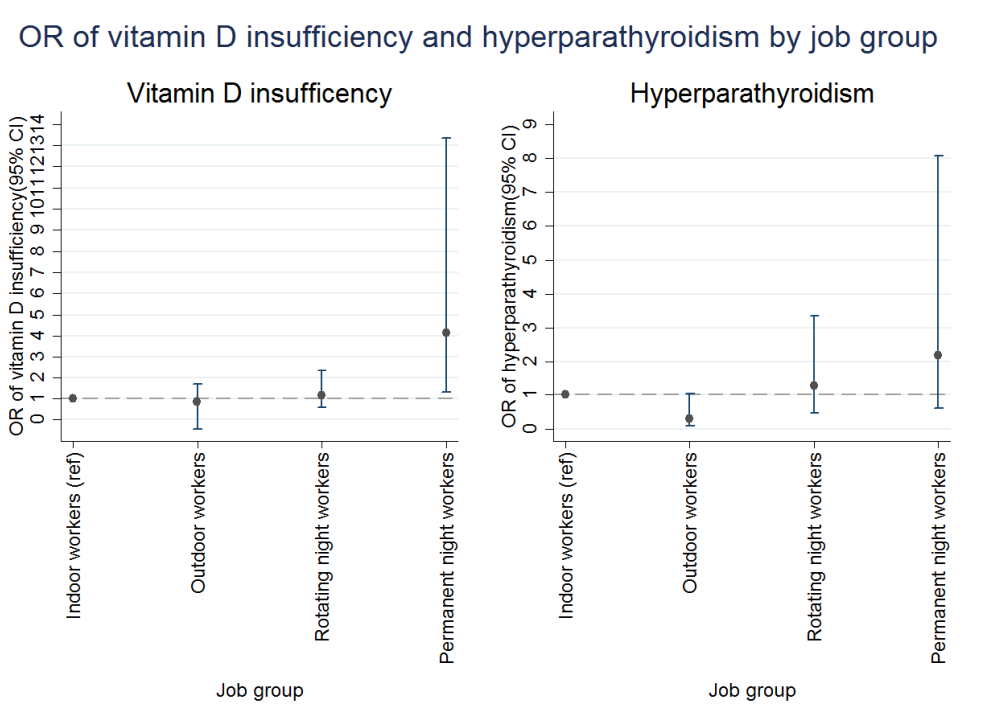
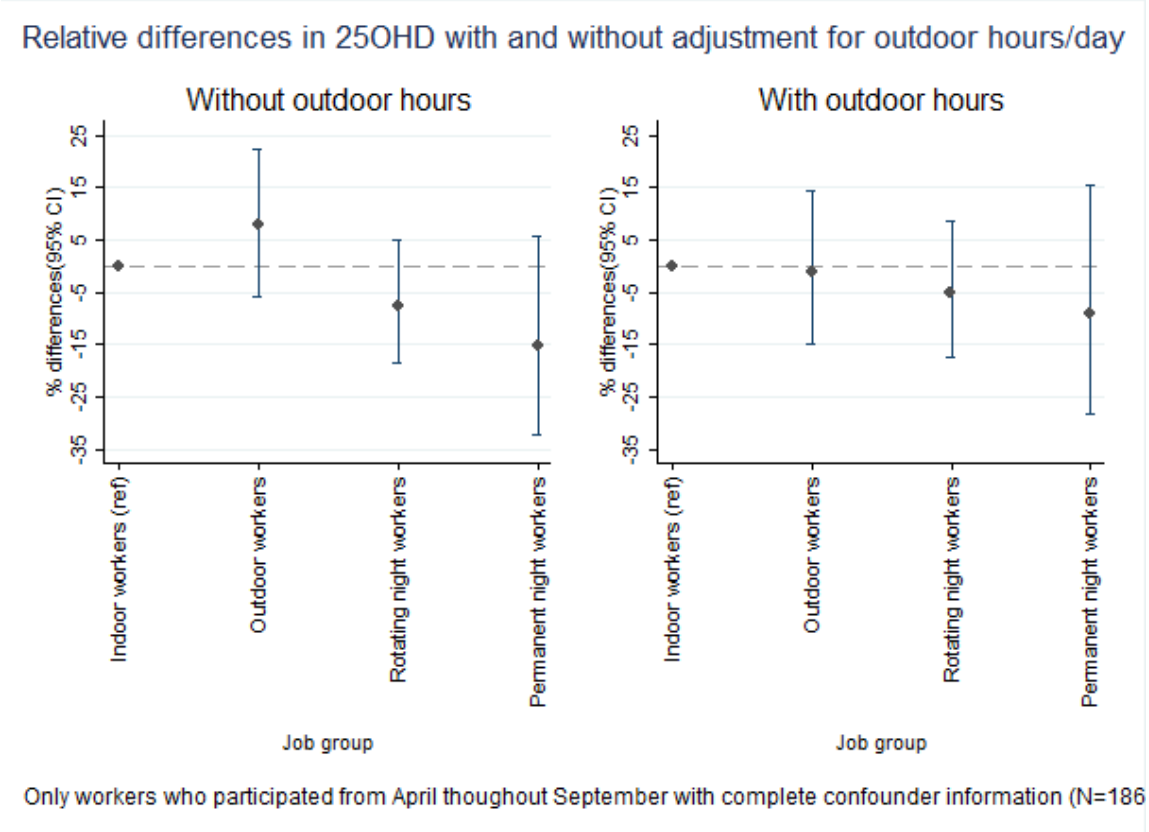


Figure 6. OR of having vitamin D insufficiency (< 50nmol/L) or hyperparathyroidism (> 6.9 pmol/L) between indoor (n=162), outdoor (n=112), rotating night (118), and permanent night workers (n=33)



Among workers who participated from April throughout September 25OHD concentrations were 4.9% (95% CI 0.8; 9.2%) higher per hour spent outdoors on work days, but on days off there was no significant association (results not shown). Outdoor workers, participating during the summer, had 7.8% (95% CI -6.0; 22.4%) higher 25OHD concentrations than indoor workers. After adjustment for time spent outdoors this decreased to -1.2% (95% CI -15.0; 14.5%). Rotating night workers had 7.6% (95% CI -4.9; 18.6%) lower 25OHD concentrations, this only changed slightly by adjustment for demographic and lifestyle related confounders. Permanent night workers had 15.3% (95% CI -5.7; 32.1%) lower 25OHD concentration that decreased to -9.3% (95% CI -28.2; 15.6%) after adjustment (Figure 7).

Figure 7. Relative difference (%) in 25OHD concentrations with and without adjustment for hours spent outdoors/day[1] between indoor (n=81), outdoor (n=44), rotating night (n=46), and permanent night workers (n=15) participating from April throughout September.



[1] Outdoor defined as minutes with light measurements above 1,000 lux

6. DISCUSSION

6.1 KEY FINDINGS

In study I day time light exposure was higher on days with outdoor work than days with indoor work across seasons. Night time light exposure was higher on days with night work compared to days with indoor work. Meanwhile the light exposure was lower during daytime on days with night work than on days with indoor work. On days off, only few differences in light exposure were observed between indoor, outdoor and night workers. These findings applied across seasons.

In study II salivary melatonin concentrations were lower among night workers on days with night work than among day workers. No difference was observed on days off. Light exposure mediated a part of the melatonin suppression observed during the night, but not during the day.

In study III permanent night workers had lower 25OHD and higher PTH concentrations than indoor workers. Outdoor workers tended to have higher 25OHD concentration during summer, and lower PTH concentrations all year than indoor workers. The concentration of 25OHD increased by hours spent outdoor during summer. The differences between job groups were partly explained by differences in time spent outdoors.

6.2 METHODOLOGICAL CONSIDERATIONS

6.2.1 OUTCOME DEFINITIONS

In study I, mean white light intensities was chosen along with time spent above 80, 1,000 and 2,500 lux as different approaches of describing the light exposure. The thresholds were chosen on basis of previous literature describing light above these intensities to affect circadian, neuroendocrine, and

neurobehavioral responses (described in section 3.2). Furthermore, 1,000 lux was also chosen to facilitate comparison with previous studies (5, 30, 32, 33, 36).

Intensity and spectrum of the light are interrelated parameters when describing the effect on non-visual responses. Illuminance is a conventional metric of describing light, and more complex metrics have been developed (13, 117). We chose to use illuminance as outcome, as it is a clearly defined standard unit and the light measure most commonly used in previous studies. Use of blue light was another option, but the sensitivity of the blue light sensor is unique for the Actiwatches (101). Besides the unit for measuring blue light is not a clearly defined unit, which would make comparison and extrapolation difficult.

In study II we calculated mean melatonin concentrations within four hour intervals because participants were asked to collect saliva samples at specified time periods 4 hours apart. Still within these 4-h intervals exact time of sampling may have an impact on melatonin concentrations and the estimated difference between day and night workers. We therefore included exact time of sampling in additional analyses. However, this only changed estimates marginally. We did not assess circadian phase, which obviously would have been an outcome of interest. However this was not possible. Participants only collected saliva during awakening hours, and, except for days with night work, few samples were collected during the night, where variation is largest. This caused wide confidence intervals and problems to estimate circadian phase. Assessment of circadian phase was furthermore hampered by the lack of criteria for lightening conditions before saliva sampling, because of the masking effect of ambient light. It was, however, not feasible to impose any light criteria as these would be difficult to comply with during working hours.

In study III, we used 50 nmol/L as cut off for vitamin D insufficiency as recommended by Danish guidelines, but this cut-off is still a matter of debate as described in section 3.6. We used 6.9 pmol/L as cut-off of hyperparathyroidism, as this is the upper reference limit used in Danish laboratories. This level is defined in a normative manner i.e. represents the highest 2.5% in a population. It has therefore been questioned whether this limit is too high, as vitamin D insufficiency is common in general populations, and PTH may be pathologically increased in a substantial part of a normal population (87). The consequences for this study would be an underestimation of the prevalence of "true" vitamin D insufficiency and hyperparathyroidism. This would most likely affect all job groups equally causing non-differential misclassification and attenuation of results.

6.2.2 EXPOSURE ASSESSMENT

We defined type of work differently within each study, in order to get the most relevant exposure. In study I, we defined the work type from the diary, because we were interested in the exposure during the week of participation. The cut-off between indoor and outdoor work was arbitrary, and the between-worker variability of exposure was higher among outdoor than indoor workers. However we chose to define outdoor workers as one joint group because of power considerations.

In study II, we chose to define light exposure as time above 80 lux, as this is a well-documented threshold for melatonin suppression and reflects peak exposures. Average light exposure measures do not capture these peaks and assumes a dose-response relationship that is not present below 80 lux. Because we had the specific time point for each saliva sample, we were able to use light measurements from the relevant time window increasing the accuracy of the observed associations.

In study III, we were interested in all over exposure to UVB inducing synthesis of 25OHD. The UVB intensity is highest during summer, and larger areas of bare skin exposed because of higher temperatures. The definition of an outdoor worker was therefore based on questionnaire information on hours of outdoor work from June-August. We chose the same cut-off of two hours/day as in study I equalling ten or more hours/week. Unfortunately, we lacked information on frequency of night shifts among the rotating night workers, and the exposure level in this group may vary substantially.

6.2.3 SELECTION BIAS

Participants were recruited from a wide range of occupations, had a wide age span, included men and women. As participation in the field study was voluntary it is unknown whether the participants are representative. Potential participants were told the aim was to study if low light intensities during indoor work affect health, and if light at night affect sleep quality and circadian rhythms. Otherwise they received as little information of the specific aims as possible. Self-selection into the study may have caused participants with poor health not to participate, or an overrepresentation of workers with a special interest in health, or workers who worry about their health. This does however not depend on job group. Compared to the general working population women, health care workers and child care workers are overrepresented. Health care workers were mainly indoor and rotating night workers, and may in all-over be healthier than many other workers. In study I, this may give rise to an overestimation of light exposure outside work hours among indoor and rotating night workers. In study III, it may cause an overestimation of the difference between indoor and permanent night workers, and an underestimation of the difference between indoor and outdoor workers. In study II, this is less likely a problem as melatonin is less affected by lifestyle and the melatonin profile mainly determined by genetics (46). There were twice as many day workers with

morning preference than night workers. It has been suggested morning types are more susceptible to night work and light at night in terms of more melatonin suppression (38, 56). Morning types have further been shown to have lower night work tolerance, and may therefore be more likely to change job (118). If the proportion of workers with morning and evening preference is representative for Danish night workers, this is not a problem. But if participants with morning preference have chosen not to participate, the effect of working nights may be underestimated. We were, however, not able to demonstrate an effect of diurnal preference in this study.

6.2.4 INFORMATION BIAS

In study I, days with indoor, outdoor, and night work were classified by diary information. Days with night work are less likely subject to misclassification, as participants reported the exact working hours each day. Some misclassification has probably occurred between days with indoor and outdoor work. In addition to recall bias, participants were asked if they spent 20 minutes or longer outdoors each hour, but this was always interpreted as 60 minutes. Days with more than 120 minutes self-reported outdoor work were classified as outdoor days, but the true duration of outdoor work may be shorter. The light exposures may therefore be underestimated on days with outdoor work, as well the observed differences between indoor and outdoor work days.

The light measurements were obtained using personal dosimetry. To ensure the Actiwatch was actually worn, we excluded hours where it was reported not worn, and periods where the participant reported to be awake, but no movement was recorded for 20 minutes or longer. The light exposure assessment has some limitations. First of all light is measured at the upper arm and does not represent retinal exposure. Light intensities have been shown to be underestimated when measured at the wrist (119), and the placement on the upper arm is preferable as it represents viewing

direction most of the time. Aarts et al (120) investigated the performance of personally worn light exposure measurement equipment, and concluded that the location of these instruments had an impact on the results. Although, the placement of the Actiwatch was not directly comparable to the recommended position at eye-level, it was still placed in viewing direction and therefore reasonable accurate when referring to light exposure of indoor, outdoor and night workers.

The measurements may differ from the true light levels during some light conditions, because the measured light (lux) depends on the angle of the light on the Actiwatch, and the spectral composition of the light (119, 121). This causes misclassification of unknown directions, and this may differ between jobs groups as the spectrum of light sources, in particular sunlight, differs from each other causing differential misclassification. The differences in study I may thus be biased in both directions.

In study II, we expect the reports of working day or night time to be precise (122). Melatonin has a pronounced diurnal rhythm, and time of sampling is of uttermost importance when analysing data. Participants noted the exact date and time on a blank label on each sample enhancing the chances of the time noted is accurate compared to prefabricated labels. Therefore inaccurate information on time of sampling is not likely a source of bias. The light measurements are prone to the same errors as described above causing a non-differential misclassification of the mediator, which causes an underestimation of the mediating effect (123).

LC-MS/MS was used to analyse salivary melatonin. The LOD of this method is lower than previous methods, and the accuracy to measure low melatonin concentrations during the day better (48). Melatonin concentrations were below the lower limit of detection 3.73 pmol/l (LOD) in 2% of the samples. All of these were sampled during the day and evening where melatonin concentrations are

expected low. These measurements do, however, still represents a value, and dropping them would overestimate mean melatonin concentrations, and depending on the distribution between job groups cause differential or non-differential misclassification and bias. Therefore, they were given a random value from a normal distribution centered around 2/3 of the LOD. Four of the samples from day time had unrealistically high concentrations (1261-5000 pmol/L). The biochemical analyses were rerun with similar results, and the questionnaire inspected for possible explanations. Since these may have a major impact on the statistical analysis, they were excluded along with 14 samples below the limit of detection (LOD) in accordance with Grubbs outlier test (108) to avoid bias. Biochemical analyses are always subject to some variation, but this does not depend on exposure. This results in non-differential misclassification and bias towards the null.

In study III, job group was based on questionnaire information that has been shown to provide accurate information on rotating and permanent night work (122). The reporting of outdoor work during summer is prone to recall bias, but this is most likely not related to vitamin D and PTH status, and causes non-differential misclassification and bias towards the null. The limitations of the light measurements are less important in this study, as the light merely is used to separate indoor from outdoor stay. Serum 25OHD and plasma PTH were analysed with the most precise laboratory methods, but the biochemical analyses are associated with various levels of imprecision (see section 4.4). As described for melatonin causes bias towards the null.

6.2.5 CONFOUNDING AND EFFECT MODIFICATION

In study I, we did not adjust for confounders as the study was mainly descriptive.

A priori, we selected potential confounders in study II and III based on a review of the literature. In study II, we adjusted for time of sampling, age, sex, BMI, current smoking, diurnal preference and use of antidepressant medication. We lacked information on menopausal status, oestrogen medication, parity, or time since last menstrual period, which may affect melatonin concentrations (124). Night workers were slightly younger than day workers, and the proportion of pre-menopausal women may differ between groups. However, we adjusted for age, which is highly correlated with menopausal status. We have no reason to believe the distribution of the other factors should differ between job groups and confound results. Time of day is a strong predictor of melatonin concentrations, as already discussed in section 6.2.1. We further hypothesized that time of day was an effect modifier of the effect of night work on melatonin concentrations. Therefore an interaction term of type of work and four-hour intervals was included, but there was no significant interaction, except for the sub-analyses of permanent night workers. Chronotype has been suggested to be an effect modifier of the association between night work and melatonin suppression (38, 56, 125). We were not able to demonstrate this in our study (data not shown). However, the the four item question used in this study was crude compared to comprehensive chronotype questionnaires used by previous studies. A true interaction may therefore exist.

In study III, results were adjusted analyses in two steps: 1. adjusting for only season, 2.adjusting for season, sex, age, SES, use of vitamin D supplements, BMI, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to freezing. This approach was chosen to estimate the all-over difference between job groups, and to investigate whether differences were due to lifestyle factors. Estimates for differences between indoor workers and outdoor and permanent night workers changed when adjusted for lifestyle factors and socio-economic status. This indicates that lifestyle factors associated with job group affect the results besides occupational

UVB exposure. A priori we hypothesized that season was an effect modifier, but there was no interaction between job group and season. This may however owe to lack of power, as results from workers participating through the light half year indicated that outdoor workers had higher 25OHD concentrations than indoor workers. We believe that adjustment for the chosen confounders has reduced the possibility of confounded associations in study II and III. However the possibility of residual confounding and unknown confounders is still present.

6.3 MAIN FINDINGS IN THE LIGHT OF OTHER STUDIES

Study I

In study I, the time indoor workers spent above 1,000 lux was comparable to what previous field studies have reported (5, 30, 32, 33). Except for one study (36), where only 36 min. was spent above 1000 during a 24-h day in September, but this may be explained by longer work hours. Outdoor workers had higher light exposure than indoor workers on work days. To our knowledge this has not previously been studied, but UVR exposure was previously found higher among outdoor workers compared to indoor workers (89, 91). In accordance with previous literature, night workers had higher light exposure during night work than day workers within the same time window (38, 59). The day after a night shift, night workers had lower light exposure than day workers. This has not previously been studied, but most studies reported lower 24-h light exposure on days with night shift than days with day shift (34, 38, 39). Similar median light intensities (60), as well as higher average light exposure on days with night work (35) have, however, also been reported. In the latter study, the workers did 12 hour shifts, whereas our population mainly did 8 hour shifts explaining the conflicting findings.

Study II

In study II, we found 15-16% lower melatonin concentrations among night workers during days with night work compared to day workers. This is in line with previous studies (38, 54-57, 61, 62) except one (58). Other studies that estimated percentage differences reported higher differences than we found. The size of melatonin suppression depends on light intensities (18) and numbers of consecutive night shifts (56, 63, 64). Dissimilarities of these two factors would cause true different results. In addition different sampling methods, protocols and methods of analysis were used and these may cause variance in the estimated differences. The study by Leung et al. yielded the results most comparable to our findings. They collected spot urine across a 24-h day and estimated mean aMT6s levels with cosinor analyses. Results showed -25% rotating night workers had 25 % (95% CI: 9.8; 37.7 %) lower aMT6s levels (56). Gomez-Acebo et al. also used cosinor analysis of aMT6s concentrations from spot urine collected during rotating night workers second night shift. They reported that mean concentrations of aMT6s were 89 ng/mg creatinine among day workers and 50 ng/mg creatinine among night workers, corresponding to 43.8% lower melatonin production among night workers (55). Light exposure was not reported and may explain the greater extent of melatonin suppression. Mirick et al. and Davis et. al collected urine during different functional time periods (sleep and work), and compared total aMT6s production during some of these, but not the entire 24 hours. The permanent night workers in these two studies had worked at least two consecutive night shifts before participation. The aMT6s produced during a night shift was 68.6% (95% CI 62.5; 74.8%) and 62.0% (95% CI: 55.0; 69.0%) lower than what day workers produced during their night sleep (54, 126). If the night workers were phase delayed it is possible that their peak production occurred after the end of the shift, and the difference between the groups is overestimated. The possible overestimation along with higher exposure to night work could in addition to unknown light exposure explain the higher percentage difference observed in these

studies. Papantoniou et al. collected spot urine and derived the circadian mean aMT6sfrom a cosinor analysis and reported the circadian mean was 33.8% lower among the permanent night workers (95% CI: 15.1; 48.4%). (38) The higher difference in this study could be explained by a higher median light exposure at night (38 lux vs. 6 lux in our study) and higher exposure to night work among the permanent night workers compared to our mainly rotating night workers. On days off (on average 47 hours after completing a shift that were mainly the first or second consecutive shift) melatonin concentrations were similar to day workers. This is in accordance with Jensen et al. (63) who reported full recovery on the second day off after two consecutive night shifts, but not Hansen et. al (62) who collected urine on averagely the second day off, but did not report how many consecutive shifts the permanent and rotating night workers had had. Mirick et al. and Davis et. al compared aMT6s concentration in urine produced the first night after a shift e.g. <24 hours after and reported melatonin production was still affected, and this findings does not contradict our results.

Mediation analyses showed that exposure to light above 80 lux mediated a 6% decrease in melatonin concentrations. Personal light dosimetry have been used in few studies on night work and melatonin (38, 59, 60), none of these analyzed the mediating effect of light. All of these studies used average light at night as exposure, and did not find strong associations with melatonin concentrations. Peak exposure is probably a more relevant exposure assessment, than average levels, as melatonin is suppressed above a threshold of 80 lux, and may explain why we find a stronger association. Still, other factors than light accounted for the majority of the melatonin suppression, and this is in agreement all three studies.

Study III

In study III, we found lower 25OHD and higher PTH concentrations among permanent night workers compared to day workers. We found comparable 25OHD concentrations in indoor and outdoor worker, but a tendency towards lower PTH concentrations among outdoor workers all year and higher 25OHD concentrations during summer. Rotating workers did not differ from indoor workers in any analyses. The difference in 25OHD could partly be explained by time spent outdoors.

Regarding comparison to previous studies, it is important to be aware that the measured 25OHD concentrations vary substantially between assays and laboratories (127). This should, however, not affect the relative difference between job groups within each study population. A birth cohort study from England found that permanent night work in multivariable analysis was associated with 8% (95% CI: 2; 15%) lower concentrations among women, whilst no difference was observed among men compared to day workers of the same sex (96). This study indicated a correlation between night work and self-reported time spent outdoors, but not use of vitamin D supplements or oily fish consumption. This supports our findings; that lack of exposure to sunlight partly causes the lower vitamin D concentrations observed. Rotating night workers had similar 25OHD concentrations as indoor workers, supporting a small Japanese study on 14 male factory workers (94). Contrary, Israeli physicians with night shifts had 23% lower 25OHD concentrations than their colleagues without night shifts (93). Self-reports from this study showed that the physicians working at hospitals (who comprised the majority of night shift workers), were less sun exposed than the family doctors. Indoor workers and rotating night workers spent similar amounts of time outdoors in our study, and this may be the reason of the contrasting findings. Romano et al. (92) found a significant effect of working night shifts in adjusted analyses among 196 Italian male factory

workers. The unadjusted mean 25OHD was 39% lower among workers doing rotating shifts, but this study did not include diet or time spent outdoor. Importantly none of the studies had information on frequency of night shifts as predictor of sun exposure. Outdoor workers had regardless of spending longer time outdoors on work days not higher 25OHD concentrations than indoor workers across the year. But results pointed towards higher 25OHD concentrations from April through September, and lower PTH concentration all year. Most previous studies have reported significantly higher 25OHD concentrations among outdoor workers (88-90). Our results may in addition to lack of power owe to differences in length of work days, dressing, sun protection and the definition of outdoor work. Devgun et al. (90) studied gardeners that never worked indoors; while Azizi et al. used self-reported outdoor work two or more hours/day (89), and Pazaitou-Panayiotou et al. did not define outdoor work (38). Our results are in line with a recent Danish study comparing farmers and their indoor working spouses. However in a contemporary agriculture it is possible that a substantial part of the outdoor work was actually spent inside vehicles with exposure to UVA but not UVB. Our results from analyses of the summer population suggest that the longer time spent out on work days is counteracted by a poorer lifestyle among the outdoor workers. Similar observations were made in the study by Ward et al. (96), who found manual class was not associated with lower 25OHD though lifestyle was poorer than other workers, but might be counteracted by more time spent outdoors. In conclusion few studies have been conducted comparing job groups, but results point towards lower 25OHD concentrations among especially permanent, but also rotating, night workers. The effect can however be counteracted by a healthier lifestyle. The studies were conducted at different latitudes, but latitude has been shown not to be a strong predictor of 25OHD. In fact the highest 25OHD concentrations have been found in Northern Europe (Africa not studied), and 25OHD concentrations seems to depend more on lifestyle and behaviour (128).

7. CONCLUSION

The findings in this thesis show that indoor, outdoor and night work affect diurnal light exposure on work days, while only small differences were observed on days off. Outdoor workers were during daytime on work days exposed to higher light intensities, and spent longer time above 1,000 lux as well as 2,500 lux, than other workers. Night workers were during night work exposed to higher light intensities, and spent longer time above 80 lux, than indoor workers at home. Nevertheless, light exposure during night work was still low. The differences between job groups were observed independent of season, but all average measures and durations were higher and longer in the summer.

On work days, salivary melatonin concentrations were 15-16% lower among night workers than day workers. In total light, at night mediated a 6% decrease in melatonin concentrations, but the majority of the difference observed was caused by other factors than light. On days off (averagely 47 hours after a night shift) night workers melatonin concentration did not differ from day workers.

Permanent night workers had lower 25OHD and higher PTH concentrations than indoor workers, and this was partly caused by differences in time spent outdoors. Outdoor workers tended to have higher 25OHD concentrations during summer and lower PTH all year. Analyses indicated that the effect of outdoor work was counteracted by a poorer lifestyle among outdoor workers. In total this suggests a gainful effect of outdoor work. Rotating workers did not differ from indoor workers in any analysis.

8. PERSPECTIVES

The results presented in this study show that work hours affect light exposure on work days, but not days off. The low light exposure observed among indoor and night workers on work days may, according to previous literature, affect general well-being, mood, sleep and vitality - especially during the winter. The morning hours are a crucial time of light exposure with respect to entrainment of the circadian rhythm and treatment of depression and SAD. Indoor and night workers showed higher light exposure in the afternoon, when they didn't have to work or sleep. It is likely that employers could increase workers performance by improving light conditions, as studies have showed an increase of e.g. performance and alertness by higher exposure to light or addition of blue light during work hours. Night workers showed an acute transient suppression of melatonin that was only partly mediated by light exposure. The degree of suppression was lower than what has previously been reported. This may be interpreted as light conditions at night are favourable with respect to melatonin suppression, though it may on the other hand cause sleepiness and lower alertness, aims not included in this study. Furthermore prior light history have been shown to affect melatonin suppression, and considering the low light intensities during day time on work days, there may be a potential for prevention, which calls for more research. Time spent outdoors attenuated the associations of job group and 25OHD concentrations. Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers, and work organizers should consider the beneficial effects on health of outdoor work and outdoor recreational spaces.

These findings all indicate that the light environment and time spent outdoors during work affects human physiology, but they do not tell if the light environment cause disease in the long run. This calls for more research of the long term effects of night work and in particular indoor work.

9. ENGLISH SUMMARY

Background and aims: Currently, the population of industrialized countries spends 90% of their life inside buildings where light intensities are lower than outdoors during the day, higher than outdoors during the night, and UVB radiation not present. Indoor and night work is common and affect light exposure during work and maybe also outside work hours. Low light intensities during indoor work may affect general well-being, sleep, mood, vitality, and learning abilities, whereas light exposure during the night work may suppress melatonin production and affect circadian rhythm. Vitamin D insufficiency is common and low exposure to UVB related to work hours may affect vitamin D metabolism. The aim of the current thesis was to assess light exposure during days with night, outdoor, indoor, and off work and to examine the effects of night work on salivary melatonin concentration during and subsequent to night work and the mediating role of light. Furthermore to examine blood concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) among indoor, outdoor, night workers and the association with hours spent outdoors on work days and days off.

Methods: Light intensity from 535 indoor, outdoor and night workers was continuously recorded for seven days across the year with a personal light recorder. Participants completed a work diary and a sleep diary, and a questionnaire on background characteristics. A subset of participants (N=404) collected up to seven saliva samples during a 24 h work day (day or night) and a day off. Another subsample provided a blood samples (N=459). Average light intensity and time spent above 80, 1,000 and 2,500 lux were depicted and computed for 6-hour intervals on work days and days off work during summer and winter among 509 workers. Differences between night, outdoor and indoor workers were analysed with multivariate linear regression. Salivary melatonin concentrations were analysed, samples from 341 workers were included in multilevel regression to assess the difference between day and night work. The mediating effect of light was analysed by

boot strapping. Linear and logistic regression models were used to evaluate the associations of time spent outdoor, indoor, outdoor, rotating and permanent night work and 25OHD and PTH concentrations.

Results: On work days outdoor workers had higher light exposure than indoor workers at daytime. Night workers had higher light exposure during night work than indoor workers, but lower during daytime. On days off few differences was observed between the job groups. On work days, night workers showed 15% lower salivary melatonin concentrations than day workers. This effect was partly mediated by light during night, but not day time. On days off, we observed no difference in melatonin concentrations between day and night workers. Permanent night workers had 24.6 % (95 % CI: 11.1; 36.1 %) lower 25OHD and 14.2 % (95 % CI: 0.2; 30.6 %) higher PTH concentrations and outdoor workers comparable 25OHD but 7.3 % (95 % CI: -0.7; 14.7 %) lower PTH concentrations compared to indoor workers. Concentration of 25OHD increased by 5.3 % (95 % CI: 1.8; 9.1 %) per hour spent outdoor at workdays in the summer.

Conclusion: Night workers had higher light exposure at night than day workers, but exposure to light intensities able to suppress melatonin was short. Melatonin was transiently suppressed, and this was partly mediated by light. The indoor and night workers' light exposure during day time at work days was at a level that may reduce general well-being and mood, especially during winter. Outdoor workers experienced anti-depressive levels of light exposure during summer. Concentrations of 25OHD was lower and PTH higher among permanent night workers. Concentrations of 25OHD increased by time spent outdoors on work days. Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers and work organizers should consider the beneficial effects of outdoor work and recreational spaces.

10. DANSK RESUME

Baggrund og formål: I øjeblikket tilbringer befolkningen i de industrialiserede lande ca. 90 procent af døgnet indendørs, hvor lyset adskiller sig fra udendørs lys. Indendørs lys indeholder ikke UVB stråler, og lysintensiteten er om dagen lavere indendørs end udendørs, mens den om natten er højere. Både indendørs- og natarbejde er hyppigt, og påvirker lyseksponeringen i løbet af, og muligvis også udenfor, arbejdstiden. De lave lysintensiteter under indendørsarbejde kan påvirke det generelle velbefindende, søvn, humør, vitalitet og indlæring, mens lys om natten kan undertrykke melatonin-produktion og forskyde døgnrytmen. Vitamin-D mangel er hyppig, og lav UVB-eksponering i arbejdstiden kan muligvis påvirke D-vitamin niveauet. Formålet med denne afhandling var at beskrive lyseksponering på arbejdsdage med indendørs-, udendørs- og natarbejde samt i fritiden. At undersøge betydningen af natarbejde og lyseksponering under natarbejde for melatonin-produktionen, og at undersøge betydningen af indendørs-, udendørs- og natarbejde og tid brugt udendørs på arbejds- og fridage på koncentrationerne af 25-hydroxyvitamin-D (25OHD) og parathyroidea hormon (PTH).

Metoder: Vi rekrutterede 535 indendørs-, udendørs- og natarbejdere, der gennem en uge bar en lysmåler på overarmen. Målingerne blev foretaget fordelt over året. Deltagerne udfyldte en arbejds- og søvndagbog samt et spørgeskema om arbejde og livsstil. Vi indsamlede spytprøver fra 404 deltagere gennem et arbejdsdøgn (dag eller natarbejde) og på en fridag. Blodprøve blev taget fra 459 deltagere. Gennemsnitlige lysintensiteter og tid brugt over 80, 100 og 2500 lux blev beregnet i seks-timers intervaller på arbejds- og fridage; sommer og vinter. Vi brugte multivariat lineær regression til beregning af forskelle i lyseksponering mellem job grupperne samt til at estimere forskelle i melatonin koncentration mellem dag- og natarbejdere. Den medierede lyseffekt blev estimeret med bootstrapping. Lineære og logistiske regressionsmodeller blev brugt til at analysere

sammenhængen mellem indendørs-, udendørs- og skifteholdsarbejde samt permanent natarbejde og 25OHD og PTH-koncentrationer.

Resultat: På arbejdsdage med udendørsarbejde var lysniveauer i dagstid højere end på dage med indendørsarbejde. Natarbejdere var på arbejdsdage eksponeret for højere lysniveauer end indendørsarbejderne om natten. I dagstid var natarbejderne eksponere for lavere lysniveauer end indendørsarbejderne. På fridage var lysniveauerne mere ens mellem de tre jobgrupper, og vi fandt kun få signifikante forskelle. På arbejdsdage havde natarbejdere 16,5 % (95 % CI: 0,2; 30,5 %) lavere melatonin koncentration i spyttet end dagarbejdere. Denne effekt var delvist medieret af lys om natten, men ikke om dagen. På fridage var der ingen signifikant forskel mellem dag- og natarbejdere. Faste natarbejdere havde 24,6 procent (95 % CI: 11,1; 36,1 %) lavere 25OHD og 14,2 procent (95 % CI: 0,2; 30,6 %) højere PTH-koncentrationer. Udendørsarbejdere og indendørsarbejdere havde sammenlignelige 25OHD-koncentrationer, mens PTH var 7,3 procent (95 % CI: -0,7; 14,7 %) lavere. Koncentrationen af 25OHD øgedes 5,3 % (95 % CI: 1,8; 9,1 %) pr time brugt udendørs på arbejdsdage om sommeren.

Konklusion: Natarbejdere havde højere lyseksponering om natten end indendørsarbejdere, men varigheden af lys, der forventes at påvirke melatonin var kort. Melatonin koncentrationen var forbigående nedsat under natarbejde og delvist medieret af lys. Dagslysniveauerne var på arbejdsdage blandt indendørs- og natarbejdere så lave lysniveauer, at det kan påvirke det generelle velbefindende og humøret – specielt om vinteren. Udendørsarbejdere var om sommeren eksponeret for lysniveauer sammenlignelige med de, der bruges til depressions behandling. Permanente natarbejdere havde lavere 25OHD og højere PTH end indendørsarbejdere. Koncentration af 25OHD steg signifikant pr time brugt udendørs på sommer arbejdsdage. Klinikere bør være opmærksomme på, at D-vitamininsufficiens kan være udbedt hos personer med permanent natarbejde, og arbejdsgivere bør overveje de gavnlige effekter af udendørs arbejde og pausearealer.

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12. SUPPLEMENTARY MATERIAL

1. Overview of fields studies on work and light exposure

2. Overview of Field studies on night work and salivary melatonin or urinary 6-sulfatoxymelatonin (aMT6s)

3. Overview of Field studies on job group and vitamin D levels

4. Questionnaire [In Danish]

5. Diary [In Danish]

Supplementary table 1 Field studies on work and light exposure

Reference	Population	Device	Latitude and time of the study	Results average light	Results time above thresholds
Indoor workers					
Koller et al. 1993	6 day guards working 6:00-18:00h 6 night guards working 18:00-6:00h	BPW21 Telefunken fixed on a spectacle frame	Vienna November-March 48 hours with night or day duty 48 hours off ork		Minutes above 500 lux:: Day guards Work days: 125 min Days off: 176 min Night guards Work days: 37 min Days off: 10 min Minutes above 1500 lux:: Day guards Work days: 52 min Days off: 89 min Night guards Work days: 13 min Days off: 3 min
Heil et al. 2002	11 employees of a cardiac pulmonary rehabilitation center working 8:00-17:00h	CSA monitor work on the wrist	Bozeman US 45°N September Mondag 12:00h-Friday 12:00h		Minutes above 1000 lux: 36 min
Aan het Rot 2006	30 day workers, who worked >30 hours/week	Acti-watch-L, mini mitter On the wrist	Montréal, Canada 45 °N Summer and winter 20 days measurements		Average minutes above 1000 lux Winter: 26 min (0.5-116) Summer: 91.2 min (19.5-296) Light levels were higher on weekends.
Hubalek et al. 2010	23 office workers Length of workday: 7-9 hours	Lux Blick Head mounted	Zurick , Switzerland, 47°N 3 weeks during April and June Only awake time	Median Illuminance (25^{th}-75^{th} percentile) All awakening hours 183 lux (118-249 lux) Time in office 308 lux (202-572 lux)	Median duration over: (25^{th}-75^{th} percentile) All awakening hours 100 lux : 534 min (436-626) 1000 lux : 105 min (61-187) 2500 lux : 43 min (16-92) Time in office: 100 lux : 240 min (204-283) 1000 lux : 16 min (2-48)

					2500 lux : 1 min (0-8)
Smolder et al. 2013	42 office workers and students (10 participated twice)	Daysimeter at eye level	Einhoven, Netherlands 51 ºN 3 consecutive days Device worn 8am-8pm October 2010-11 14 spring 10 summer 12 autumn 16 winter		Distribution of light levels across hours (from figure) < 50 lux: 33% 50-200 lux: 32% 200-500 lux: 19.5% 500 -1000 lux: 7% > 1000 lux: :8.5%
Boubekri et al. 2014	49 office workers working 8:00-17:00h 27 working in windowless environments 22 working in workplaces with daylight	Acti-watch-L, mini mitter On the wrist	Urbana Champaign, US 40 ºN 2 weeks Late spring and summer		Average Log lux/min Work days Mornings No windows; 2.38 Windows: 2.57 p= 0.32 Work hours No windows: 2.58 Windows: 3.00 p=0.02 Evenings No windows: 1.93 Windows: 2.50 p=0.008 Free days No windows: 2.37 Windows: 3.03 p=0.003
Figueiro et al. 2014	11 office workers, 8 who also participated in the summer Working 8:00-17:00h	Daysimeter worn as pendant	Grand Junction, Colorado US 39 ºN 7 days May-June	Works hours mean light : Winter: 72 lux Summer: 179 lux Work hours median light: Winter 74 lux Summer 122 lux Total out of bed hours mean: Winter 36 lux Summer 111 lux Median daytime lux winter 32 summer 112	

				Mean workday lux winter 83 summer 178 Median workday lux winter 76 summer 122 Mean post workday lux winter 24 summer 64 Median post workday lux winter 19 summer 74	
Crowley et al. 2014	14 office workers, 6 who also participated in the winter Work day start 8.30-10.30 h and end 16.30-18:00 h	Actiwatch Spectrum Phillips Respironics One around the neck and one wrist worn	Chicago, US, 41°N 7 days (24 h) The Actiwatch next to bed during sleep August-September and January-March		Mean minutes above 1000 lux Summer Workday 134 min Day off 160 min Winter: Workday 73 min Day off 82 min
Night workers					
Burch et al. 2005	71 day workers 62 evening workers 32 night workers Employed at the same factory doing 8 hour shifts	Acti-watch-L On the wrist	40 °N June-January 24 hours measurements	Time weighted average lux Day shift: 770±495 lux Evening shift 1338±1260 lux Night shift: 427±347 lux	
Borugian et al. 2005	5 day time health care officers 17 shift working nurses doing 12 hour shifts	Stowaway light data logger around the neck	Vancouver, Canada, 44°N Season not reported 7 days measurements	24 h average lux(range) Day workers Day off: 4.57 (1.62-26.30) Work day 2.63 (1.15-6.76) Shift workers Day off: 3.02 (0.09-14.79) Day work day: 2.29 (0.71-4.57) Night work day: 6.61 (0.79-28.84)	
Grundy et al. 2011	123 rotating night workers nurses	Stowaway light data logger around the neck On the night table during sleep	Kingston, Canada 44°N Across a year 48 hours with a day shift and 48 hours with a night shift	Log lux mean (SE) between 00:00-05:00h Day shift -2.14 (0.06) = 0-1 lux Night shift -0.06 (0.06) = 0.9 lux	
Dumont et al. 2012	13 rotating night workers Employed in a	Actiwatch L (Mini mitter) around the neck	Canada 44°N unknown season	Median light lux (SD) Work hours	

	telecommunication center		48 hours with a day shift and 48 hours with a night shift	Night shift 72.5 +/-54.9 Day/evening shift 64.7 +/-50.8 24 hours **log** lux Night shift 1.23 +/- 0.26 = Day/evening shift 1.13 +/-0.19
Papantoniou et al. 2014	42 Day workers 75 Night workers	Hobo ware at shoulder level	Barcelona, Spain 41ºN March-June 24 hours	Day workers mean 24 h: 1061 lux Mean during work hours: Hospital: 822 lux Car industry = 1342 lux Railway company: 1950 lux Night workers Mean 24h= 996 Mean during work hours = 60 lux Mean 00-05 h= 38 lux

Supplementary table 2 Field studies on night work and salivary melatonin or urinary 6-sulfatoxymelatonin (aMT6s),

Reference	Study Population	Outcome	Exposure	Results		
Studies without light measurements						
Jensen et al. 2017	Male police officers 73 rotating NW	Salivary melatonin collected every 4th hour during awakening hours.	Second, forth and seventh consecutive night shift	Numbers of consecutive night shifts	Highest melatonin concentration (pmol/L)	95% CI
				Second night shift	87.5	73.3; 104.5
				Fourth night shift	65.0	54.5; 77.5
				Seventh night shift	66.4	55.8; 79.0
				p-value	0.001	
				Decrease per night worked	4.9%	(1.4; 8.2)
Leung et al. 2016	Female hospital employees 114 rotating NW 147 DW	Urinary aMT5s Spot urine from all voids during 48-hours work period where NW had a day shift and a night shift	Night shift	Type of work and day	Adjusted mean % change in Mesor (circadian mean) from cosinor analyses	95% CI
				DW	ref	ref
				NW days with night shift	-25.0	-37.7; -9.8
				NW days with day shift	-7.0	-21.4; 0.74
				NW workers type of day	Geometric mean mesor (ng/mg)	95% CI
				Day rotation	15.2	13.7; 16.7
				Night rotation	13.6	11.3; 15.9
				p-value	<0.05	
Gomez-Acebo et. al 2014	Female health care workers and teachers 63 rotating NW 73 DW	Urinary aMT6s Spot urine from all voids during a 24-hours work day.	Second night shift	Mesor (circadian mean) from cosinor analyses (ng aMT6s/mg creatinine) between workers comparison. No statistical test of difference.		
				Day workers	88.79	
				Night workers	50.26	
Mirick et al. 2013	Male health care workers 185 permanent NW 158 DW	Urinary aMT6s Collected during: -Work -Leisure -Sleep (NW	Second night shift or more	Model	% difference	95% CI
				Between workers		
				NW day sleep relative to DW night sleep	-57.5	-66.1; -48.9
				NW night work relative to DW night sleep.	-62.0	-69.0; -55.0

		collected both during day time sleep after a shift and during the following nights sleep)		NW night sleep relative to DW night sleep.	-39.8	-50.5; -29.1
				With-in night workers		
				NW day sleep relative to NW night sleep.	-28.7	-44.5; 13.1
				NW night work relative to NW night sleep	-37.5	45.7; -29.2
Peplonska et al. 2012	Female nurses and midwifes 354 rotating NW 370 DW	Urinary aMT6s from a spot morning urine	Night shift		Adjusted mean morning MT6s (ng/mg Cr)	95% CI
				NW	47.2	42.9; 48.6
				DW	45.7	44.2; 50.2
				p-value	0.490	
Davis et al. 2012	Women working in health care 172 permanent NW 151 DW	Urinary aMT6s Collected during: -Work -Sleep (NW collected both during day time sleep after a shift and during the following nights sleep)	Second night shift or more	Model	% difference	95% CI
				Between workers		
				NW day sleep relative to DW night sleep	-62.5	-69.8; -55.1
				NW night sleep relative to DW night sleep.	-41.7	-53.1; -30.3
				NW night work relative to DW night sleep.	-68.6	-74.8; -62.5
				With-in night workers		
				NW day sleep relative to NW night sleep.	-37.5	-47.8; ??
				NW night work relative to NW night sleep	-47.3	-54.5; -40.0
Hansen 2006	Female nurses 50 NW with fixed night schedule 82 NW with mixed work schedule 27 DW 12 evening workers	Urinary aMT6s Spot urine from all voids on a workday and a day off	Night shift, on average the second consecutive night shift.	Results from mixed linear regression model		*p*-value
				Effect of working schedule (mixed/fixed) × shift (day/evening/night) × work day (yes/no)		0.01
				Between workers		
				Fixed and mixed NW compared to DW on work days		0.01
				Fixed NW compared to mixed NW		0.16
				Within night workers		
				DW workers work days compared to days off		NS
				Fixed and mixed NW work days compared to days off		0.001

Schernhammer 2004	Female nurses 80 rotatingNW	Urinary aMT6s Spot morning urine	1.4 and >4 night shifts within the last 2 weeks	Night shifts worked the last 2 weeks	aMT6s (ng/mL)	
				0	27	
				1-4	18	
				>4	12	
				Spearman correlation coefficient	-0.30	
				p-value	0.008	
Yamauchi 2004	Female nurses 9 rotating NW (3 pregnant)	Urinary aMT6s Spot urine from all voids during 24 hours days with day shift, night shift and days off.	Night shifts	Pregnant and non pregnant participants had lower aMT6s concentrations during work nights than other nights The aMT6s concentrations during daytime (07:00-23:00 h) did not differ between days with day work, night work and days off.		
Studies with light measurements						
Papantoniou et al. 2014	Male and female health care workers and employees at, a car manufacturer and a railway company 75 permanent NW 42 DW	Urinary aMT6s Urine samples from all voids during a 24-hour work day.	Night work Light measured at shoulder level. Mean light (lux) 22:00-07:00 h 00:00-05:00 h.	Mesor (circadian mean) from cosinor analyses: adjusted % difference (95% CI)		
				Type of work	Adjusted % difference	95% CI
				DW	Ref.	Ref
				NW	-33.8	(-48.4; -15.1)
				Mean light (lux) between 00:00- 05:00 h	Adjusted % difference	95% CI
				DW	Ref.	
				≤14 -30	-30.3	(-49.9; -3.1)
				15-40	-36.3	(-54.6; -10.7)
				41-315	-35.0	(53.0;-10.0)
				Mean light (lux) between 22:00- 07:00 h	Adjusted % difference	95% CI
				DW	Ref.	Ref
				<38	-27.3	(-47.8; 1.3)
				38-55	-35.3	(-53.1;10.8)
				55-246	-37.7	(-55.1; -13.6)
Dumont et al.	Female and male	Urinary aMT6s	Night shift	Measures of aMT6s	Day work days	Night work days *p*-value

2012	employees in telecommunication 13 rotating NW	All urine produced during -Work -Leisure -Sleep On a 24-hours night work day	Light measured from a necklace worn light logger.	Total 24-h excretion	15.568 ± 7879 ng	14.522 ± 4589 ng	0.47
				Averaged hourly excretion	641 ± 304 ng/h	559 ± 199 ng/h	0.14
				Association between median light during night work and aMT6s production during the night shift and the 24-h day with night work			
				Measures of aMT6s			*p*-value
				Total aMT6s (ng) excreted during work hours			>0.5
				Hourly aMT6s (ng/h) excreted during work hours			>0.5
				Total aMT6s (ng) excreted during 24-h			0.02
				Hourly aMT6s (ng/h) excreted during 24-h			0.01
Grundy et al. 2011	Female nurses 123 rotating NW	Salivary melatonin from -Awakening -Mid-shift -Before sleep -Awakening Urinary aMT6s from -Before sleep -Awakening Samples from a day work day and a night work day, summer and winter. .	Night shift (24-h day) Light measured from a necklace worn light logger.	Comparison of salivary melatonin and urinary aMT6s by time of day			
				Chronological time	*p*-value		
				3PM-5PM	0.99		
				11PM-1AM	0.84		
				5-7AM	0.004		
				Morning aMT6s	0.65		
				Change in aMT6s	0.80		
				Association between average light 00:00-05:00h and urinary aMT6s measures during days with day work and night work			
				Model	Regression coefficient		*p*-value
				Night work days			
				Peak aMT6	-0.04		0.07
				Change aMT6	-0.05		0.04
				Day work days			
				Peak aMT6	-0.08		0.47
				Change aMT6	0.04		0.75

Abbreviations: 6-sulfatoxymelatonin (aMT6s), 95% confidence interval (95% CI), Night workers (NW), Day workers (DW)

Supplementary table 3 Field studies on job group and vitamin D level

Reference	Study Population	Outcome	Exposure	Results 25OHD/PTH concentrations	Results Prevalence of vitamin D insufficiency	Results Comparison between job groups	Results UV exposure/time spent outdoors
Devgun et al. 1981	18 gardeners outdoor work 8 hospital indoor workers Dundee Scotland 56.30° N Blood sample each month throughout a year	25OHD competitive protein binding assay	Indoor work	Mean January-March Outdoor 43 nmol/L Indoor 33 nmol/ L Mean August-October Outdoor 80 nmol/ L Indoor 58 nmol/ L		Indoor workers had significantly lower vitamin D than outdoor workers	
Haney et al. 2004	32 Internal medicine residents Portland,USA 45°N	25OHD analyzed with Radio immune assay PTH analysed with chemiluminescent assay Prevalence 25OHD<50nmol	Rotating shifts Questionnaire obtained sunshine exposure	25OHD mean Fall 61.8-±20 nmol/L Spring 51.0 ±19nmol/L PTH Fall 4.55 ± 2.13 pmol/L Spring 5.28±1.97 pmol/L			Sunshine exposure predicted 25OHD concentration (p 0.015) I multivariable linear regression
Azizi et al. 2009	226 male and females 104 indoor workers 122 outdoor workers	25OHD analyzed with competitive protein binding assay	Outdoor work defined as more than 2 hours outdoor/day between 08:00-14:00h	Mean 25OHD Outdoor workers Winter 64.8±21.2 nmol/l Spring 61.5±19.8 nmol/l Summer 73.8±22.3 nmol/l Autumn 70.8±20.0 nmol/l Indoor workers Winter 51.0±19.8 nmol/l Spring 52.5±20.5 nmol/l Summer 65.8±20.5 nmol/l Autumn 61.3±19.3 nmol/l		25OHD were significantly higher among outdoor workers during all seasons	
Pazaitou-Panayiotou et al.2011	489 male and females 419 indoor workers 70 outdoor workers Greece 40 °N April/may	25OHD analyzed by immunoassay	Outdoor work (no definition)	25OHD mean Outdoor workers 58.7 ± 16.5nmol/L Indoor workers 50.1 ±16.7 nmol/L		t-test comparing indoor and outdoor workers p 0.0002 Pearson correlation between 25OHD and indoor/outdoor work	

Itoh et al. 2011a	14 male factory workers 6 day workers 4 day/evening 4 rotating night workers Japan 34.5°N July	25OHD analyzed by Radio immune assay	Rotating night work	Median (IQR) 25OHD Indoor day workers 65.0 (48.8-73.8) Day evening 65.0 (58.8-69.5) Rotating night workers 65.0 (58.8-69.5)	Indoor day workers 33.3% Day/evening 25.0% Rotating night workers 25.0%	No association of night shift and 25OHD levels	
Itoh et al. 2011b	4 male factory workers Japan 34.5°N 6 blood samples within 14 days in February and October	25OHD analyzed by Radio immune assay PTH analyzed by electrchemiluminescence immunoassay	Indoor day workers	Mean (SD) P25OHD nmol/L Feb: 44.3(6.9) Oct: 55.3(4.3) Mean PTH nmol/L Feb 4.78(1.48) Oct 3.50 (0.47)			
Ward et al. 2011	6154 employed Caucasians 382 with night work England 52°N All seasons	5OHD analyzed with ELISA	Permanent night works Selfreported time spent outdoors			Female night workers: -8% (-15.0: -2%) Male night workers no association	Suggestion of an association between night work and time spent outdoors, significant in univariate but not multivariate model
Growdon et al. 2012	102 male and female doctors with rotating shifts Boston, USA 42°N March	5OHD analyzed by Radio immune assay PTH analysed with chemiluminescent assay	Rotating shifts	Mean 25OHD 67±26 nmol/L Median PTH (IQR) 3.43 (2.64 ; 4.51) pmol/L	25%		
Wallington et al. 2013	83 Female nurses Canada 44°N Spring/winter and summer/autumn (62 participated both seasons)	25OHD analyzed with Radio immune assay	Rotating shifts Self reported hours spent outdoors 11:00.15:00 h	25OHD mean Summer 93.8 nmol/L Winter 42.2 nmol/L	Summer 9% Winter 13%		Outdoor hours not correlated with 25OHD
Kim et al. 2013	4.009 economically active subjects 18-50 years 20.9% worked other than daytime Korea 40°N	25OHD analyzed with Radio immune assay	Regular and irregular night work	Mean 25OHD Daytime 44.0 nmol/l Other than daytime 40.8 nmol/l Other than daytime includes rotating/permanent night workers and evening worker. Evening workers		Regular and irregular shift workers serum 25OHD levels were similar with those of daytime workers	

				had the lowest 25OHD			
Cinar et al. 2013	118 male and female office workers Turkey 39N August and February	25OHD analyzed with High liquid chromatography PTH analyzed with immunoradiometric assay	Indoor work Self reported exposure to sunlight	Mean 25OHD August: 71 nmol/l February: 34.5 nmol/l Mean PTH August: 3.5 pmol/l February: 5.3 pmol/l	August: 24.6% February: 83.9%		Selfreported sunlight exposure – not associated with vit D in winter or summer
Bodekær et al. 2014	44 Farmers working outdoor 44 Spouses working indoor Denmark 55°N October and February	25OHD analyzed with Liquid chromatography–mass spectrometry	Outdoor work UVR measured by UVR meter (Sunsaver)	End summer Farmers 67.2(17.4) nmol/l Spouses 68.3 (18.0) nmol/l Winter Farmers 44.0 (16.0) nmol/l Spouses 48.5 (20.0) nmol/l	All workers October: 16% February: 61%	No difference between spouses and farmers.	Farmers spend more time outdoors and had higher UVR than spouses on work days but on non work days there was no difference UVR measures with positive correlation with vitamin D in summer and winter.: Daily UVR dose, accumulated UVR dose, UVR dose on days off, beach days and sunscreen days
Romano et al. 2015	196 male factory workers 100 day workers 96 rotating shift workers Italy 45°N April	25OHD analyzed by immunoassay Prevalence 25OHD<50nmol	Rotating shift work	25OHD mean Day workers: 54.5 nmol/l Shift workers: 33.5 nmol/l	All workers 67%	Shift work significantly associated with – 17.8 nmol/L	
Munter et al. 2015	81 Physicians 43 hospital physicians (79% with night shifts) 38 community based (8% with night shifts) (44 DW 37 rotating NW) Israel 32°N, Winter	25OHD analyzed with chemiluminescent assay	Rotating shift works	Mean 25OHD With night shifts 37.0 nmol/l Without night shifts 48.3 nmol/l	Hospital 77% Community based 68%	Shift work significantly associated with lower 25OHD levels	

DAGBOG

LUX@R

Videnskabelig undersøgelse om arbejde og lys

Aarhus Universitetshospital

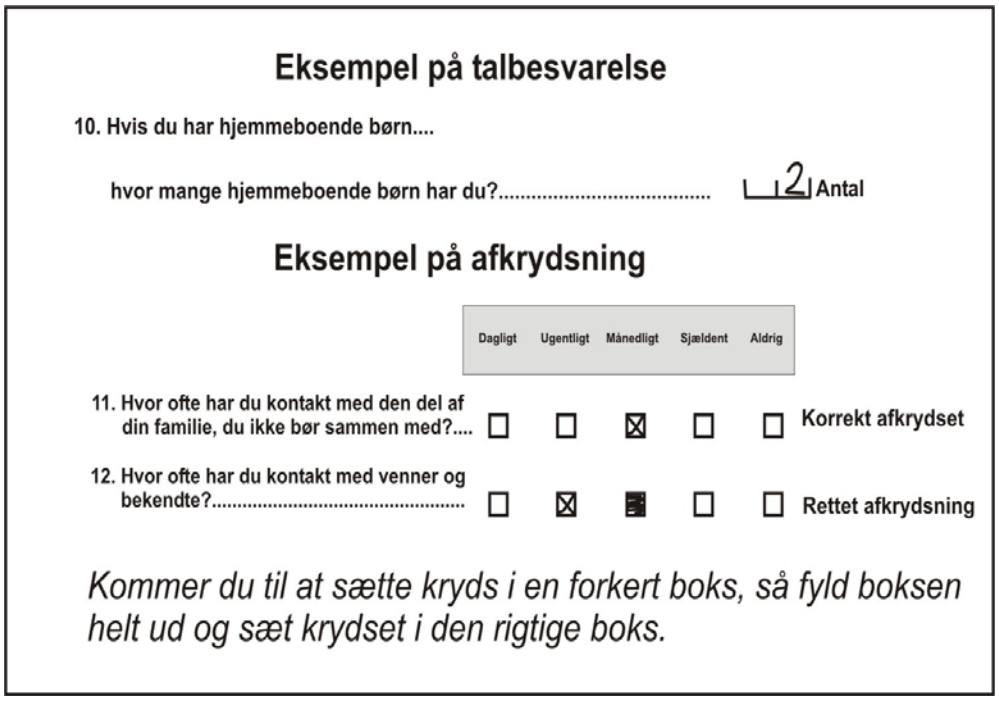
DET NATIONALE
FORSKNINGSCENTER FOR ARBEJDSMILJØ

Instruktion

Dagbogen skal udfyldes to gange dagligt: én gang efter opvågning og én gang før sengetid. Hvis du er natarbejder og sover om dagen, udfylder du dagbogen før og efter din søvn.

Du skal ikke bruge for lang tid på spørgsmålene, men give det svar, som først falder dig ind. Nogle af sprøgsmålene kan minde om hinanden, men de er ikke helt ens og de undersøger noget forskelligt.

Du bedes udfylde skemaet med kuglepen. Nedenfor ser du et eksempel på, hvordan forskellige sprøgsmål kan besvares.



Hvis du ønsker, at spørge om noget, mens du udfylder skemaet, kontakt venligst:

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8000 Aarhus C
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Anne Helene Garde
Det Nationale Forskningscenter
for Arbejdsmiljø
Lersø Parkallé 105
2100 København Ø
Tlf.: 3916 5258
E-mail: ahg@arbejdsmiljoforskning.dk
Mobil: 2253 4699

Overblik over undersøgelsens 7 dage

Bagerst i dagbogen finde du en vejlening i brugen af lysmåleren samt en vejledning til hvordan du taget spytprøver

	1. DØGN		2. DØGN		3. DØGN		4. DØGN		5. DØGN		6. DØGN		7. DØGN		8. DØGN	
LYSMÅLER																
Dagarbejde	Dag	Nat	Dag	Nat	Dag	Nat	Dag	Nat	Dag	Nat	Dag	Nat	Dag	Nat	Dag	Nat
Natarbejde	Vågen	Sover	Vågen	Sover	Vågen	Sover	Vågen	Sover	Vågen	Sover	Vågen	Sover	Vågen	Sover	Vågen	Sover
DAGBOG																
Overarm	X		X		X		X		X		X		X		X	
Håndled*																
Natbord*																
SPYTPRØVER																
	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng	Når du vågner	Når du går i seng
		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
*																

* Udfyldes i samarbejde med en projektmedarbejder

1. DØGN – Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ☐☐☐

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

2. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det <u>svært at falde i søvn</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du <u>uroligt</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du <u>for tidligt</u> uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det <u>let at stå op</u>? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor <u>udhvilet</u> er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

2. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ☐☐☐

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

3. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ___ ___ 20___

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ___ : ___

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ___

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ___ : ___

6. Var det <u>svært at falde i søvn</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du <u>uroligt</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du <u>for tidligt</u> uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det <u>let at stå op</u>? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor <u>udhvilet</u> er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

3. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ____ ____ 20__

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ____

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

4. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det <u>svært at falde i søvn</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du <u>uroligt</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du <u>for tidligt</u> uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det <u>let at stå op</u>? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor <u>udhvilet</u> er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

4. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ☐☐ : ☐☐ Dato (dag, måned) ☐☐ - ☐☐

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ☐☐☐

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

5. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det svært at falde i søvn? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du uroligt? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du for tidligt uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det let at stå op? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor udhvilet er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

5. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ____ ____ 20__

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ____

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

6. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det <u>svært at falde i søvn</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du <u>uroligt</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du <u>for tidligt</u> uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det <u>let at stå op</u>? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor <u>udhvilet</u> er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

6. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ___ ___ 20___

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ___ : ___ Dato (dag, måned) ___ - ___

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ___ : ___ Dato (dag, måned) ___ - ___

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ___

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

7. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det svært at falde i søvn? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du uroligt? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du for tidligt uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det let at stå op? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor udhvilet er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

7. DØGN - Udfyldes inden du lægger dig til at sove

1. Dato: (dag, måned, år) ____ ____ 20__

2. Har du været på arbejde i dag? *Sæt også X i "Ja", hvis du inden for det seneste døgn har været på nattevagt*

- ☐ Ja
- ☐ Nej, jeg har haft fri
- ☐ Nej, jeg har holdt egen sygedag
- ☐ Nej, jeg har holdt barnets sygedag

} **Gå til spørgsmål 6**

3. Hvornår startede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

4. Hvornår sluttede din arbejdsdag? *Skriv et tal i hver boks*

Klokken ____ : ____ Dato (dag, måned) ____ - ____

5. Har du været på nattevagt i nat? *Sæt kun ét X*

☐ Ja ☐ Nej **Hvis ja**, besvar nedenstående spørgsmål. **Hvis nej**, gå til spørgsmål 6.

Hvor lang tid sov du sammenlagt i løbet af nattevagten? Antal minutter ____

6. Har du drukket følgende indenfor de seneste 6 timer?

Sæt gerne flere X'er ☐ Ja, kaffe ☐ Ja, te ☐ Ja, cola ☐ Nej, ingen af delene

7. Har du benyttet lysterapilampe i dag?

Sæt kun ét X ☐ Ja ☐ Nej

8. Indenfor det seneste døgn, hvornår har du da i minimum 20 minutter:

Sæt gerne flere X i én linje, hvis du fx både har været udendørs og indendørs indenfor samme time

	Ikke haft lysmåler på	Været udendørs	Været indendørs	Anstrengt dig så meget fysisk, at du svedte og blev forpustet: På arbejde	I din fritid
Kl. 00 - 01	☐	☐	☐	☐	☐
Kl. 01 - 02	☐	☐	☐	☐	☐
Kl. 02 - 03	☐	☐	☐	☐	☐
Kl. 03 - 04	☐	☐	☐	☐	☐
Kl. 04 - 05	☐	☐	☐	☐	☐
Kl. 05 - 06	☐	☐	☐	☐	☐
Kl. 06 - 07	☐	☐	☐	☐	☐
Kl. 07 - 08	☐	☐	☐	☐	☐
Kl. 08 - 09	☐	☐	☐	☐	☐
Kl. 09 - 10	☐	☐	☐	☐	☐
Kl. 10 - 11	☐	☐	☐	☐	☐
Kl. 11 - 12	☐	☐	☐	☐	☐
Kl. 12 - 13	☐	☐	☐	☐	☐
Kl. 13 - 14	☐	☐	☐	☐	☐
Kl. 14 - 15	☐	☐	☐	☐	☐
Kl. 15 - 16	☐	☐	☐	☐	☐
Kl. 16 - 17	☐	☐	☐	☐	☐
Kl. 17 - 18	☐	☐	☐	☐	☐
Kl. 18 - 19	☐	☐	☐	☐	☐
Kl. 19 - 20	☐	☐	☐	☐	☐
Kl. 20 - 21	☐	☐	☐	☐	☐
Kl. 21 - 22	☐	☐	☐	☐	☐
Kl. 22 - 23	☐	☐	☐	☐	☐
Kl. 23 - 24	☐	☐	☐	☐	☐

8. DØGN - Udfyldes når du vågner

1. Dato: (dag, måned, år) ☐☐ ☐☐ 20☐☐

2. Hvor har lysmåleren været placeret, mens du sov? *Sæt ét X*

☐ På håndleddet ☐ Ved siden af sengen

3. Hvornår lagde du dig til at sove?

Skriv det klokkeslæt, hvor du lagde dig til at sove. Bemærk, at nogle personer går i seng før de ønsker at sove, fx. fordi de læser

Klokken ☐☐ : ☐☐

4. Hvor længe var du om at falde i søvn? *Skriv ét tal*

Minutter ☐☐☐

5. Hvornår vågnede du? *Skriv det klokkeslæt, hvor du vågnede*

Klokken ☐☐ : ☐☐

6. Var det <u>svært at falde i søvn</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

7. Sov du <u>uroligt</u>? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

8. Vågnede du <u>for tidligt</u> uden at kunne sove videre? *Sæt kun ét X*

☐ Slet ikke ☐ Meget lidt ☐ Noget ☐ Ganske meget ☐ Meget

9. Hvor mange gange vågnede du i løbet af natten? *Sæt kun ét X*

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 eller flere

10. Var det <u>let at stå op</u>? *Sæt kun ét X*

☐ Meget let ☐ Let ☐ Hverken let eller svært ☐ Svært ☐ Meget svært

11. Hvor <u>udhvilet</u> er du? *Sæt kun ét X*

☐ Helt ☐ Meget ☐ Ganske ☐ Lidt ☐ Slet ikke

12. Indtog du følgende umiddelbart inden du faldt i søvn? *Sæt kun ét X*

☐ Ja, sovemiddel ☐ Ja, alkohol ☐ Ja, smertestillende ☐ Nej, ingen af delene

13. Har du i løbet af natten/søvnen haft lyset tændt i samme rum som dig?
Sæt kun ét X

☐ Nej ☐ Ja

Instruktion til lysmåleren Actiwatch

Lysmåleren registrerer intensitet og spektralsammensætningen af det lys du udsættes for, dvs. den registrerer hvor svagt eller kraftigt lyset er samt indholdet af fx blåt eller rødt lys. Derudover registrerer lysmåleren også bevægelse, dvs. at den måler, hvornår du bevæger den arm, som lysmåleren sidder på. Det er ikke muligt at se, hvad du laver, men kun at du bevæger dig. Vi bruger det til at undersøge kvaliteten af din søvn.

Sådan bæres lysmåleren mens du er vågen:

- Lysmåleren bæres på **overarmen** af den dominante arm, dvs. hvis du er højrehåndet, skal du sætte den på højre arm.
- Måleren bæres på overarmen alle 7 dage mens du er vågen.
- Lysmåleren bæres uden på det tøj du har på. Det gælder også overtøj.
- Måleren kan holde til at komme med i bad i op til 30 minutter.

Undgå, at tildække måleren med tøj, hår eller lignende, da det således ikke er muligt at se, hvor meget lys du er blevet udsat for.

Sådan bæres lysmåleren mens du sover:

- Lysmåleren bæres som udgangspunkt på **håndleddet** mens du sover, for at kunne vurdere din søvnkvalitet. Du skal sætte den på din dominante arm, dvs. hvis du er højrehåndet, skal du sætte den på højre arm.
- To nætter skal lysmåleren dog ligge ved siden af dig på et natbord eller et sted ved siden af sengen. Disse to nætter aftales med en projektmedarbejder ved undersøgelsens opstart.
    - Hvis du er dagarbejder skal lysmåleren ligge på natbordet én nat op til en arbejdsdag og én nat op til en fredag. Dvs. to nætter i alt.
    - Hvis du er natarbejder skal måleren ligge på natbordet 1 gang i forbindelse med en nattevagt (dvs. hvor du sover om dagen), og 1 gang i forbindelse med, at du sover om natten.
- Når du vågner, registrerer du i dagbogen ud for det relevante spørgsmål, om lysmåleren har været på håndleddet eller på natbordet ved siden af dig.

Hvad betyder symbolerne på lysmålernes skærm?

I tabellen nedenfor kan du se betydningen af nogle af de vigtigste symboler som lysmålerens skærm kan vise. Hvis du er i tvivl om din lysmåler fungerer korrekt, så kontakt os da venligst via kontaktoplysningerne som du finder på bagsiden af denne dagbog.

Symbol:	Betydning:
	Uret indsamler data og har registreret kontakt med huden.
	Uret indsamler data, men viser ikke klokken, da det ikke kan registrere kontakt med huden.
	Uret har indsamlet data, og har nået det på forhånd programmerede stoptidspunkt.
	**Uret indsamler ikke data.** Kontakt os venligst på mobilnummer **2037 3718** (Århus) eller **2253 4699** (København).

Instruktion til spytprøverne

Det er ikke alle deltagere der skal tage spytprøver. Du vil blive informeret ved starten af undersøgelsen, hvis du er blevet udvalgt til at tage spytprøver.

Hvornår skal du tage spytprøverne?
Du har sammen med den projektmedarbejder, der udleverede undersøgelsesmateriale aftalt, hvilke dage du skal indsamle spytprøver.

Du skal tage max 14 prøver i alt. 7 på en arbejdsdag og 7 på en fridag.

Prøverne tager du:

- I din seng første gang du vågner uanset hvad klokken er. Det er derfor nødvendigt, at du har et rør og en etiket klar ved siden af din seng.
- Derefter tager du en prøve hver 4. time, så det ca. passer med tidspunkterne:
    - Kl. **07**, kl. **11**, kl. **15**, kl. **19**, kl. **23** og kl. **03**

  Spring det tidspunkt over, hvor du sover.
- Sidste gang du tager en prøve er når du lægger dig til at sove, uanset hvad klokken er.

Sådan tager du spytprøverne
Det tager højst fem minutter at tage en spytprøve. Du skal bruge et rør og en etiket til hver spytprøve. Du må **ikke spise ½ time** før prøvetagningen.

1. "Knæk" proppen af røret.
2. Fyld røret med ca. 1 ml spyt (til mærket) – det tager ca. to minutter. Lad det tynde spyt løbe ned i røret eller skub det ned i røret med tungen. Tænk på en citron, hvis du er tør i munden.
3. Udfyld etiketten og sæt den på røret.
4. Læg prøven i et køleskab eller en fryser, når du kan komme til det.

Du kan aflevere spytprøverne sammen med spørgeskemaerne og lysmåleren, når vi efter de 7 undersøgelsesdage kommer ud på din arbejdsplads igen.

LUX@R udføres i et samarbejde mellem Arbejdsmedicinsk Klinik ved Aarhus Universitetshospital, Det Nationale Forskningscenter for Arbejdsmiljø, Statens Byggeforskningsinstitut, VELUX A/S, Arbejds- og Miljømedicinsk Afdeling ved Bispebjerg Hospital samt Aarhus Universitetshospital, Risskov.

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Projektmobil: 2253 4699

SPØRGESKEMA

LUX@R

Videnskabelig undersøgelse om arbejde og lys

Aarhus Universitetshospital

DET NATIONALE
FORSKNINGSCENTER FOR ARBEJDSMILJØ

Instruktion

Du skal ikke bruge for lang tid på spørgsmålene men give det svar, som først falder dig ind. Nogle af spørgsmålene kan minde om hinanden, men de er ikke helt ens, og de undersøger noget forskelligt.

Bemærk - ikke alle spørgsmål skal besvares!
I spørgeskemaet vil der være nogle spørgsmål, som du måske ikke behøver at svare på. Læg derfor mærke til, når du henvises til at springe nogle spørgsmål over.

Du bedes udfylde skemaet med kuglepen. Nedenfor ser du et eksempel på, hvordan forskellige sprøgsmål kan besvares.

Eksempel på talbesvarelse

10. Hvis du har hjemmeboende børn....

hvor mange hjemmeboende børn har du?..... 2 **Antal**

Eksempel på afkrydsning

	Dagligt	Ugentligt	Månedligt	Sjældent	Aldrig	
11. Hvor ofte har du kontakt med den del af din familie, du ikke bør sammen med?....	☐	☐	☒	☐	☐	**Korrekt afkrydset**
12. Hvor ofte har du kontakt med venner og bekendte?.....	☐	☒	■	☐	☐	**Rettet afkrydsning**

Kommer du til at sætte kryds i en forkert boks, så fyld boksen helt ud og sæt krydset i den rigtige boks.

Hvis du ønsker at spørge om noget, mens du udfylder skemaet, kontakt venligst:

Helene Tilma Vistisen
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Aarhus Universitetshospital
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Mobil: 2253 4699

BAGGRUNDSOPLYSNINGER

De følgende spørgsmål handler om dine personlige baggrundsoplysninger

1. Jeg er ... ☐ Mand ☐ Kvinde

2. Hvilket år er du født? 19__

3. Hvis du er kvinde: Er du gravid? ☐ Ja ☐ Nej

ERHVERVSARBEJDE

De følgende spørgsmål handler om dit nuværende erhvervsarbejde og inkluderer også bibeskæftigelse men **ikke** frivilligt arbejde

4. Hvad er din nuværende stillingsbetegnelse ...

Skriv fx "sygeplejerske på børneafdeling" i stedet for blot "sygeplejerske" eller "montør for køkkenfirma" i stedet for blot "montør". *Skriv venligst med BLOKBOGSTAVER.*

4.A for din hovedbeskæftigelse? _____

4.B for dit bijob? _____

5. Hvilken arbejdstid har du sædvanligvis?

Sæt ét X

Fast dagarbejde (ca. mellem kl. 06 og 16)	☐
Fast aftenarbejde (ca. mellem kl. 15 og 24)	☐
Fast natarbejde (ca. mellem kl. 23 og 08)	☐
Skiftende arbejdstider som også inkluderer natarbejde	☐
Skiftende arbejdstider som ikke inkluderer natarbejde	☐

Hvis anden arbejdstid, skriv hvilken: _____

6. Hvor mange timer er du sædvanligvis indendørs om ugen i forbindelse med dit erhvervsarbejde?

Sæt ét X i hver linje

	0 timer/ uge	1-4 timer/ uge	5-9 timer/ uge	10-19 timer/ uge	20-29 timer/ uge	30-39 timer/ uge	Mere end 40 timer/ uge
Forår (mar., apr. og maj)	☐	☐	☐	☐	☐	☐	☐
Sommer (jun., jul. og aug.)	☐	☐	☐	☐	☐	☐	☐
Efterår (sep., okt. og nov.)	☐	☐	☐	☐	☐	☐	☐
Vinter (dec., jan. og feb.)	☐	☐	☐	☐	☐	☐	☐

7. Befinder du dig i bil eller andet lukket transportmiddel i forbindelse med dit erhvervsarbejde? *Sæt ét X*

Nej ☐ **Gå til spørgsmål 9**

Ja ☐ Hvilket transportmiddel _____

8. Hvor mange timer befinder du dig sædvanligvis i bil eller andet lukket transportmiddel i forbindelse med dit arbejde?

Sæt ét X i hver linje

	0 timer/ uge	1-4 timer/ uge	5-9 timer/ uge	10-19 timer/ uge	20-29 timer/ uge	30-39 timer/ uge	Mere end 40 timer/ uge
Forår (mar., apr. og maj)	☐	☐	☐	☐	☐	☐	☐
Sommer (jun., jul. og aug.)	☐	☐	☐	☐	☐	☐	☐
Efterår (sep., okt. og nov.)	☐	☐	☐	☐	☐	☐	☐
Vinter (dec., jan. og feb.)	☐	☐	☐	☐	☐	☐	☐

9. Arbejder du på noget tidspunkt udendørs i forbindelse med dit erhvervsarbejde?

Sæt ét X

Nej ☐ **Gå til spørgsmål 11**

Ja ☐

10. Hvor mange timer er du sædvanligvis udendørs om ugen i forbindelse med dit erhvervsarbejde?

Sæt ét X i hver linje

	0 timer/ uge	1-4 timer/ uge	5-9 timer/ uge	10-19 timer/ uge	20-29 timer/ uge	30-39 timer/ uge	Mere end 40 timer/ uge
Forår (mar., apr. og maj)	☐	☐	☐	☐	☐	☐	☐
Sommer (jun., jul. og aug.)	☐	☐	☐	☐	☐	☐	☐
Efterår (sep., okt. og nov.)	☐	☐	☐	☐	☐	☐	☐
Vinter (dec., jan. og feb.)	☐	☐	☐	☐	☐	☐	☐

11. Hvad er din gennemsnitlige ugentlige arbejdstid?

Skriv antal timer

Hovedbeskæftigelse ___ timer/uge

Bijob ___ timer/uge

12. Hvor fysisk anstrengende er dit arbejde sædvanligvis?

Sæt ét X

Det er mest stillesidende arbejde, som ikke kræver fysisk anstrengelse	☐
Det er mest stående eller gående arbejde, som ikke kræver fysisk anstrengelse	☐
Det er stående eller gående arbejde med en del løfte- eller bærearbejde	☐
Det er tungt eller hurtigt arbejde, som er fysisk anstrengende	☐

De følgende spørgsmål handler om det erhvervsarbejde, du har haft gennem hele dit liv, og inkluderer også bibeskæftigelse men **ikke** frivilligt arbejde

13. Hvor mange år har du sammenlagt haft erhvervsarbejde?

|__|__| år

14. Hvor lang tid har du sammenlagt arbejdet indenfor de forskellige <u>arbejdstider</u> i hele dit arbejdsliv?

Skriv ét tal i hver linje

	År	Mdr.
Fast dagarbejde (ca. mellem kl. 06 og 16)	|__|__|	|__|__|
Fast aftenarbejde (ca. mellem kl. 15 og 24)	|__|__|	|__|__|
Fast natarbejde (ca. mellem kl. 23 og 08)	|__|__|	|__|__|
Skiftende arbejdstider som også inkluderer natarbejde	|__|__|	|__|__|
Skiftende arbejdstider som ikke inkluderer natarbejde	|__|__|	|__|__|
Andet _____	|__|__|	|__|__|

15. Hvor mange år har du sammenlagt haft erhvervsarbejde, hvor du har arbejdet <u>udendørs</u> mindst 5 timer om ugen i gennemsnit?

|__|__| år

HELBRED OG LIVSSTIL

De følgende spørgsmål handler om dit helbred og din livsstil

16. Hvor høj er du, og hvor meget vejer du?

Skriv et tal i hver boks

Hvor høj er du (uden sko)? ___ cm

Hvad vejer du (uden tøj)? ___ kg

17. Tager du på nuværende tidspunkt medicin?

Sæt ét X

- ☐ Nej
- ☐ Ja, sovemedicin
- ☐ Ja, melatonin
- ☐ Ja, medicin mod depression

Hvis anden medicin, skriv hvilken: _____

_____

18. Tager du dagligt en multivitamintablet?

Sæt ét X

☐ Nej ☐ Ja

Hvis ja, hvad hedder tabletten? _____

19. Tager du dagligt tilskud af D-vitamin?

Sæt ét X

☐ Nej ☐ Ja, 1 tablet ☐ Ja, 2 tabletter ☐ Ja, 3 eller flere tabletter

Hvis ja, hvad hedder tabletten? _____

20. Tager du tilskud af levertran?

Sæt ét X

☐ Nej ☐ Ja

21. Hvor ofte spiser du i gennemsnit fisk eller skaldyr?

Sæt ét X

Aldrig	1-3 gange pr. måned	1 gang om ugen	2-3 gange om ugen	4-6 gange om ugen	Dagligt
☐	☐	☐	☐	☐	☐

22. Hvor ofte går du i solarium?

Sæt ét X

☐ Flere gange/uge ☐ Ca. 1 gang/uge ☐ Ca. 1 gang/måned ☐ Få gange om året ☐ Aldrig

23. Ryger du?

Sæt ét X

Ja ☐

Nej, men jeg har røget ☐

Nej, jeg har aldrig røget ☐

Hvis du ryger eller har røget, besvar nedenstående spørgsmål. Hvis du aldrig har røget, gå til spørgsmål 23.

I hvor mange år har du røget?

☐☐ år

24. Hvor meget ryger/røg du om dagen i gennemsnit?

Skriv et tal i hver boks

Antal cigaretter pr. dag ☐☐

Antal cerutter pr. dag ☐☐

Antal pibestop pr. dag ☐☐

25. I løbet af de sidste 4 uger hvor meget har du været genereret af ...

Sæt ét X i hver linje

	Slet ikke	Lidt	Noget	En hel del	Virkelig meget
at føle dig nedtrykt?	☐	☐	☐	☐	☐
en følelse af ingenting af være værd?	☐	☐	☐	☐	☐
tanker om at gøre en ende på dit liv?	☐	☐	☐	☐	☐
en følelse af at være fanget i en fælde?	☐	☐	☐	☐	☐
at føle dig ensom?	☐	☐	☐	☐	☐
selvbebrejdelser?	☐	☐	☐	☐	☐
at føle dig træt?	☐	☐	☐	☐	☐
at føle dig udkørt?	☐	☐	☐	☐	☐

26. Hvordan kommer du sædvanligvis til og fra arbejde?

Sæt ét X ud for hver årstid, som viser, hvordan du sædvanligvis kommer på arbejde.
Sæt ét kryds i hver linje

	Bil	Bus	Tog	Cykel	Gående	Andet
Forår (mar., apr. og maj)	☐	☐	☐	☐	☐	☐
Sommer (jun., jul. og aug.)	☐	☐	☐	☐	☐	☐
Efterår (sep., okt. og nov.)	☐	☐	☐	☐	☐	☐
Vinter (dec., jan. og feb.)	☐	☐	☐	☐	☐	☐

Hvis andet, skriv: _____

27. Hvor meget tid har du i gennemsnit brugt på hver af følgende fritidsaktiviteter i det sidste år?

Medregn også transport til og fra arbejde.
Sæt ét kryds i hver linje

	Over 4 timer/ uge	2-4 timer/ uge	Under 2 timer/ uge	Dyrker ikke denne fritidsaktivitet
Gang, cykling eller anden lettere motion, hvor du ikke bliver forpustet eller sveder	☐	☐	☐	☐
Motionsidræt, tungt havearbejde eller hurtig gang/cykling, hvor du sveder og bliver forpustet	☐	☐	☐	☐
Hård træning eller konkurrenceidræt	☐	☐	☐	☐

SØVN

Spørgsmålene i dette afsnit handler om dit søvnmønster

28. I løbet af de sidste 4 uger, hvor ofte ...

Sæt ét X ud for hvert spørgsmål

	Aldrig	Sjældent	En gang imellem	For det meste	Altid
har du haft svært ved at falde i søvn?	☐	☐	☐	☐	☐
har du haft svært ved at vågne?	☐	☐	☐	☐	☐
er du vågnet for tidligt uden at kunne falde i søvn igen?	☐	☐	☐	☐	☐
har du følt, at du ikke var udhvilet, når du vågnede?	☐	☐	☐	☐	☐
er du vågnet flere gange og har haft svært ved at falde i søvn igen?	☐	☐	☐	☐	☐
har du sovet dårligt og uroligt?	☐	☐	☐	☐	☐
har du følt dig udmattet ved opvågning?	☐	☐	☐	☐	☐

29. Hvis du skal beskrive dig selv som morgenmenneske eller aftenmenneske, hvad er du så?

Sæt ét X

Helt sikkert morgenmenneske	☐
Mere morgenmenneske end aftenmenneske	☐
Mere aftenmenneske end morgenmenneske	☐
Helt sikkert aftenmenneske	☐

30. Er du interesseret i at høre nærmere om eventuelt andre projekter omkring lysmiljøet, fx sammenhængen mellem lysmiljø og knogleskørhed?

Sæt ét X

☐ Nej ☐ Ja

HAR DU KOMMENTARER TIL SPØRGESKEMAET:

_____

_____

_____

_____

_____

_____

_____

_____

Tak fordi du tog dig tid til at udfylde spørgeskemaet!

LUX@R udføres i et samarbejde mellem Arbejdsmedicinsk Klinik ved Aarhus Universitetshospital, Det Nationale Forskningscenter for Arbejdsmiljø, Statens Byggeforskningsinstitut, VELUX A/S, Arbejds- og Miljømedicinsk Afdeling ved Bispebjerg Hospital samt Aarhus Universitetshospital, Risskov.

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Projektmobil: 2253 4699

Paper I

Light exposure during days with night, outdoor and indoor work

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Jakob Markvart

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Helene Tilma Vistisen

Henrik Kolstad

Abstract

Objective: To assess exposure to diurnal and seasonal light during days with night, outdoor, and indoor work and days off work to increase knowledge of light exposure to be used in studies of effects of light exposure on human health and well-being

Methods: Light intensity was continuously recorded for seven days across the year among indoor (n=170), outdoor (n=151) and night workers (n=188) equipped with a personal light recorder. Average light intensity and time spent above 80, 1,000 and 2,500 lux were depicted and computed for six-hour intervals on work days and days off work during summer and winter.

Results: Indoor and night workers' exposure to mean light intensity only intermittently exceeded 1,000 lux during standard working hours in the summer and never in the winter. Contrary to this, outdoor workers exceeded 2,500 lux during standard working hours in the summer and 1,000 lux without reaching 2,500 lux in the winter. Night workers spent on average 13-14 minutes above 80 lux during night work, which were about eight times as long as indoor workers. During days off work, indoor and night workers were more exposed to light than during work days, but only marginal differences were seen between indoor, outdoor and night workers.

Conclusion: The night workers of this study were only exposed to light intensities above 80 lux expected to suppress melatonin for a few minutes during night time. The indoor and night workers' exposure to light during day time at work days was at a level that may reduce general well-being and mood, especially during the winter. Outdoor workers were exposed to anti-depressive levels of light exposure during the summer.

Introduction

Currently, the population in industrialized countries spend 90% of their life inside (Klepeis et al., 2001; Schweizer et al., 2007), where light intensities are often lower during the day and higher during the night compared to outdoors.

During indoor work during the daytime, average light intensities between 120 and 300 lux have been reported in the summer and about 80 lux in the winter (Figueiro & Rea, 2014; Hubalek et al., 2010). Office workers, nurses and other indoor workers were exposed to light intensities above 1,000 lux for around 15 min. during working hours in the summer (Heil & Mathis, 2002; Hubalek et al., 2010). During entire work days including hours before and after work, indoor workers were exposed to light above 1,000 lux between 36 and 150 min. in the summer and between 26 and 73 min. in the winter (Crowley et al., 2015; Heil & Mathis, 2002; Hubalek et al., 2010; Koller et al., 1993; Savides et al., 1986).

During night work, average light intensities between 43 and 73 lux have been reported (Dumont et al. , 2012; Papantoniou et al., 2014). During 24-hour where participants did a night shift, average light intensities between 427 and 996 lux have been reported (Burch et al., 2005; Papantoniou et al., 2014). Koller et al. observed that night workers spent 13 min. above 1500 lux during a 24-hour day, with a night shift, during the winter (Koller et al., 1993).

Ultraviolet radiation (UVR) exposure has been extensively studied in outdoor workers (Bodekær et al., 2014; Boniol et al., 2015; Gies & Wright, 2003; Schmalwieser et al.,

2010; Serrano et al., 2013; Thieden et al., 2004; Wolska, 2013). To our knowledge, there are no studies of visible light exposure of outdoor workers.

Light exposure has constantly been reported higher on days off than on work days among indoor workers (aan het Rot et al., 2008; Borugian et al., 2005; Crowley et al., 2015; Hubalek et al., 2010; Koller et al., 1993). During days off, people have been reported to be exposed to light intensities above 1,000 lux for 160-200 min. in the summer (Crowley et al., 2015; Hubalek et al., 2010) and 82-89 min. in the winter (Crowley et al., 2015; Koller et al., 1993).

General well-being, mood, vitality, and learning ability have been associated with increasing light intensities and duration of exposure to bright light (Espiritu et al., 1994; Figueiro & Rea, 2014; Hahn et al., 2011; Hubalek et al., 2010; Marqueze et al., 2015). Depression and seasonal affective disorder (SAD) respond to 60-120 min. light therapy above 2,500 lux applied in the morning (Tuunainen et al., 2004; Wirz-Justice et al., 1996). A cut off of 1,000 lux has been used as an indicator of exposure to outdoor daylight (Figueiro et al., 2017), e.g. in studies on alertness, arousal, sleep, performance, vitality, mood, and EEG activity (aan het Rot et al., 2008; Espiritu et al., 1994; Kaida et al., 2006). Light intensities above a threshold of 80-100 lux during evening and night have been shown to suppress melatonin production (Figueiro et al., 2006a; Figueiro et al., 2006b; Revell & Skene, 2007a; Zeitzer et al., 2000), affect circadian rhythm (Shanahan et al., 1997), and increase alertness (Cajochen et al., 2000).

Our aim was to assess exposure to diurnal and seasonal light during days with night, outdoor, and indoor work and days off work to increase knowledge of light exposure to be used in studies of effects of light exposure on human health and well-being.

Materials and methods

Study setup

Participants (N=535) were recruited through employers, advertisements in magazines and on web-pages with the aim to recruit equal numbers of indoor day, outdoor day, and night workers. Participants were followed for seven consecutive days. They completed a questionnaire on background characteristics. Light intensities were continuously recorded during all seven days with a light recorder and accompanied by a diary. The data collection was carried out from March 2012 until May 2013. All participants gave written informed consent and the study was approved by the Danish Data Protection Agency (J.nr. 2011-41-6850) and the Central Denmark Region Committee on Health Research (M-20110214) in Denmark.

Participants

We defined a day with ≥120 minutes (min.) work between 00:00 and 05:00 a.m. as a night work day and a day with ≥120 min. of outdoor work as an outdoor work day according to the diary information (mean time reported outdoors was 6 hrs. 5 min. (SD 2 hrs. 18 min.) in the summer, and 4 hrs. 31 min. (SD 2 hrs. 1 min.) in the winter). Work days, not fulfilling these criteria, were classified as indoor work days (mean time reported outdoors was 43 min. (SD 24 min.) in the summer and 44 min. (SD 22 min.) in the winter). Days with no recorded work were classified as days off work. Workers were classified into three job groups: Workers with ≥1 night work day were classified as *night workers*, workers with no night work days and ≥1 outdoor work day as *outdoor workers* and workers with no night or outdoor work days as *indoor workers*. Twenty-five participants with incomplete diary information to

classify workdays as indoor, outdoor or night were excluded. The final study population comprised 509 participants (170 indoor workers, 151 outdoor workers, 188 night workers). A total of 484 participants provided valid (see below) light measurements from workdays and 485 from days off (Table 1).

Light measurements from 504 participants were included for analyses of time spent above three light intensities according to criteria described below. Women comprised 72.2% of the population and the mean age of all participants was 42.2 years. Indoor workers included teachers, hospital employees, child care worker, factory workers, mechanics, gardeners, residential social workers, craftsmen, and work environment inspectors. Outdoor workers included child care worker, gardeners, craftsmen, teachers, work environment inspectors, physiotherapists, and residential social workers. Night workers included hospital employees, factory workers, and residential social workers.

We only included indoor work days for indoor workers, outdoor work days for outdoor workers, night work days for night workers; all days off work were included (Table 1).

Questionnaire and diary

At study start, participants filled in a questionnaire that included information on occupation. In a diary, participants recorded bedtime, time of waking up, and working hours during the study period. For each hour of the day, participants reported if the light recorder was not worn for more than 20 min. and if more than 20 min. were spent outdoors.

Light assessment

The seven-day study period started at different days of the week and at different times of the day depending on participants' work schedules. Participants were instructed to wear a Philips Respironics Actiwatch Spectrum (Actiwatch) outside clothes on the upper arm during all hours awake except during showers and swimming. While sleeping, the Actiwatch should be kept next to the bed with the front pointing upwards. Light and actigraphy (movement counts) were recorded with 1 minute epochs. The Actiwatch sensor measures light in the red, blue, and green wavelength bands. The white light (lux) output is derived from the light received by these three bands.

All Actiwatches were calibrated using a side-by-side calibration method as described by Markvart et al. (Markvart et al., 2015) . The white light output was calibrated under overcast sky conditions against a cosine corrected photometer with a spectral sensitivity that closely relates to the luminosity function V (λ) established by the Commission Internationale de l'Éclairage (CIE). The calibrated white light output will in this study be referred to as light.

In total, 4,222,732 min. of light measurements were collected from days off and days with indoor, outdoor, and night work. Measurements from workers without information on job group (outdoor, indoor, night work) were omitted (286,703). Likewise, data were omitted when the Actiwatch was reported to be worn on the wrist during sleep (1,007,316 min), not worn when awake (212,081 min), and if no physical activity was recorded for 20 min. by actigraphy (209,997 min). In total, 2,506,635

min. corresponding to 41,777 hours with light measurements from 2,638 days were used for analyses of mean light intensity. On average 15 hrs. and 45 min. of light measurements were available per day. Data were also analyzed according to minutes spent above three light intensities: 80, 1,000 and 2,500 lux. For these analyses we required ≥ 90% valid light measurements within four six-hour intervals according to criteria specified later. In total, 1,573,729 min. of light measurements from 4,461 six-hour intervals, and 2,290 days were included for 504 workers.

Statistical analysis

To depict individual light exposure across the day we smoothed the graphs by a moving window equal to the mean of each worker's light intensities of the last 20 min. The arithmetic means of these smoothed light intensities were plotted for indoor, outdoor and night workers by time of the day on work days, days off and all days and stratified by season.

Data were also (not being averaged) presented as arithmetic means, medians, 10th percentiles, and 90th percentiles computed across six-hour intervals (00:00-05:59h (night), 06:00-11:59 (morning), 12:00-17:59 (afternoon) and 18:00-23.59 (evening). We presented these results separately for work days and days off and stratified by season (summer, winter as defined by standard time and daylight saving time) as these are significant predictors of light exposure caused by the rotation of earth.

Within each of the strata, we also tabulated median minutes and interquartile ranges (IQR) spent above 80, 1,000 and 2,500 lux to represent thresholds for melatonin suppression and induction of alertness (Cajochen et al., 2000; Zeitzer et al., 2000),

outdoor vs. indoor stay during daytime (aan het Rot et al., 2008; Crowley et al., 2015; Figueiro et al., 2017; Heil & Mathis, 2002; Hubalek et al., 2010; Partonen & Lonnqvist, 2000; Smolders et al., 2013), and light therapy for depression (Tuunainen et al., 2004).

To investigate the lower limit of detection (LOD), the Actiwatches were placed in complete darkness for four eight-hour sessions. The highest measured intensity was 1.20 lux, corresponding to light intensities between 0 and 1.20 lux. We used the exact value of all measurements instead of assigning new values to measurements below a certain LOD criteria to keep as much exposure information as possible in the data (Whitcomb & Schisterman, 2008). Light measurements with 0.000 lux were replaced by 0.001 lux (1.0 % of all light measurements included in analyses) and six-hour intervals with 0 min. above the thresholds were replaced by 1 min. before log transformation (1.0 % of six-hour intervals).

Light intensities and time spent above the thresholds showed right skewed distributions and were log transformed prior to further statistical analyses. They were analysed with multivariate linear regression to estimate differences between night, outdoor and indoor workers with the latter as the reference. Analyses of light intensities were adjusted for hour of sampling within the four six-hour intervals. Analyses were carried out using a mixed procedure with an autoregressive structure. Participants were entered as an independent random variable because each participant was measured multiple times. All analyses were carried out using STATA 13.0 (StataCorp, College Station, Texas).

Results

Figure 1 depicts the smoothed arithmetic mean light intensities for indoor, outdoor and night workers across the day on work days, days off and stratified by summer and winter. On summer workdays, the smoothened mean light intensities for outdoor workers reached a maximum of 6,000 lux around noon, which was about four times the maximum mean intensity reached by indoor and night workers. On summer workdays, outdoor workers' mean light intensity exceeded 2,500 lux during standard work hours (from 08:00 to 15:00); this was only intermittently seen for indoor and night workers, who first exceeded this level from 15:00 h to 18:00. On summer days off work, outdoor workers were exposed to slightly higher light intensities than night and indoor workers in the morning reaching a maximum of 5,000 lux. All three job groups peaked between 12:00-16:00 and showed mean light intensities exceeding 2,500 lux from 12:00 until about 18:00.

On winter work days, mean light intensities during the day were also higher among outdoor compared with indoor and night workers and exceeded 1,000 lux from about 10:00 until about 15:00 but only briefly exceeded 2,500 lux. Indoor and night workers' exposure to light intensities showed no noticeable peaks and never exceeded 1,000 lux.

At winter days off, outdoor workers' mean light intensities were lower than on workdays, while indoor and night workers showed higher light intensities than on work days.

Table 2 presents six-hour interval light intensities. On work days, outdoor workers' arithmetic mean light intensity was above 4,000 lux during summer afternoons (12:00-17:59) and above 1,000 lux during winter. During night work (00:00-05:59), mean light intensities were between 25 and 38 lux during summer and winter; this was 2-10 times the intensities recorded in outdoor and indoor workers and during days off. On days off, few differences were observed, outdoor workers were exposed to lower mean light intensities than indoor workers in summer evenings (18:00- 23:59h), and light intensities during winter nights differed, although all light intensities were low.

Tables 3, 4 and 5 show time (min.) spent above 80, 1,000, and 2,500 lux (median and interquartile range (IQR)) for indoor, outdoor and night workers across the day and during summer and winter for work days and days off.

Outdoor workers spent on average eight times (846%) longer time above 2,500 lux between 06:00-12:00 in the summer and four times (436%) longer in the winter compared with indoor workers. Outdoor workers' median time spent above 1,000 lux between 06:00-11:59 was 124 min. (IQR: 68-209) in the summer and 47 min. (IQR: 27-85) in the winter (Table 4). Indoor workers' corresponding median time was 22 min. (IQR: 7-42) in the summer and 2 min. (IQR: 0-13) in the winter. On days off, outdoor workers spent on average 127 % longer time above 2,500 lux during summer mornings (06:00-12:00) and 15.3% shorter time above 80 lux during summer afternoons. Otherwise, outdoor workers experienced light exposure similar to indoor workers on days off, regardless of season.

Night workers' exposure to light above 80 lux on workdays was on average up to 847 % longer than indoor workers during the night (00:00-06:00). Night workers' median time spent above 80 lux between 00:00-06:00 was 14 min. (IQR: 4-33) in the summer and 13 min. (IQR: 2-25) in the winter. This was about eight times more than indoor workers (773% in summer and 847% in winter). Night workers had up to 59.3 % less exposure to light above 1,000 and 2,500 lux during day time on workdays. On days off, night workers spent 35.3 % and 43.1 % less time than indoor workers above 80 lux in the morning, and 47.0 % and 39.7% less time in the evenings. Otherwise, light exposure did not differ significantly from indoor workers.

Discussion

Indoor and night workers' mean exposure to light only intermittently exceeded 1000 lux during standard working hours in the summer and never in the winter. Contrary to this, outdoor workers exceeded 2,500 lux during standard working hours in the summer and 1,000 lux in the winter, but without reaching 2,500 lux. Compared with indoor workers, outdoor workers spent seven times longer time above 2,500 lux in the summer and three times longer time above 1,000 lux in the winter. Night workers on average spent 13-14 minutes above 80 lux during night work, which was about eight times longer than indoor workers. During days off, indoor and night workers were exposed to more light than during work days, but only marginal differences were seen between indoor, outdoor and night workers.

The time indoor workers spent above 1,000 lux was comparable to results from previous field studies (aan het Rot et al., 2008; Crowley et al., 2015; Hubalek et al., 2010; Smolders et al., 2013) except Heil et al. (Heil & Mathis, 2002) who reported a shorter duration of only 36 min. during a 24-hour day in September.

There is limited data on light exposure during outdoor work, but higher exposure to UVR has been reported compared with indoor workers (Azizi et al., 2009; Bodekær et al., 2014). It was not surprising that we observed light intensities were higher among outdoor workers compared to indoor workers on work days. In particular, we expected to see differences during the winter, where a short photo-period in the Northern hemisphere leaves very few hours of daylight for indoor workers to spend outdoors outside standard work hours.

In agreement with previous studies, night workers in our study were exposed to higher light intensity during days with night work than day workers (Grundy et al., 2011; Papantoniou et al., 2014). During daytime, night workers spent shorter time above all three thresholds than indoor workers during daytime in agreement with most previous studies (Burch et al., 2005; Koller et al., 1993; Papantoniou et al., 2014), except (Borugian et al., 2005; Dumont et al., 2012). These discrepancies could be attributed to different length of work days, as 12-hour shifts (Borugian et al., 2005) allow more time to spend outdoors compared to 8-hour shifts, which was most common in our sample.

In our study, indoor and in particular night workers were exposed substantially longer to light intensities above 1,000 lux and 2,500 lux on days off compared to work days, in line with other studies on indoor workers (aan het Rot et al., 2008; Crowley et al., 2015; Koller et al., 1993), but not night workers (Borugian et al., 2005; Koller et al., 1993).

Laboratory studies with polychromatic light have found melatonin suppression (Rea et al., 2005; Revell & Skene, 2007b; Zeitzer et al., 2000) and alerting effects of light at night (Cajochen et al., 2000) beginning at 80-100 lux. Night workers were during work nights on average exposed for 13-14 min. above 80 lux, and in general most of the time light intensities were too low to induce melatonin suppression and exert alerting effects.

The relatively short exposure to light above 1,000 lux we observed among indoor and night workers, especially during winter work days may affect general well-being,

mood, vitality, and learning abilities. Aan het Rot et al. found that exposure to light above 1000 lux for more than 19.6 min. was associated with better mood, less quarrelsome and more agreeable behavior (aan het Rot et al., 2008). However, no association between duration of exposure to light above 1,000 lux and mood has also been reported (Hubalek et al., 2010). Some types of depression can be treated by exposure to 2,500 lux for two hours in the morning (Tuunainen et al., 2004), and a one hour outdoor morning walk can improve SAD symptoms (Wirz-Justice et al., 1996). In the winter, few participants in our study reached this exposure intensity, but even in the summer it was only among outdoor workers that more than half of the participants spent an hour above 1,000 lux in the morning on workdays. In the winter, night workers were almost never exposed to light above 1,000 lux on work days even if they were not at work when the sun is up, and therefore, in principle, have the possibility to go outside.

Strengths and limitations

Participants noted time of work and sleep every day, and this information is not very prone to recall bias. We used diary and actigraphy data to ensure that light measurements represented personal light exposure, because participants were not observed during the study period. Light measurements were calibrated to account for variation between the Actiwatches (Markvart et al., 2015). We included subjects of both sexes from a range of different occupations within the three job groups. Furthermore, light measurements were carried out on both work days and days off across all seasons, possibly affecting total light exposure. To our knowledge, this study is the largest field study of this kind to date.

Light measurements were conducted by Actiwatches placed at the upper arm and do not represent retinal light exposure accurately (Figueiroet al., 2013). Intensities are shown to be lower when measured at the wrist than at the eye (Figueiro et al., 2013), and therefore a discrete placement of the device on the upper arm was preferred. However Aarts et al (Aarts et al., 2017) investigated the performance of personally worn light exposure measurement equipment where they summarized that the placement of these instruments has an impact on the results. Although, the subjects in this study used a measurement device not directly comparable to the recommended position at eye-level, it was placed in viewing direction and is still reasonably accurate when referring to light exposure of indoor, outdoor and night workers. Moreover, light measurements depend on arm movements and positions, and the measured light may differ from actual light intensities during certain light conditions because of the mismatch between the spatial and spectral sensitivity of the Actiwatch towards a standard classified illuminance sensor (Figueiro et al., 2013; Price et al., 2012). Light exposure was therefore subject to some misclassification of unknown direction.

Conclusion

The night workers of this study were only exposed to light intensities above 80 lux expected to suppress melatonin, for a few minutes during night time. The indoor and night workers' exposure to light during day time was at a level that may reduce general well-being and mood, especially during the winter. Outdoor workers were exposed to anti-depressive levels of light during summer.

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Table 1 Numbers of participants and days with light measurements by type of worker and type of day

	Indoor workers		Outdoor workers		Night workers		All Workers	
Type of day	N workers	N Days	N workers	N Days	N workers	N Days	N workers	N Days
Work days	169	693	134	351	181	420	484	1,464
Days off	167	454	140	320	178	400	485	1,174
All days	170	1,147	151	671	188	820	509	2,638

Figure 1 Smoothed arithmetic mean light intensities for indoor, outdoor and night workers across the day on work days, days off and stratified by summer and winter.

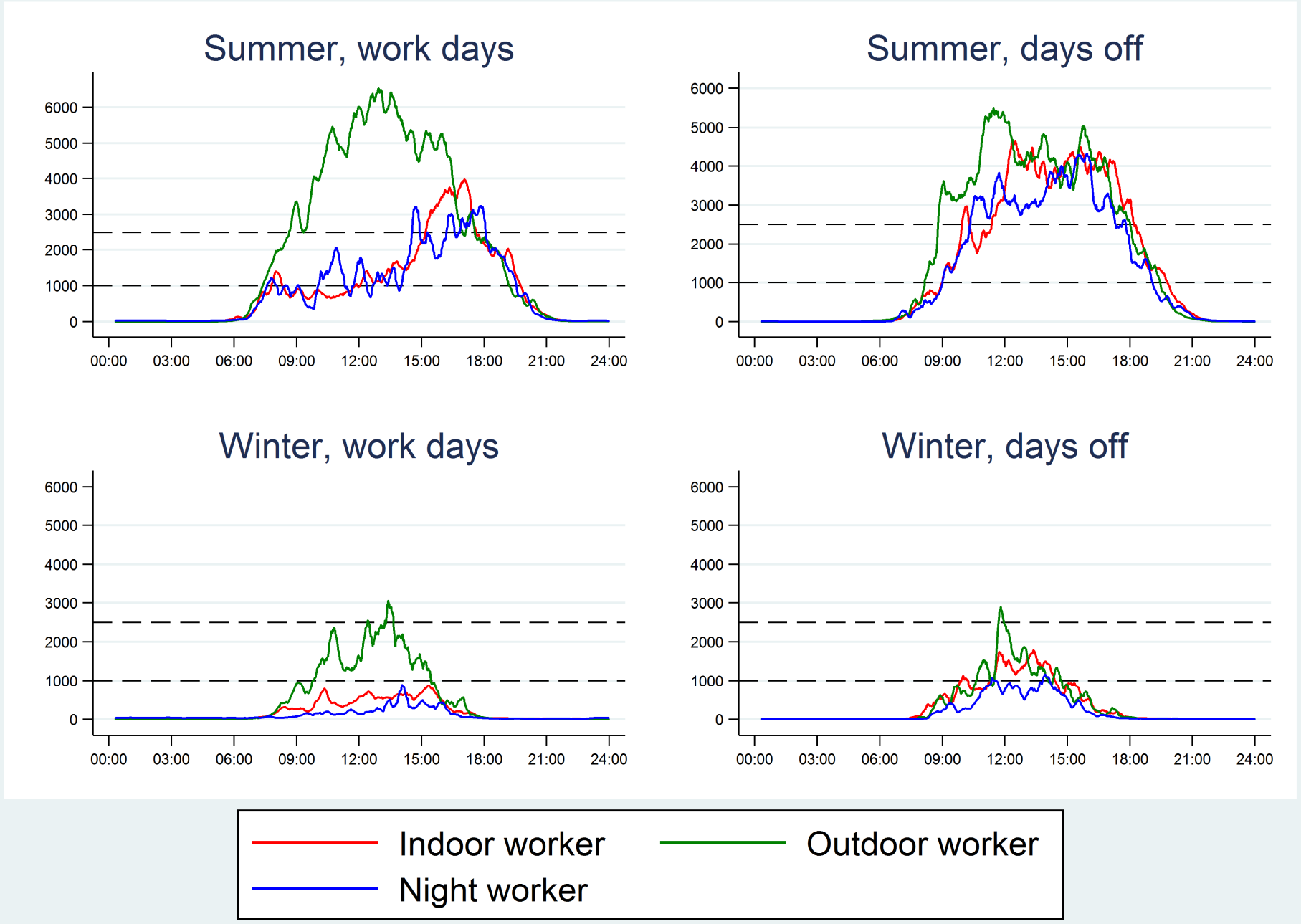

Table 2 **Six**-hour light intensities of indoor, outdoor and night workers during work days and days off by season and time of day.

		Indoor workers (N=170))					Outdoor workers (N=151)							Night shift workers (N=188)						
		Hours	Light (Lux)				Hours	Light (Lux)						Hours	Light (Lux)					
Time periods by day and season		N	Mean[a]	Median	10 %[b]	90 %[b]	N	Mean[a]	Median	10 %[b]	90 %[b]	% diff[c]	*p*-value[c]	N	Mean[a]	Median	10 %[b]	90 %[b]	% diff[c]	*p*-value[c]
Summer																				
00:00-05:59	Work day	688	13.6	0.2	0.0	15.4	513	5.2	0.2	0.0	12.1	-46.9	0.049	1,240	25.9	18.4	2.8	57.2	1298	<0.001
	Day off	646	5.5	0.2	0.0	7.0	675	5.5	0.2	0.0	4.8	-43.3	0.054	520	3.5	0.2	0.0	9.9	-3.0	0.921
06:00-11:59	Work day	1,880	755	242	36.7	1,794	1,466	3,148	944	34.9	8,948	159	<0.001	855	753	53.1	0.4	1,560	-57.2	<0.001
	Day off	1,138	1,511	209	2.0	3,934	984	2,733	219	0.9	8,070	13.6	0.497	957	1,623	168	0.5	4,618	-27.9	0.110
12:00-17:59	Work day	2,315	2,428	562	96.2	6,678	1,559	4,715	2,089	109	12,774	80.3	<0.001	843	2,085	307	1.2	5,760	-75.2	<0.001
	Day off	1,328	4,064	949	84.3	11,332	1,120	3,986	969	32.2	11,910	-16.5	0.254	1,122	3,176	781	60.9	9,341	-11.6	0.479
18:00-23:59	Work day	2,110	596	28	1.6	1,180	1,298	528	16.0	0.5	900	-50.0	<0.001	991	498	30.4	3.4	644	23.3	0.141
	Day off	1,245	573	26	1.7	921	1,033	476	11.6	0.4	748	-34.5	0.001	1,096	407	18.1	1.5	515	-2.1	0.884
Winter																				
00:00-05:59	Work day	465	2.8	0.2	0.0	5.0	141	2.8	0.2	0.0	5.6	218	0.001	1,056	38.1	22.6	3.7	101	6951	<0.001
	Day off	555	2.5	0.2	0.0	2.5	310	1.5	0.2	0.0	2.1	105	0.034	353	4.5	0.3	0.0	12.8	315	<0.001
06:00-11:59	Work day	1,334	308	107	9.4	617	399	867	183	9.7	3,593	87.0	<0.001	726	79.3	19.6	0.4	149	-51.4	<0.001
	Day off	903	611	49	0.2	1,249	474	708	39.4	0.2	1,229	13.5	0.530	652	351	39.6	0.3	758	-21.8	0.188
12:00-17:59	Work day	1,626	472	136	12.5	993	422	1301	283	10.9	3,593	40.9	0.039	718	232	24.7	0.6	432	-72.1	<0.001
	Day off	1,040	775	106	7.4	1,804	538	787	88.0	6.8	1,792	-16.3	0.283	806	465	77.3	7.7	1,082	-8.6	0.565
18:00-23:59	Work day	1,431	19.7	8.5	0.7	47	348	14.4	7.0	0.7	38.7	-10.4	0.462	868	20.2	12.0	1.5	48.5	54.6	<0.001
	Day off	976	16.6	6.8	0.6	42	506	13.1	6.0	0.9	28.8	15.0	0.443	730	12.9	6.6	1.0	30.2	3.3	0.841

[a] Arithmetic mean [b] Percentiles [c] *p*-values computed from a mixed linear regression analyses comparing log transformed light with indoor workers as reference group and adjusted for hour of sampling.

Table 3. Median time (min) spent above 80 lux for indoor, outdoor and night workers during work days and days off by season and, time of day.

Time periods by day and season	Indoor workers (N=170)		Outdoor workers (N=151)				Night workers (N=185)			
	6-hour periods N	Median (IQR[a])	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]
Summer										
Work days										
00:00-05:59	78	0 (0-0)	58	0 (0-0)	-9.8	0.609	157	14 (4-33)	773	<0.001
06:00-11:59	196	237 (175-275)	177	263 (210-309)	18.9	0.144	56	50 (28-95)	-79.0	<0.001
12:00-17:59	320	285 (226-315)	210	297 (254-322)	5.4	0.486	48	204 (111-281)	-45.9	<0.001
18:00-23:59	163	82 (42-146)	76	60 (16-109)	-38.9	0.011	123	75 (35-134)	-11.0	0.489
Days off										
00:00-05:59	75	0 (0-0)	80	0 (0-0)	8.2	0.503	60	0 (0-0)	-1.7	0.893
06:00-11:59	63	166 (111-204)	60	164 (115-226)	-17.6	0.334	49	154 (90-195)	-35.3	0.036
12:00-17:59	161	273 (214-316)	140	256 (191-311)	-15.3	0.012	136	258 (197-306)	-6.7	0.291
18:00-23:59	108	81 (36-137)	85	65 (22-119)	-17.0	0.405	90	55 (25-101)	-47.0	0.037
Winter										
Work days										
00:00-05:59	62	0 (0-0)	17	0 (0-0)	-1.1	0.978	161	13 (3-70)	847	<0.001
06:00-11:59	129	168 (97-215)	47	171 (134-230)	11.2	0.664	49	23 (8-99)	-85.6	<0.001
12:00-17:59	234	180 (123-224)	56	195 (149-232)	10.0	0.552	43	53 (16-143)	-73.6	<0.001
18:00-23:59	102	8 (2-25)	20	4 (0-21)	-10.3	0.763	88	13 (2-25)	25.9	0.292
Days off										
00:00-05:59	69	0 (0-0)	40	0 (0-0)	-3.2	0.733	35	0 (0-0)	-0.5	0.958
06:00-11:59	39	125 (62-173)	29	108 (54-171)	-19.0	0.459	26	70 (31-141)	-43.1	0.048
12:00-17:59	125	137 (85-198)	61	136 (59-191)	-9.7	0.478	98	128 (89-186)	-5.5	0.651
18:00-23:59	65	6 (2-15)	34	3 (0-11)	-37.6	0.139	63	2 (0-14)	-39.7	0.060

[a] IQR interquartile (25^{th}–75^{th} percentile) range

[b] Values computed from a mixed linear regression analyses with indoor workers as reference group.

Table 4 Median time (min) spent above 1,000 lux for indoor, outdoor and night workers during work days and days off by season and, time of day.

Time periods by day and season	Indoor workers		Outdoor workers				Night workers			
	6-hour periods N	Median (IQR[a])	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]
Summer										
Work days										
00:00-05:59	78	0 (0-0)	58	0 (0-0)	-8.2	0.105	157	0 (0-0)	-8.4	0.038
06:00-11:59	196	22 (7-42)	177	124 (68-209)	459	<0.001	56	11 (0-23)	-59.4	<0.001
12:00-17:59	320	75 (37-106)	210	152 (94-205)	102	<0.001	48	66 (21-123)	-32.4	0.008
18:00-23:59	163	14 (0-47)	76	6 (1-30)	-2.6	0.927	123	5 (0-29)	-24.6	0.264
Days off										
00:00-05:59	75	0 (0-0)	80	0 (0-0)	0.0[c]	-	60	0 (0-0)	0.0[c]	-
06:00-11:59	63	28 (15-67)	60	67 (19-110)	43.9	0.206	49	34 (15-65)	-18.3	0.490
12:00-17:59	161	98 (44-175)	140	102 (48-168)	2.9	0.847	136	89 (51-145)	2.2	0.883
18:00-23:59	108	8 (0-45)	85	6 (0-28)	-2.9	0.916	90	4 (0-19)	-26.4	0.260
Winter										
Work days										
00:00-05:59	62	0 (0-0)	17	0 (0-0)	0.0	1.000	161	0 (0-0)	3.3	0.188
06:00-11:59	129	2 (0-13)	47	47 (27-85)	600	<0.001	49	0 (0-0)	-54.4	0.003
12:00-17:59	234	11 (2-32)	56	53 (30-90)	360	<0.001	43	1 (0-24)	-56.6	0.002
18:00-23:59	102	0 (0-0)	20	1 (1-1)	-3.1	0.559	88	0 (0-0)	-3.1	0.326
Days off										
00:00-05:59	69	0 (0-0)	40	0 (0-0)	0.0[c]	-	35	0 (0-0)	0.0[c]	-
06:00-11:59	39	17 (0-39)	29	15 (2-76)	8.8	0.856	26	11 (0-25)	-20.6	0.623
12:00-17:59	125	20 (4-48)	61	21 (3-65)	-4.3	0.877	98	19 (6-42)	-7.2	0.578
18:00-23:59	65	0 (0-0)	34	0 (0-0)	0.0[c]	-	63	0 (0-0)	0.0[c]	-

[a] IQR interquartile (25^{th}–75^{th} percentile) range

[b] Values computed from a mixed linear regression analyses with indoor workers as reference group.

[c] All measurements are below 1,000 lux

Table 5 Median time (min) spent above 2,500 lux by occupation, season, type of day and time of day with interquartile (25^{th}–75^{th} percentile) range (IQR)

Time periods by day and season	Indoor workers		Outdoor workers				Night workers			
	6-hour periods N	Median (IQR[a])	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]	6-hour periods N	Median (IQR[a])	% diff[b]	*p*-value[b]
Summer										
Work days										
00:00-05:59	78	0 (0-0)	58	0 (0-0)	0.0[c]	-	157	0 (0-0)	0.0[c]	-
06:00-11:59	196	5 (0-15)	177	71 (25-131)	846	<0.001	56	2 (0-11)	-31.1	0.104
12:00-17:59	320	40 (19-67)	210	100 (58-155)	158	<0.001	48	40 (8-80)	-27.2	0.111
18:00-23:59	163	3 (0-22)	76	1 (1-13)	-11.1	0.646	123	1 (0-10)	-20.7	0.296
Days off										
00:00-05:59	75	0 (0-0)	80	0 (0-0)	0.0[c]	-	60	0 (0-0)	0.0[c]	-
06:00-11:59	63	14 (2-43)	60	42 (7-90)	127	<0.001	49	17 (4-38)	3.8	0.911
12:00-17:59	161	58 (22-125)	140	61 (22-127)	0.9	0.964	136	58 (25-108)	2.5	0.893
18:00-23:59	108	0 (0-15)	85	0 (0-8)	-3.9	0.865	90	0 (0-5)	-29.2	0.137
Winter										
Work days										
00:00-05:59	62	0 (0-0)	17	0 (0-0)	0.0[c]	-	161	0 (0-0)	0.0[c]	-
06:00-11:59	129	0 (0-2)	47	18 (2-33)	436	<0.001	49	0 (0-0)	-27.5	0.146
12:00-17:59	234	1 (0-13)	56	22 (4-51)	352	<0.001	43	0 (0-3)	-37.6	0.068
18:00-23:59	102	0 (0-0)	20	0 (0-0)	0.0[c]	-	88	0 (0-0)	0.0[c]	-
Days off										
00:00-05:59	69	0 (0-0)	40	0 (0-0)	0.0[c]	-	35	0 (0-0)	0.0[c]	-
06:00-11:59	39	3 (0-26)	29	4 (0-32)	2.1	0.961	26	1 (0-12)	-38.0	0.272
12:00-17:59	125	4 (0-25)	61	5 (0-30)	13.7	0.650	98	2 (0-16)	-27.6	0.185
18:00-23:59	65	0 (0-0)	34	0 (0-0)	0.0[c]	-	63	0 (0-0)	0.0[c]	-

[a] IQR interquartile (25^{th}–75^{th} percentile) range

[b] Values computed from a mixed linear regression analyses with indoor workers as reference group.

[c] All measurements are below 2,500 lux

Paper II

Night work, light exposure and melatonin on work days and days off

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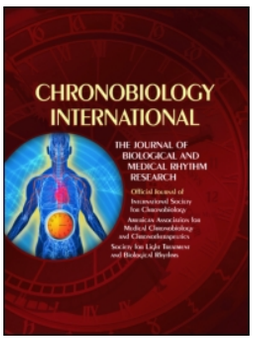

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Night work, light exposure and melatonin on work days and days off

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ABSTRACT

We aimed to examine the effects of night work on salivary melatonin concentration during and subsequent to night work and the mediating role of light. We included 254 day workers and 87 night workers who were followed during 322 work days and 301 days off work. Each day was defined as the 24 hour period starting from the beginning of a night shift or from waking in the mornings with day work and days off. Light levels were recorded and synchronized with diary information (start and end of sleep and work). On average, participants provided four saliva samples per day, and these were analyzed for melatonin concentration by liquid chromatography tandem mass spectrometry (LC-MS/MS). Differences between day and night workers on work days and days off were assessed with multilevel regression models with melatonin concentration as the primary outcome. All models were stratified or adjusted by time of day. For light exposure, we estimated the total, direct and indirect effects of night work on melatonin concentrations obtaining 95% confidence intervals through bootstrapping. On work days, night workers showed 15% lower salivary melatonin concentrations compared with day workers (−15.0%; 95% CI: −31.4%; 5.2%). During the night, light exposure mediated a melatonin suppression of approximately 6% (−5.9%, 95% CI: −10.2%; −1.5%). No mediating effect of light was seen during the day time. On days off, we observed no difference in melatonin concentrations between day and night workers. These findings are in accordance with a transient and partly light-mediated effect of night work on melatonin production.

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Night Work, melatonin suppression, light exposure, field study

Introduction

Epidemiological studies have suggested increased risk of breast cancer following shift work (Kolstad, 2008; Lin et al., 2015; Wang et al., 2013). A recent meta-analysis of 10 follow-up studies found little or no effect on breast cancer incidence (Travis et al., 2016). However, previous epidemiological studies have some methodological limitations making interpretation of the results difficult. Yet, a working group convened by the International Agency for Research on Cancer (IARC) in 2007 classified shift work that involves circadian disruption, as probably carcinogenic to humans based on sufficient evidence in animals and limited evidence in humans (Straif et al., 2007).

Light exposure during night shifts and suppression of melatonin synthesis has been hypothesized as pivotal causal elements linking shift work and cancer (Costa et al., 2010; Schernhammer & Schulmeister, 2004; Stevens et al., 2014). Melatonin is a circadian hormone produced primarily by the pineal gland during the night. Production peaks around 02:00 h in humans entrained to the ambient 24-hour light/dark cycle (Skene & Arendt, 2006). Melatonin may have oncostatic effects through various pathways such as inhibition of tumor growth, reduction of oxidative DNA damage or change of estrogen levels (Hill et al., 2015).

During work days, the majority of field studies have observed lower salivary melatonin or urinary 6-sulfatoxymelatonin (aMT6s, the major melatonin metabolite) concentrations in night workers compared with day workers (Davis et al., 2012; Gómez-Acebo et al., 2015; Hansen et al., 2006; Leung et al.,

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Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/icbi.

2016; Mirick et al., 2013; Papantoniou et al., 2014;; Schernhammer et al., 2004), but this was not observed in all studies (Peplonska et al., 2012). Comparisons within night workers have shown lower (Jensen et al., 2016; Leung et al., 2016; Mirick et al., 2013; Yamauchi, 2004) or similar (Dumont et al., 2012; Gibbs et al., 2007; Grundy et al., 2011) melatonin or aMT6s levels on days with night work compared to days with day work. Studies including day and night workers during work days and days off found lower urinary aMT6s levels in night workers, compared with day workers on work days as well as during the first night sleep period after a night shift (Davis et al., 2012; Mirick et al., 2013), and this has also been found during the second day after a night shift (Hansen et al., 2006). Melatonin production was thus still affected 12–36 hours after completing a night shift. However, a recent study measuring salivary melatonin found full recovery of the melatonin profile on the second day off (Jensen et al., 2016).

From laboratory studies it is well established that retinal exposure to polychromatic light at night acutely suppresses melatonin concentration depending on intensity, duration and spectrum of the light with substantial inter-individual variation of the effect (Bojkowski et al., 1987; Figueiro et al., 2006a; Rea & Figueiro, 2014; Rea et al., 2005; Revell & Skene, 2007).

Average and median light levels measured at shoulder or neck level during night shifts have been reported below 80 lux among health care and industrial workers (Borugian et al., 2005; Dumont et al., 2012; Grundy et al., 2011; Papantoniou et al., 2014). These averaged levels are expected to have relatively low impact on melatonin synthesis (Figueiro et al., 2006a). The response to light also depends on peak exposures, the individual and their photic history (Burgess & Fogg, 2008; Hebert et al., 2002).

Few field studies have included objective measures of light at night when studying melatonin production during night work. Papantoniou et al. (2014) found that night workers in the highest tertile of light exposure during night work had lower 24-h aMT6 than the lowest tertile. Dumont et al. (2012) made similar observations, but they did not observe an association between light at night and melatonin production during night. Grundy et al. (2011) observed no consistent association between light exposure and melatonin production among nurses working rapidly rotating shifts. As far as we are aware, no field studies have analyzed to what extent light exposure mediates the effect of night work on melatonin levels.

The objectives of the current study were to examine melatonin concentrations during and subsequent to night work and the mediating role of light exposure.

Materials and methods

Population

Participants were recruited through employers, advertisements and via the homepage of the National Research Centre for the Working Environment. The aim was to recruit equal numbers of indoor day workers, outdoor day workers and night workers. Enrolment of participants took place at two centers (Aarhus, latitude 56°90′N longitude 20°12′E and Copenhagen, latitude 55°40′N longitude 12°34′E). In total, 535 subjects participated and 404 (76%) collected saliva samples. The study was carried out from March 2012 to May 2013. All participants gave written informed consent, and the study was approved by the Danish Data Protection Agency (J.nr. 2011–41-6850) and the Regional Ethics Committee (M-20110214) in Denmark.

For the present study, five participants were excluded due to pregnancy which may alter melatonin metabolism (Kivela, 1991; Lew, 1987). Fifty-eight rotating night workers were excluded as they did not provide saliva samples during days with night work. The study population thus comprised 341 participants (64%), hereof 87 night workers and 254 day workers. The night workers were defined as those working more than three hours between 00:00 h and 05:00 h on a regular (n = 19) or a rotating basis (n = 68) (Stevens et al., 2011). Day workers were a mix of indoor and outdoor workers who never worked between 00:00 h and 05:00 h.

The night workers were hospital employees (n = 75), factory workers (n = 10) or residential social workers (n = 2). The day workers were nursery workers (n = 61), hospital employees (n = 56), teachers (n = 47), gardeners and pavers (n = 34), factory workers (n = 18), craftsmen (n = 13), mechanics (n =

8), office workers (n = 8), dentist or dental assistants (n = 7) or residential social workers (n = 2).

Light exposure assessment

Light levels and actigraphy (movement counts) were recorded for seven consecutive days with a Philips Respironics Actiwatch Spectrum (Actiwatch). The Actiwatch was worn outside clothes on the upper arm. During sleep, the Actiwatch was placed next to the bed except for two sleep periods where it was worn on the wrist for sleep measures (not reported here). The Actiwatch was set to one-minute sampling epochs and recorded white light (lux). After data collection was completed, the light sensor outputs from the Actiwatches were calibrated as described by Markvart et al. (Markvart et al., 2015).

Light measurements were synchronized with diary information on the start and end of sleep and work. In the diary, each participant reported if they had worn the Actiwatch for less than 20 minutes within every hour. If the participant did not report wearing the Actiwatch, or the Actiwatch recorded no movement for 20 consecutive minutes, we inspected the light and actigraphy measurements and assessed if the light recordings should be included or not. Light measurements were excluded if there was no movement, or a constant light level was recorded.

In laboratory studies, melatonin production was not suppressed by polychromatic light intensities below 80 lux (Zeitzer et al., 2000), and suppression has been shown to occur within 30 minutes of light exposure (Bojkowski et al., 1987; Revell & Skene, 2007; Thapan et al., 2001). Comparable thresholds have been reported by other studies (Figueiro et al., 2006a, 2006b). We therefore classified light exposure by the duration of light exposure above 80 lux occurring 30 minutes before each saliva sample (0–30 minutes).

Questionnaire and diary

The questionnaire included information on sex, age (years), pregnancy (current yes/no), occupation (current), height (centimetres), weight (current kilograms), smoker (current, former or never), use of melatonin supplementation (yes/no), antidepressant medications (yes/no) and diurnal preference (response categories: definitely a morning person, more a morning person than an evening person, more an evening person than a morning person, definitely an evening person). Three night workers and two day workers reported occasional use of melatonin supplementation. Their melatonin profiles were inspected, and none of them indicated the presence of exogenous melatonin administration.

The diary recorded the start and end of sleep and work, whether the day was a work day or a day off work, and if the Actiwatch was worn for less than 20 minutes within every hour of the day.

Collection of saliva and assessment of melatonin

For each participant, we aimed at including saliva samples during one work day (a day with night work or a day with day work) and a day off. The participants decided themselves on which days in the 7-day study period to collect saliva. Participants were instructed to collect the first sample at the first awakening from their primary sleep. Following the first sample, participants were asked to collect saliva at 07:00 h, 11:00 h, 15:00 h, 19:00 h, 23:00 h and 03:00 h when awake. An additional sample was collected just before bedtime. Night workers followed the same instructions, but on days with night work sampling started in the afternoon at awakening, and the next sample was collected at 15:00 h or 19:00 h, depending on waking time. The sampling period ended the following morning, when night workers went to bed. Eating was not allowed 30 minutes prior to sampling. The sampling tube should contain approximately 1 ml saliva. No instructions were given on light conditions when sampling. Just after sample collection participants noted the date and exact time on a label on the saliva tube and stored the sample at 5°C whenever possible until the end of the 7-day study period. Melatonin in saliva is stable at room temperature for at least seven days (Jensen et al., 2011).

Samples from day workers were classified as work day measurements if sampled within 24 hours after awakening on a work day. Samples from night workers were classified as work day measurements if sampled within 24 hours after the beginning of a night shift. Samples from day workers obtained within 24 hours after awakening on a day off were classified as day off samples. Samples from night workers were classified as day off samples according the same criteria as the day workers but in addition requested that

samples should be obtained more than 24 hours after ending a night shift. This additional criterion was included to obtain a well defined day off category.

In total, 3579 saliva samples were collected. We excluded 430 saliva samples from rotating night workers during days with day shift, 47 samples without valid light measurements, 45 samples from pregnant participants, four samples above and 14 samples below three standard deviations (636 nmol/L and 0.4 nmol/L) of the geometric mean of all samples according to Grubb's outlier test (Grubbs, 1950), 34 samples obtained on a day off less than 24 hours after the end of a night shift and 161 samples from night workers before the beginning of their first night shift, leaving 2842 samples for analyses. A total of 1541 saliva samples were collected on 322 work days, and 1301 saliva samples were collected on 301 days off (Table 1. Of the night workers, 44 (50%) collected saliva samples during the day of the first night shift, 38 (44%) during the day of the second night shift and five (6%) during the day of the third to fifth night shift during the follow up period. On average the night workers day off, saliva samples were provided 47 hours (range 25–116 hours) after the end of the last night shift.

Melatonin analyses were carried out using liquid chromatography tandem mass spectrometry (LC-MS/MS) as described in Jensen et al. (Jensen et al., 2011). A volume of 25 µL was injected into an Agilent 1200 HPLC (Agilent technologies, Santa Clara, CA, USA) equipped with a C18 2.1 mm x 50mm 2.6µm Kinetex column (Phenometex, Torrance, CA, USA). A linear gradient was run over 3 minutes from 10% to 100% methanol (MeOH) and kept at 100% for two and a half minutes, followed by one minute of equilibration at 10% MeOH. The mass spectrometer, an Agilent 6460 QQQ equipped with jet stream electrospray ionization (ESI) ion source, was operated in a positive ion mode. The quantification was achieved by using the mass spectrometer in multiple reaction monitoring modes. A single precursor ion-product ion transition was measured for each hormone and its internal standard. The transitions were as follows: m\z 233.2 -> m\z 174.1. The limit of detection (LOD) was 3.73 pmol/L, and 74 samples (2%) had concentrations below LOD. For a concentration below LOD, the sample was given a random number from a normal distribution with 2/3 of the LOD as the mean. To test equivalence between analyses, reference samples at two levels (28–43 pmol/L, intra assay coefficient of variation (CV): 20%; 80–152 pmol/L, CV = 13%) were analyzed with every 14 samples. Westgard control charts (Westgard et al., 1981) were used to document that the LC-MS/MS method remained under statistical and analytical control. Samples that failed analysis were rerun once. If the concentration was above 490 pmol/L, solutions were diluted and reanalysed.

Statistical analysis

Characteristics of the study population were presented as numbers (%), means and range. Light and melatonin concentrations were log normally distributed and were therefore naturally log transformed. Mean levels per 4-hour time intervals and type of worker (day worker, night worker) were calculated and expressed as geometric means with 95% confidence intervals. We compared geometric mean light exposure and duration above 80 lux between day and night workers with Student's t-test. All analyses comparing night and day workers were stratified into work days and days off. Geometric mean melatonin levels by duration of light exposure above 80 lux were computed separately for day (08:00–19:59 h) and night hours (20:00–07:59 h).

We also compared melatonin concentration between day and night workers on work days and days off work with multivariate multilevel linear regression (STATA mixed procedure) to account for the repeated measurements. For each individual, we used a random intercept with a variance component covariance structure and

Table 1. Numbers of participants and saliva samples by type of worker and type of day.

	Day workers		Night workers		Total	
	Participants *N*	Samples *N*	Participants *N*	Samples *N*	Participants *N*	Samples *N*
Work day	235	1204	87	337	322	1541
Day off	230	1021	71	280	301	1301
Total	254	2225	87	617	341	2842

repeated statement for the samples with an autoregressive covariance structure. Type of worker (day worker, night worker) and time of day (01:00–04:59 h, 05:00–08:59 h, 09:00–12:59 h, 13:00–16:59 h, 17:00–20:59 h, 21:00–00:59 h) were included as categorical variables. Potential confounders included were age (continuous, years), sex (male, female), body mass index (BMI, kg/cm^2,calculated as weight/height^2, continuous), current smoking (yes, no), diurnal preference (morning type: definitely a morning person, more a morning person than an evening person, evening type: more an evening person than a morning person, definitely an evening person) and use of antidepressant medication (yes, no). These factors were identified *a priori* based on a review of the literature (Bhatti et al., 2014; Burgess & Fogg, 2008; Leung et al., 2016; Papantoniou et al., 2014; Schernhammer et al., 2006).

To assess if light exposure mediated the effect of night work on melatonin levels, we conducted mediation analyses. These were restricted to work days, since no difference in melatonin concentrations was observed between day and night workers on days off. Work days were stratified into day (08:00–19:59 h) and night hours (20:00–07:59 h) because time of day is a significant modifier of the effect of light. Light exposure was included as duration above 80 lux occurring 30 minutes before each saliva sample. The minimum value was therefore 0 minutes and the maximum 30 minutes.

We estimated the direct, indirect (mediated by light exposure) and total effects of night work with classical path analysis methods combining the results of two regression analyses (Hayes, 2009). Firstly, we regressed log-melatonin on night work, light exposure and covariates. Secondly, we regressed light exposure on night work and covariates:

$$E[\log(melatonin)] = \beta_0 + \beta_{Night\ work} \times Night\ work + \beta_{Light\ exposure} \times Light\ exposure + \beta_{Covariates} \times Covariates$$

$$E[\text{Light exposure}] = \alpha_0 + \alpha_{Night\ work} \times Night\ work + \alpha_{Covariates} \times Covariates$$

The direct effect, indirect and total effects of night work on log-melatonin were then defined as:

$$\text{Direct effect} = \beta_{Night\ work}$$
$$\text{Indirect effect} = \alpha_{Night\ work} \times \beta_{Light\ exposure}$$
$$\text{Total effect} = \beta_{Night\ work} + \alpha_{Night\ work} \times \beta_{Light\ exposure}$$

We estimated 95% confidence intervals using 1000 bootstrap samples. The relative effects of night work (%) on melatonin were found by the exponentials. Note that, as the effects on log melatonin are assumed to be additive/linear, the effects on melatonin are multiplicative/relative.

In a separate internal analysis among night workers only, we examined if night workers' melatonin production was lower on days with night work compared with days off. Analyses that compared permanent night workers only (n =19) with day workers (n =254) were also carried out.

In additional analyses, we included the exact time of saliva sampling in addition to the 4-hour time categories. This only changed estimates marginally and was thus not included in the presented analyses. To examine if melatonin concentrations between day and night workers varied across the day, we included an interaction term between type of worker and 4-hour time intervals of the day. Since the interaction term was not significant in any of the models except for the analyses of the permanent night workers, this was not included in the other models. All statistical analyses were carried out using Stata 13.1 (Stata.corp, TX, USA)

Results

Table 2 presents characteristics of the 254 day workers and 87 night workers. Night workers were younger, more often women, were less often smokers and were more often evening types in their diurnal preference. Almost twice as many night workers as day workers used antidepressant medication. Of the day workers, 26 % had previously worked night shifts.

Table 3 presents geometric mean salivary melatonin concentrations in 4-hour intervals during work days and days off for night and day workers. Night workers' mean melatonin concentrations were lower than day workers at all times of the day except between 01:00 and 04:59 h.

Table 4 presents geometric mean light levels and mean duration of light exposure above 80 lux for day and night workers by time of day during work days

Table 2. Characteristics of the study population (n = 341) and saliva samples (n = 2842).

	Day workers (n = 254)					Night workers (n = 87)				
	Participants *N*	%	Saliva samples *N*	Mean	Range	Participants *N*	%	Saliva samples *N*	Mean	Range
Age	254			44.4	17–68	87			40.6	24–58
BMI (kg/m^2)[a]	247			24.8	16.9–45.3	87			25.3	17.1–42.6
Years of night work[b]	65			4.5	0.25–33	86			12.1	0.5–37
Sex										
Male	83	32.7	709	–	–	8	9.2	55	–	–
Female	171	67.3	1516	–	–	79	90.8	562	–	–
Current smoker										
Yes	40	15.7	307			16	18.4	110		
No	214	84.3	1918			79	81.6	507		
Diurnal preference[c]										
Morning type	159	63.3	1444	–	–	29	33.3	215	–	–
Evening type	92	36.7	754	–	–	58	66.7	402	–	–
Use of antidepressants										
Yes	11	4.5	89	–	–	7	8.8	50	–	–
No	243	95.5	2136	–	–	80	91.2	567	–	–

Number of participants with missing information [a]7, [b]1 [c]3.

and days off. On work days, night workers were exposed to significantly higher light levels than day workers between 21:00 and 05:00 h, and day workers were exposed to significantly higher light levels than night workers between 09:00 and 21:00 h. During days off, similar light levels among night and day workers were observed.

Table 5 presents geometric mean melatonin concentration during the night and day by duration of light exposure above 80 lux occurring in the past 30 minutes. When light exposure lasted more than 10 minutes during the night hours, melatonin concentrations were almost half of the level seen for a shorter light duration. Melatonin concentrations during the day were not affected by light exposure duration.

Table 6 presents crude and adjusted relative difference (%) in melatonin concentration in day workers compared with night workers from the multilevel linear regression analyses. On work days night workers showed 16.5% (95% CI −0.2; −30.5) lower melatonin concentrations than day workers in the adjusted analysis that differed only marginally from the crude analysis. On days off work, no differences in melatonin concentration between night workers and day workers were observed.

Table 7 presents results from the mediation analyses. During night and day, night shift workers showed, respectively, 15.0% and 16.2% (−15.0 % [95% CI: −31.4%; 5.2%] and −16.2 % [95% CI: −34.6%; 7.5%]) lower melatonin concentrations than the day workers (the total effects). During the night, light exposure mediated a 5.9 % decrease (−5.9% [95% CI: −10.2%; −1.5%]) in melatonin levels in the night workers compared with day workers. No mediating effect of light exposure was seen during the day. The direct effects of night work were −9.6% (95% CI −27.0; 11.9) during the night and −18.3% (95% CI −36.7; 5.4) during the day.

Figure 1 shows the adjusted geometric mean melatonin levels in day and night workers by time of day during work days and days off. Results are presented for a male, 40 year old, BMI 25kg/m^2, non-smoker, no antidepressant medication and morning preference. The relative difference between day and night workers on work days did not differ across the day, whereas the absolute difference was largest at night. Night workers' mean melatonin concentrations were lower at all times of a work day compared to a day off. Day workers showed a higher mean melatonin concentration between 05:00 and 08:59 h on work days compared to days off. Apart from this, mean melatonin concentration was similar on work days and days off among day workers.

In the night workers, the difference in adjusted melatonin concentrations between night shifts and days off was −15.4% (95% CI −30.6%; 2.8%), being lower on days with night work compared to days off work (data not shown). On work days, the

Table 3. Geometric mean salivary melatonin concentration by time of day among day and night workers on work days and days off.

	Day workers (N = 254)					Night workers (N = 87)				
Time of day	Mean time of sampling (SD*)	Samples N	Participants N	Geometric mean melatonin concentration (pmol/L)	95% CI	Mean time of sampling (SD*)	Samples N	Participants N	Geometric mean melatonin concentration (pmol/L)	95% CI
Work days										
01:00–04:59	03:03 (80)	29	28	46.1	34.8; 61.0	02:52 (70)	70	68	48.9	38.8; 61.7
05:00–08:59	06:31 (52)	269	212	32.7	29.2; 36.7	07:14 (62)	78	66	26.8	21.2; 33.8
09:00–12:59	10:49 (57)	236	212	10.2	9.1; 11.5	10:54 (75)	25	23	8.1	4.9; 13.2
13:00–16:59	14:51 (57)	224	199	9.2	8.1; 10.5	15:13 (56)	52	47	6.8	5.3; 8.9
17:00–20:59	18:51 (60)	217	188	9.7	8.4; 11.2	18:58 (57)	47	43	8.4	6.2; 11.3
21:00–00:59	22:35 (47)	229	191	35.9	31.7; 40.6	22:52 (70)	65	59	27.7	20.8; 37.0
Total	14:08 (633)	1204	235	17.0	15.9; 18.1	12:30 (445)	337	87	19.3	16.8; 22.1
Days off										
01:00–04:59	02:40 (83)	25	22	54.0	37.9; 75.8	02:34 (74)	8	7	87.2	44.9; 172.2
05:00–08:59	07:17 (57)	188	173	21.4	18.7; 24.6	07:26 (61)	28	27	26.8	17.9; 40.1
09:00–12:59	10:52 (67)	218	197	11.2	9.8; 12.7	10:33 (68)	65	58	13.2	10.1; 17.3
13:00–16:59	14:52 (55)	180	168	9.0	7.8; 10.3	14:34 (61)	61	58	8.0	6.1; 10.5
17:00–20:59	18:50 (56)	204	182	9.5	8.3; 10.9	18:46 (64)	55	53	9.5	7.0; 12.9
21:00–00:59	22:36 (48)	216	175	30.2	26.3; 34.6	22:42 (53)	63	57	26.2	19.6; 34.9
Total	14:42 (351)	1021	230	14.9	13.9; 15.9	15:14 (340)	280	71	14.7	12.7; 16.9

Note. SD* given as minutes.

Table 4. Light exposure levels on day and night workers by time of day on work days and days off. Results are presented as geometric means and durations of light above 80 lux.

	Day workers (*N* = 254)		Night workers (*N* = 87)			Day workers (*N* = 254)		Night workers (*N* = 87)		
Time of day	Geometric mean light exposure (lux)	95% CI	Geometric mean light exposure (lux)	95% CI	*p*–Value*	Mean duration of light above 80 lux (minutes)	95% CI	Mean duration of light above 80 lux (minutes)	95% CI	*p*–Value*
Work days										
01:00–04:59	0.0	0.0; 0.1	6.0	4.6; 7.9	0.000	0.1	0.0; 0.3	24	15; 33	0.000
05:00–08:59	17	13; 20	13	10; 17	0.27	68	62; 74	45	37; 54	0.000
09:00–12:59	194	173; 221	3.6	1.9; 6.8	0.000	166	159; 173	35	20; 50	0.000
13:00 – 16:59	187	158; 212	26	17; 41	0.000	156	147; 163	72	58; 87	0.000
17:00–20:59	27	21; 32	16	11; 22	0.02	76	41; 69	55	67; 84	0.01
21:00–00:59	1.3	0.9; 1.6	6.0	4.9; 7.5	0.000	7	5; 8	18	11; 24	0.000
Days Off										
01:00–04:59	0.0	0.0; 0.1	0.2	0.1; 0.4	0.001	1.1	−0.3; 2.5	0.6	0.1; 1.1	0.75
05:00–08:59	2.2	1.3; 2.7	2.1	1.2; 3.6	0.73	26	21; 31	21	14; 28	0.31
09:00–12:59	152	125; 186	97	71; 134	0.02	141	133; 148	127	113; 141	0.09
13:00 – 16:59	152	118; 186	128	90; 182	0.50	140	131; 148	130	114; 146	0.27
17:00–20:59	24	19; 29	17	12; 24	0.20	69	61; 77	59	45; 72	0.20
21:00–00:59	1.0	0.8; 1.2	2.2	1.7; 2.7	0.001	6	5; 7	5	3; 7	0.27

*Comparison of light exposure between day and night workers by Students t-test.

Table 5. Geometric mean melatonin concentrations by duration of light exposure above 80 lux 30 minutes prior to saliva sampling during night and day.

Time of day	Duration of light exposure above 80 lux	Mean time of sampling (SD*)	Samples *N*	Participants *N*	Geometric mean melatonin concentration (pmol/L)	95% CI
Night 20:00 – 07:59	< 10 min	01:41 (235)	1142	334	31.8	30.0; 33.7
	10–20 min	01:41 (284)	56	47	16.9	12.6; 22.8
	20–30 min	01:32 (295)	50	45	16.7	12.0.; 23.4
	All samples	01:41 (239)	1248	337	30.1	28.4; 31.9
Day 08:00 – 19:59	< 10 min	13:37 (2273)	667	287	10.7	9:9; 11.6
	10–20 min	13:51 (220)	269	188	10.3	9.1; 11.6
	20–30 min	13:42 (183)	658	270	9.2	8.5; 9.8
	All samples	13:42 (231)	1594	334	10.0	9.5; 10.5
Total	< 10 min	13:53 (440)	1809	338	21.3	20.2; 22.4
	10–20 min	13:54 (269)	325	210	11.3	10.0; 12.7
	20–30 min	13:46 (208)	708	279	9.6	8.9; 10.2
	All samples	13:51 (377)	2842	341	16.2	15.5; 16.9

*SD given as minutes.

Table 6. Crude and adjusted relative difference (%) in salivary melatonin concentration in night workers compared with day workers.

			Crude		Adjusted*	
	Samples *N*	Participants *N*	% difference	95% CI	% difference	95% CI
Work days	1541	322	−17.0	−29.1; −1.6	−16.5	−30.5; −0.2
Days off	1301	301	3.2	−12.8; 22.1	8.5	−9.3; 29.8

*Adjusted for time of day, age, sex, BMI, smoking, diurnal preference and use of antidepressant medication.

Table 7. Adjusted[a] total, direct, and indirect effects of light exposure[b] on the association of night work with salivary melatonin concentration by time of the day. Results from 87 night workers and 254 day workers followed for 24 hours since starting on the work shift.

		Total effect		Direct effect		Indirect effect	
	Samples *N*	% difference	95% CI	% difference	95% CI	% difference	95% CI
Night 20:00 – 07:59	726	−15.0	−31.4; 5.2	−9.6	−27.0; 11.9	−5.9	−10.2; −1.5
Day 08:00 – 19:59	791	−16.2	−34.6; 7.5	−18.3	−36.7; 5.4	3.0	−2.8; 9.1

[a]Adjusted for time of day, age, sex, BMI, smoking, diurnal preference and use of antidepressant medication.
[b]Light exposure is the duration of measurements above 80 lux 30 minutes prior to each saliva sample.

difference in adjusted melatonin concentrations between permanent night workers (n =19) and day workers was −27.4% (95 % CI −47.3; −0.1).

Discussion

The effect of night and day work and the mediating effect of light exposure on melatonin levels have been examined in 254 day workers and 87 night workers. As far as we are aware, we were the first to show a mediating effect of light among night shift workers. Light exposure appeared to mediate a 6% decrease in melatonin concentration during night. On days off, we observed no difference in melatonin concentration between day and night workers. On work days, night workers showed 15–16 % lower salivary melatonin concentrations compared with day workers. When night workers' work days were compared with their days off, melatonin concentrations were 15.4% lower. On days off, we observed no difference in melatonin concentration between day and night workers.

The observation of lower melatonin concentrations on work days, when comparing night workers with day workers, is in agreement with most previous field studies (Davis et al., 2012; Gómez-Acebo et al., 2015; Hansen et al., 2006; Leung et al., 2016; Mirick et al., 2013; Papantoniou et al., 2014; Schernhammer et al., 2004;) except one (Peplonska et al., 2012). This is also the case for the lower melatonin concentration observed on work days compared with days off in our analyses of night workers (Davis et al., 2012; Hansen et al., 2006; Jensen et al., 2016; Leung et al.,

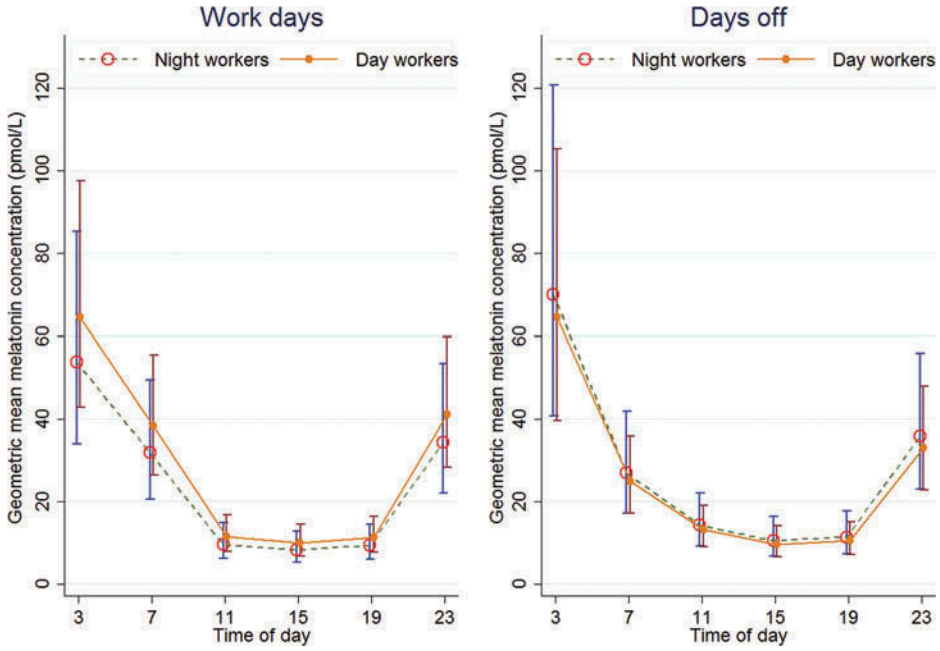

Figure 1. Estimates of geometric mean (95% CI) of salivary melatonin concentrations for day and night workers within 4-hour intervals on work days and days off. The figure shows the estimated melatonin concentrations of a worker with the following characteristics: male 40 year old, BMI=25kg/m^2, non–smoker, no antidepressant medication and morning preference.

2016; Mirick et al., 2013; Yamauchi, 2004), but conflicting results exist (Dumont et al., 2012; Gibbs et al., 2007; Grundy et al., 2011). The similar melatonin concentrations we observed for night and day workers during days off were, however, not in accordance with previous studies (Davis et al., 2012; Hansen et al., 2006; Mirick et al., 2013). This discrepancy may be because we mainly included rotating night workers and that the day off samples of the night workers were collected later after the last night shift (on average 47 hours) than in the referred studies. Our findings are on the other hand in agreement with the recent results of Jensen et al. (2016)

Our observation of lower melatonin levels with higher light exposure during night is partly in line with two previous studies, showing an inverse association between light at night and 24-hour aMT6s (Dumont et al., 2012; Papantoniou et al., 2014). However, Dumont et al. did not find an association with night time melatonin production, and Grundy et al. did not find an association between light exposure and melatonin levels in rotating shift nurses (Grundy et al., 2011).

Our observation of an mediating effect of light at night is as expected from laboratory studies (Bojkowski et al., 1987; Figueiro et al., 2006a; Rea & Figueiro, 2014; Rea et al., 2005; Revell & Skene, 2007). As far as we are aware, we are the first to show a mediating effect among workers on the night shift.

The effects of night work on melatonin concentrations during the daytime were unexplained by light exposure (the direct effect). This may be the result of adaptation to the new work schedule and the altered light, sleep, wake or meal patterns. This is supported by a laboratory study of simulated night work demonstrating melatonin suppression, despite light conditions that were designed not to induce suppression (Dumont & Paquet, 2014).

We observed lower melatonin levels in night workers than in day workers on work days, except between 01:00 and 04:59 h, the latter finding not being expected. This unexpected effect was mainly due to two night workers with melatonin concentrations above 200 pmol/L that disappeared in the adjusted analyses and was probably an accidental finding due to the low number samples in this time period.

Most of the night workers worked rotating shifts and 94 % only worked a single or two consecutive nights during the 7-day study period. Melatonin suppression has been reported to increase with the number of consecutive nights worked (Dumont & Paquet, 2014; Jensen et al., 2016; Leung et al., 2016). A recent field study showed a 5% decrease in salivary

melatonin concentration per night worked (Jensen et al., 2016). The difference in melatonin concentrations observed would therefore likely be larger if the night workers had worked more consecutive nights.

Previous studies, addressing the effect of light exposure on melatonin concentration during night work, classified participants by the mean or median light level without taking threshold or a recent time window into account (Dumont et al., 2012; Grundy et al., 2011; Papantoniou et al., 2014). This may explain why we find a more prominent effect of light than these earlier studies.

In the present study, light measurements were multiplied with a calibration factor before statistical analysis to account for variation between the light monitors (Markvart et al., 2015). Light was measured using the same procedure for all participants with the Actiwatch positioned at the upper arm, but not at eye level as suggested by Figuerio (Figueiro et al., 2013). Because of the Actiwatch positioning, there may have been a difference in perceived light at eyelevel compared to actual measured light exposure. Differences may also arise during certain light conditions due to the mismatch between the spatial and spectral sensitivity of Actiwatch toward a standard classified illuminance sensor (Figueiro et al., 2013; Price et al., 2012). This misclassification of light exposure is probably not only non-differential because light spectra may differ between night and day workers at the same time of the day. However, we expect an overall underestimation of the effects of light on melatonin concentration.

Non-visual light responses, such as circadian rhythm resetting and melatonin suppression, have a distinct spectral sensitivity compared to the visibility curve of the CIE standard observer V(λ) and appear to be most sensitive to blue light (Thapan et al., 2001). Unfortunately, however, there is no consensus of a weighted unit for the non-visual light responses (Lucas et al., 2014). Therefore, the measured light does not equal the circadian effectiveness of the light, and the estimated effect of light may be over or underestimated depending on the present light conditions.

Night work often causes phase delay (Gibbs et al., 2002; Gómez-Acebo et al., 2015; Leung et al., 2016; Papantoniou et al., 2014), and this phase shifting may induce melatonin suppression independent of light, as shown in a study of simulated night work (Dumont & Paquet, 2014). However, our data did not show an interaction between time of day and being a day worker or night worker, except in the analyses of the few permanent night workers. This finding indicates that the difference in melatonin concentration between day workers and rotating night workers was similar across the 24 h day. It also implies that a phase shift did not occur among these night workers, or the effect was masked by other effects (Jensen et al., 2016). Ninety-four % of the night workers collected saliva samples after one or two consecutive night shift, and this may be insufficient to induce a phase shift. It is, however, possible that our 4-hour sampling intervals preclude observing a minor phase shift.

Assessment of melatonin onset under dim light conditions would have made it possible to assess circadian phase because of the masking effect of ambient light. However, since our primary aim was to assess the concentrations of melatonin under real-life circumstances, no lighting conditions were imposed.

Analysis of saliva provided melatonin concentrations at specific time points. We were therefore able to estimate the association of melatonin levels with light exposure during relevant time windows (Bojkowski et al., 1987; Revell & Skene, 2007; Thapan et al., 2001). This is contrary to studies relying on urinary aMT6s measurements, which provide estimates of the cumulated melatonin production between each urine void, and where the effect of light within a shorter period may be diluted.

Salivary melatonin concentrations were analyzed with a LC-MS/MS method. The LOD of this method is lower, than what has previously been possible. Hence, the possibilities to measure melatonin concentrations during the day are better (Jensen et al., 2011). For obvious reasons, participants had to be awake to provide saliva samples. During the night, few samples were collected, especially among the day workers, confidence intervals were wider, and an effect of night work harder to demonstrate. In addition, the relative few samples at night where variation is largest made it difficult to estimate time of the acrophase, and this may add to why we did not observe a phase delay among these predominantly rotating night workers.

We adjusted for several known predictors of melatonin levels, but not for menopausal status, estrogen

medication, parity, or time since last menstrual period, that may affect melatonin concentration (Schernhammer et al., 2006). Night workers were slightly younger and probably had a higher proportion of pre-menopausal women, but this should not have confounded our results because all results were adjusted for age.

Twice as many day as night workers had morning preference. Chronotype has been suggested as an effect modifier, and night workers with morning as well as evening preference (Bhatti et al., 2014; Leung et al., 2016; Papantoniou et al., 2014) have been found to have larger melatonin suppression. Adjustment for diurnal preference did not alter the results in this study; however, the four item question was crude compared to comprehensive chronotype questionnaires.

In the mediation analyses, we conditioned on light exposure and may thus have introduced collider stratification bias if light exposure and melatonin share predictors (mediator-outcome confounders) (Richiardi et al., 2013). Age, sex, BMI, diurnal preference and depression may predict melatonin level (Bhatti et al., 2014; Burgess & Fogg, 2008; Leung et al., 2016; Papantoniou et al., 2014; Schernhammer et al., 2006), possibly also light exposure levels, and we controlled for these factors. However, little is known about individual predictors of light exposure, and residual confounding of the direct effect of night work cannot be excluded.

Conclusions

On work days, night workers showed lower salivary melatonin concentrations compared with day workers. Light exposure seemed to mediate a substantial part of the difference seen during the night, but no mediating effect of light was observed during the day time. On days off, we observed no difference in melatonin concentrations between day and night workers. These findings are in accordance with a transient and partly light-mediated effect of night work on melatonin production.

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Paper III

Indoor, outdoor, and night work and blood concentrations of vitamin D and parathyroid hormone.

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Abstract

Objectives: To examine blood concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) among indoor, outdoor, and night workers and the association with hours spent outdoors on and off work days.

Methods: Blood samples were collected from 425 workers *(*162 indoor, 112 outdoor, 118 rotating night and 33 permanent night workers) throughout all seasons. Serum concentrations of 25OHD and PTH were analyzed by isotope dilution liquid chromatography-tandem mass spectrometry (LC MS/MS) and an automated immune analyzer, respectively. Personal light exposure levels were continuously recorded and used to estimate hours spent outdoors.

Results: Permanent night workers had a 24.6% (95% CI: 11.1; 36.1%) lower 25OHD concentration and a 14.2% (95% CI: 0.2; 30.6%) higher PTH concentration and outdoor workers had a comparable 25OHD concentration but a 7.3% (95% CI: -0.7; 14.7) lower PTH concentration compared to indoor workers. Concentration of 25OHD increased by 5.3% (95% CI: 1.8%; 9.1%) per hour spent outdoor at workdays in the summer.

Conclusion: Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers and employers work organizers should consider the positive effects of outdoor work.

Introduction

The importance of vitamin D in maintaining calcium homeostasis and skeletal health is well established (1). The anti-proliferative and immunomodulatory effects of vitamin D (2, 3) as well as the presence of vitamin D receptors in tissues not related to calcium metabolism (4) suggest that vitamin D has pleiotropic effects beyond calcium metabolism. Epidemiological studies have reported an association between low vitamin D and increased risks of extraskeletal diseases such as colorectal cancer (5), cardiovascular disease (6, 7), multiple sclerosis (8), and allergy (9). Vitamin D insufficiency has been hypothesized to be part of a causal pathway between shift work and cancer (10).

Vitamin D is a fat-soluble pro-hormone mainly derived from synthesis by the skin upon exposure to ultraviolet B radiation (UVB) from sunlight; only a minor part is obtained from foods such as milk, fish, and meat (11). In Denmark (latitude 55-56^{o}N), vitamin D synthesis is only induced by UVB from March till September and summer sun exposure is important for vitamin D concentration around the year (12).

Vitamin D status is defined by plasma concentrations of 25-hydroxyvitamin D (25OHD), but the cut-off value to define vitamin D insufficiency is not yet defined. Concentrations below 50 nmol/L has been considered an appropriate threshold for defining a state of vitamin D inadequacy in terms of skeletal outcomes (13), although it has also been suggested that a sufficient vitamin D status requires concentrations above 75-80 nmol/L (14). Importantly, the optimal 25OHD concentration in non-skeletal health outcomes has not yet been clarified (15). Vitamin D insufficiency is

common worldwide, also in Denmark where studies have suggested a prevalence of vitamin D insufficiency as high as 52.2% among healthy adults (16).

Previous studies have found higher 25OHD concentrations among outdoor workers (17-19) and lower concentrations among night workers compared to day worker (20-22). However, studies do not agree (23-25).

Parathyroid hormone concentrations (PTH) are inversely correlated with 25OHD concentrations. A rise in PTH signals that insufficient 25OHD concentrations start to negatively affect bone metabolism (26). The 25OHD concentration at which PTH concentrations start to increase has substantial inter-individual variation. Increased PTH concentrations have independently of 25OHD concentrations been associated with increased risk of fractures (27), cardiovascular disease (28), and overall mortality (29).

As vitamin D insufficiency is common, easily treatable and may have major health consequences for the individual, it is important to identify current risk factors for vitamin D insufficiency. Low 25OHD concentrations in indoor and night workers may be explained by limited exposure to sunlight during work and leisure time, differences in intake of vitamin D supplement, dietary habits, or lifestyle factors. The aim of this study was to examine blood concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) among indoor, outdoor, and night workers and the association with hours spent outdoors on and off work days.

Material and methods

Study set up

Participants were recruited through employers and public advertisements in magazines and on webpages aiming at recruiting an equal numbers of indoor, outdoor and night workers.

A research assistant met the participants at their place of work, provided instructions, handed out a questionnaire to get data on background characteristics and collected a blood sample. For continuous measurement of light levels, participants wore a light recorder during seven days both at and off work. Data was collected from March 2012 until May 2013. All participants gave written informed consent and the study was approved by the Danish Data Protection Agency (J.nr. 2011-41-6850) and the Central Denmark Region Committee on Health Research Ethics (M-20110214). Further details of the study design are presented elsewhere (30).

Population

A total of 535 participants were recruited and 459 provided a blood sample. Samples of eight participants could not be analysed due to insufficient blood volume. Twenty-six participants were excluded due to medical conditions or treatment potentially affecting calcium homeostasis and vitamin D metabolism: use of thiazide diuretics (n=10), pregnancy (n=7), suspected primary hyperparathyroidism (serum calcium and plasma PTH above normal) (n=2), anticonvulsants (n=1), systemic glucocorticoids (n=1), estimated glomerular filtration rate (eGFR) < 60 ml/min and metastasised breast cancer (n=1). The final population comprised 425 participants with complete confounder information except for 12 participants with missing information on body

mass index (BMI).

Indoor workers were defined as those working daytime only and working ≤ 9 hours outdoor per week during the summer (June-August) (n=162). *Outdoor workers* were defined as working daytime only and outdoors > 9 hours/week during the summer (n =112). *Night workers* were defined as working more than three hours between 00:00h and 05:00 h on a permanent (n=33) or rotating shift work basis (n=118) (31). Classification of participants into the above job groups was based on questionnaire data.

For analyses including hours spent outdoors, we only included workers who participated from April throughout September (n=227) where UVB exposure induces production of vitamin D production. We excluded 39 workers with missing information on either BMI, hours spent outdoors on or off work leaving 186 workers for analysis (81 indoor workers, 44 outdoor workers, 46 rotating shift workers, and 15 permanent night workers).

Blood samples

Blood samples were drawn at participants' place of work and collected in tubes without anticoagulation for serum and EDTA tubes for plasma and stored at 5^{o}C until processed to separate serum and plasma. Most samples (n = 407) were processed within eight hours (mean 3 hours 48 minutes), 30 samples were processed 10-33 hours after collection, and four samples were processed 94 hours after collection due to technical problems. Samples were stored at -80^{o}C after processing.

Biochemical analyses

All biochemical analyses were carried out in September 2014. Serum concentrations of 25OHD ($25(OH)D_2$ and $25OHD_3$) were analysed by isotope dilution liquid chromatography-tandem mass spectrometry (LC MS/MS) as described by Maunsell et al. (32). Calibrators were traceable to NIST SRM 972 (Chromsystems DE). The coefficient of variation (CV) for 25OHD3 was 6.4% at concentration 66.1 nmol/l and 9.4% at 25.3 nmol/l. Plasma PTH concentration was analysed using an automated immune analyzer (Cobas 6000 E; Roche Diagnostics, GmbH). The CV was 3.3% and 2.7% at PTH concentrations of 7.7 and 26.6 pmol/l, respectively. Standard laboratory methods were used for measurements of total calcium, creatinine, and albumin. The estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) study equation (33).

Questionnaire

The questionnaire included information on sex, age (years), pregnancy (yes/no), current occupation, time spent working outdoors in spring, summer, autumn, and winter (never, 1-4 hours/week, 5-9 hours/week, 10-19 hours/week, 20-29 hours/week, 30-39 hours/week, 40+ hours/week), height (centimeters), weight (kilograms), smoking (current/former/never), use of medication (yes/no), vitamin pill use (yes/no), vitamin D supplement use (no/ 10 µg/20 µg or more or cod liver oil (yes/no), tanning bed use (weekly, monthly, never), consumption of fish and shell food (never, monthly, 1 meal/week, 2-3 meals/week, > 4meals/week).

Light exposure assessment

Participants wore a Philips Respironics Actiwatch Spectrum (Actiwatch) light recorder during a 7-day study period outside clothes on the upper arm and set to one-minute sampling epochs and recorded white light (lux). Time spent outdoors was assessed as periods where the light intensity measured by the Actiwatch was 1000 lux or higher (34). Light measurements were considered not valid if the participants reported the Actiwatch was not worn or the Actiwatch recorded no physical activity for at least 20 minutes. We excluded 270 work days (26.5%) and 126 days off work (25.3%) with less than 80% valid light measurements between 07:00-19:00. Light measurements were included from 748 work days and 373 days off work.

Statistical analyses

Data was presented as numbers (%), means with standard deviations (SD)**,** or medians with interquartile (25th-75th percentiles) ranges. Concentrations of 25OHD and PTH were naturally log transformed to obtain the best approximation with normal distributions. We tested the difference of 25OHD and PTH concentrations across seasons and job groups using the Kruskal-Wallis test.

We used multivariable linear regression to estimate the relative difference of serum 25OHD and plasma PTH concentrations between outdoor, rotating night workers and permanent night workers relative to indoor workers. Models were adjusted in two steps: Model 1 included season (January-March/April-June/July-September/October-December). Model 2 also included age (continuous), sex, socio-economic status (SES) (white collar worker/ skilled blue collar worker/unskilled blue collar worker), current smoking (yes/no), BMI (continuous), vitamin D supplements or cod liver oil

(yes/no), fish and shell food consumption (< 1 meal/week/ ≥ 1 meal/week), tanning bed use (ever/never), and time from blood sampling to storage. These potential confounders were identified a priori based on a review of the literature (16, 27, 35-38). There was no interaction between job group and month of sampling, and the interaction term was thus not included.

We used logistic regression to estimate the odds ratio (OR) with 95% confidence interval (95% CI) for vitamin D insufficiency (< 50 nmol/L) and hyperparathyroidism (> 6.9 pmol/L). These analyses included the same covariates as in the linear regression models.

In linear regression analyses of the effect of time spent outdoors on 25OHD concentration, we only included the 186 workers who participated from April-September. We conducted three linear regression models; (1) job group only (2) outdoor hours on work days and days off work and (3) job group and outdoor hours on work days and days off work. These analyses were adjusted for month of sampling; otherwise covariates were similar to the previous analyses.

All analyses were carried out using STATA 13.0 (StataCorp, College Station, Texas).

Results

Prevalence of smoking was highest among outdoor and permanent night workers (Table 1). Use of vitamin D supplements was most prevalent among rotating shift and permanent night workers and least prevalent among outdoor workers. Fish and shell food consumption was lowest among permanent night workers. Indoor workers mainly participated from April-June, rotating night workers from October till December, while no permanent night workers participated July-September. Outdoor workers' participation was more equally distributed across seasons. Time from blood sampling to storage exceeded 24 hours in 33 % of the permanent night workers while this was not the case for any indoor or outdoor workers. In the sub- population of workers participating from April-September, permanent night workers had a higher mean BMI (26.5 kg/m^2 ±3.3) than indoor (24.1 kg/m^2 ±3.8), outdoor (25.4 kg/m^2 ±4.8), and rotating night workers (25.1 kg/m^2 ±5.0). Otherwise, socio-demographic characteristics were equivalent to the total population. In the sub-population, outdoor workers spent the longest time and permanent night workers the shortest time outdoors on work days. Permanent night workers also spent the shortest time outdoors on days off, but exposure in the other three groups was comparable.

Table 2 shows median 25OHD and PTH concentrations and prevalence of vitamin D insufficiency and hyperparathyroidism by job group and season. Within all job groups, 25OHD concentrations were highest and prevalence of vitamin D insufficiency lowest during July-September (no measurements available from permanent night workers). The prevalence of vitamin D insufficiency was highest from January-March (56.6%) and lowest from July-September (3.6%). From July-December, indoor workers had higher median 25OHD concentrations (68.8-95.8

nmol/L) than outdoor workers (58.8-78.8 nmol/L). Otherwise indoor, outdoor and rotating night workers had comparable 25OHD concentrations. From January-June, permanent night workers had significantly lower median 25OHD concentrations than the other job groups (19.2-36.4 nmol/L). PTH concentrations did not vary significantly within the job groups across seasons.

Table 3 presents results from the multivariable linear regression model of the relative difference in 25OHD and PTH concentrations between the four job groups. Outdoor workers had a 4.5% (95% CI -6.1; 14.1) lower and permanent night workers a 28.4% (95% CI: 11.1; 36.1%) lower 25OHD concentration than indoor workers in the season-adjusted analyses. When also adjusting for use of vitamin supplements and other expected predictors of 25OHD and PTH concentrations, outdoor workers showed a 2.0% (-7.9; 13.0) higher 25OHD concentration than indoor workers, while the result for permanent night workers only changed slightly.

Analyses of PTH concentration showed a 23.6% increased concentration for the permanent night workers in the model only adjusted for season. When further adjusted this estimate attenuated to 14.2 % difference. A decrease of approximately 7% in PTH concentrations was suggested for outdoor workers in both models. Otherwise limited differences were seen between the four job groups.

Table 4 presents job groups and OR for vitamin D insufficiency and hyperparathyroidism. Permanent night workers had a four-fold (OR=4.16 (95% CI: 1.29; 13.33)) higher odds of vitamin D insufficiency and outdoor workers tended to have lower (OR=0.29 (95% CI: 0.08; 1.04)) odds of hyperparathyroidism and perhaps

also of vitamin D insufficiency (OR=0.85, 95% CI 0.43-1.70) compared with indoor workers.

Table 5 presents the relative difference (%) in 25OHD concentrations between job groups and per hour spent outdoors in the sub-population (workers participating from April throughout September)**.** The adjusted model of job groups not including variables for outdoor hours showed a 7.8 % (95% CI: -6.0; 22.4%) higher concentration of 25OHD among outdoor workers and a 7.6% (95% CI: -18.6; 4.9%) and 15.3% (95% CI: -32.1; 5.7%) lower concentrations among rotating and permanent night workers compared with indoor workers. The adjusted model of hours spent outdoor showed a 5.3% (95% CI: 1.8; 9.1%) increase in 25OHD concentrations per hour spent outdoors on work days but only a limited increase by hours spent outdoors on days off. The final model that included outdoor hours and job group showed attenuated estimates for outdoor and permanent night workers compared with the model that did not include outdoor hours, while the effect for rotating night workers was limited.

PTH concentrations did not change by number of outdoor hours/day (data not shown).

Discussion

In the present cross-sectional study, permanent night workers had lower 25OHD and higher PTH concentrations than indoor workers. Outdoor workers tended to have a higher 25OHD concentration during summer and a lower PTH concentration irrespective of season than indoor workers. Workers with rotating night work had comparable 25OHD and PTH concentrations with indoor workers. 25OHD concentrations increased significantly by hours spent outdoors on workdays from April throughout September. The observed differences between permanent night workers, outdoor workers and indoor workers were significantly reduced in models that included time spent outdoors. This indicates that it was a significant predictor for the differences observed between the job groups.

In total, 151 (35.5%) of the participants had vitamin D insufficiency in terms of 25OHD concentrations below 50 nmol/L. As expected, prevalence was highest from January-March (56.6%), lowest from July-September 3.6% and comparable to previous findings among healthy Danes (16, 26, 39). Among indoor workers, the prevalence of vitamin D insufficiency was lower than in previous studies (21, 25, 40), but 25OHD concentrations were comparable with most previous studies (18, 19, 21, 22, 25, 40, 41) though mean 25OHD concentrations during the summer were lower in some of the studies (18, 24, 25, 40).

In contrast to most previous findings, the outdoor workers in the present study did not have higher 25OHD concentrations than indoor workers all year round but only during the summer (17-19). One explanation to this may be that outdoor workers in our study spent shorter time outdoors during summer (4½ hours on work days

according to the light recordings). Our findings are, however, in line with a recent Danish study (25) reporting similar 25OHD concentrations in outdoor working farmers and their indoor working spouses.

In accordance with our results, 25OHD concentrations did not differ between indoor and rotating night workers in some previous studies (23, 24), but 25OHD concentrations were lower among rotating night workers in other studies (21, 22). Among permanent night workers, lower 25OHD concentrations were, in agreement with our results, found among women compared to day working women, whereas no difference was observed between permanent night workers and day workers among men and a mixed population (20, 23).

Average PTH concentrations were higher among permanent night workers and lower among outdoor workers compared to indoor workers; this underpins both the adverse and positive effects of 25 OHD seen for these two job groups. To our knowledge, the association between PTH concentrations and day and night work has not previously been studied.

Despite spending more time outdoors, outdoor workers had similar 25OHD concentrations as indoor workers around the year. However, the effect estimate was higher in the summer, though not statistically significant. Moreover, there was no statistical interaction between job group and season, which may be caused by lack of statistical power. This may indicate a positive effect of outdoor work during summer, that did not last throughout the year, and that indoor workers compensate for fewer hours spent outdoors on workdays, by a lower prevalence of smoking, more use of

supplementary vitamin use, and higher socioeconomic status, but not compensating by spending more hours outdoors on days off work during the summer as in the study population of this study.

High UVB exposure can degrade newly produced vitamin D present in the skin (42), and may be another explanation for the lack of a difference between indoor and outdoor workers. The conflicting results in this and other studies (17-19) may also be explained by differences in length of workdays, dressing habits, use of sun protection and definition of outdoor work.

Among rotating night workers, 25OHD and PTH concentrations did not differ from indoor workers; this is in line with some (23, 24), but not all previous studies (21, 22). The rotating shift workers in this study were mainly health care workers, who may have a healthier vitamin D lifestyle than factory workers (22), which counteracts the lower exposure to day light on work days.

The concentration of 25OHD increased with hours spent outdoors on summer days. Studies on self-reported time outdoor have reported both similar (21, 43) and conflicting results (40, 44). In contrast to our study, a Danish study among farmers only found an association between mean daily UVR dose on days off work, but not on work days (25). This finding could perhaps be explained by farmers currently spending much of the workdays inside tractors and other vehicles, where the measured UVR mainly consists of UVA radiation, which does not induce 25OHD synthesis. No association was found between hours spent outdoors and PTH

concentrations, probably because of sufficient 25OHD production during the sunny part of the year and a maximal suppression of PTH.

The threshold value of 50 nmol/l used to define vitamin D insufficiency is based on the 25OHD concentrations, where PTH start to increase in different populations (45). However, the relevant 25OHD concentrations for vitamin D insufficiency differ between individuals (27), as not all subjects with 25OHD < 50 nmol/L show signs of vitamin D insufficient in terms of e.g. elevated PTH concentrations. The optimal 25OHD concentration with respect to extra-skeletal diseases is unknown, but has been suggested to be 75 nmol/l (14). The implication would be a higher prevalence of participants with vitamin D concentrations that are harmful to health.

Strengths and limitations

The study was cross-sectional and results should be interpreted cautiously regarding causality. However, it is not very likely that vitamin D concentrations influenced participants' decision on whether to work during the day or night. Serum 25OHD and plasma PTH concentrations were measured with the most precise laboratory methods. We excluded subjects with medical conditions or treatment with drugs potentially affecting calcium homeostasis and vitamin D metabolism. Further, we used objective measures of light to assess time spent outdoors. We adjusted for a wide range of known predictors of vitamin D concentrations, but some residual confounding can not be excluded.

Conclusion

Permanent night workers had lower 25OHD and higher PTH concentrations and outdoor workers higher 25OHD concentration during summer and lower PTH concentrations around the year compared with indoor workers. The concentration of 25OHD increased by hours spent outdoor during summer and differences between job groups were partly explained by differences in time spent outdoor. Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers, and employers should consider the positive effects on health of outdoor work.

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Declaration of interest

All authors declare no conflicts of interest.

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Table 1 Characteristics of the population

	Indoor workers N = 162				Outdoor workers N = 112				Rotating shift workers N = 118				Permanent night workers N = 33			
Characteristics	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD
Age			45.3	11.0			40.8	12.6			39.3	9.3			44.9	8.6
BMI [1]			24.0	3.8			25.8	4.8			24.7	4.6			25.7	3.2
Gender																
Female	123	75.9			58	51.8			113	96.3			17	51.5		
Male	39	24.1			54	48.2			5	4.2			16	48.5		
SES																
White collar worker	135	83.3			64	57.1			116	98.3			14	42.4		
Skilled blue collar worker	19	11.7			45	40.2			2	1.7			12	36.4		
Unskilled blue collar worker	8	5.0			3	2.7			0	0.0			7	21.2		
Current smoking																
No	141	87.0			82	73.2			105	89.0			24	72.7		
Yes	21	13.0			30	26.8			13	11.0			9	27.3		
Supplementary vitamin D use[1]																
No	103	63.6			79	70.5			72	61.0			19	57.6		
Yes	59	36.4			33	29.5			46	39.0			14	42.4		
Fish and shell food consumption																
< 1 meal/week	60	37.0			42	37.5			48	40.7			18	54.6		
≥ 1 meal/week	102	63.0			70	62.5			70	59.3			15	45.5		
Tanning bed use																
Never	158	97.5			107	95.5			111	94.0			30	90.9		
Ever	4	2.5			5	4.5			7	6.0			3	9.1		
Season of participation																
January-March	45	27.8			32	28.6			15	12.7			7	21.2		
April-June	73	45.1			36	32.1			39	33.1			20	60.6		
July-September	20	12.4			23	20.5			16	13.6			0	0.0		
October-December	24	14.8			21	18.8			48	40.6			6	18.2		
Hours from blood sampling to storage																
0-24 hours	162	100			112	100			111	94.1			22	66.6		
> 24 hours	0	0			0	0			7	5.9			11	33.3		
Minutes outdoor/day[3] [4]																
Work days	81		147	89	44		261	120	46		107	68	15		122	59
Days off	81		186	117	44		182	113	46		190	105	15		152	92

[1] 12 missing [2] Cod liver, multivitamin or vitamin D [3] An outdoor minute defined as a minute with light exposure above 1000 lux between 07:00 h and 19:00 h
[4]Information only provided for the subpopulation (N=186) of workers participating from April throughout September

Table 2. Median serum 25-hydroxyvitamin D 25OHD concentration, parathyroid hormone (PTH) concentration in plasma and percentage with vitamin D insufficiency (<50nmol/L) and hyperparathyroidism (>6.9pmol/L) by season and job group with interquartile (25^{th}–75^{th} percentile) range (IQR) and *p*-values for any difference between groups and seasons among 425 indoor, outdoor and night workers.

	Indoor workers (N=162)				Outdoor workers (N=112)				Rotating night workers (N=118)				Permanent night workers (N=33)					
		Concentration		Prev[1]		Concentrations		Prev.[1]		Concentrations		Prev[1]		Concentrations		Prev[1]	Conc.	Prev[1]
Season	N	Median	IQR	%	N	Median	IQR	%	N	Median	IQR	%	N	Median	IQR	%	*p*-value[2]	*p*-value[3]
25OHD (nmol/L)																		
January-March	45	46.9	28.5-64.7	55.6	32	48.8	31.7-64.5	56.3	15	48.0	37.4- 62.8	53.3	7	19.2	11.3-81.7	71.4	0.575	0.872
April- June	73	58.6	43.6-77.5	37.0	25	58.8	40.3-73.9	36.1	39	58.1	46.9-80.3	33.3	20	36.4	27.8-47.6	80.0	0.008	0.016
July-September	20	95.8	78.3-105.5	0.0	26	78.4	61.9-92.4	8.7	16	84.7	72.7-94.6	0.0	0	-	-	-	0.082	0.203
October-December	24	68.8	57.8-81.2	16.7	26	56.5	50.1-70.8	23.8	48	68.3	44.1-91.4	29.2	6	76.6	69.8-83.7	16.7	0.204	0.836
p-value[4]		<0.001		<0.001		<0.001		0.002		0.001		0.012		0.050		<0.001		
PTH (pmol/L)																		
January-March	45	4.6	3.6-5.7	13.3	32	3.9	3.7-4.8	3.2	15	3.5	3.4-4.2	0.0	7	4.8	4.0-6.3	14.3	0.071	0.225
April- June	72	4.5	3.4-5.6	9.6	36	4.1	3.5-5.1	0.0	39	4.4	3.6-5.3	10.3	20	5.7	4.6-6.3	15.0	0.025	0.191
July-September	20	4.4	3.6-5.0	0.0	23	4.1	3.4-4.9	4.4	16	4.7	3.6-5.8	18.8	0	-	-	-	0.513	0.074
October-December	24	4.1	3.4-5.5	4.2	21	4.5	3.6-6.1	9.5	48	4.6	3.5-5.6	8.3	6	5.5	4.6-7.2	33.3	0.224	0.175
p-value[4]		0.726		0.282		0.573		0.318		0.201		0.349		0.691		0.577		

[1]Prevalence of vitamin vitamin D insufficiency (<50nmol/L) and hyperparathyroidism (>6.9 pmol/L)

[2] Kruskal-Wallis test of any difference in concentrations between job groups

[3] Kruskal-Wallis test of any difference in prevalence of vitamin D insufficiency/hyperthyroidism between job groups

[4] Kruskal-Wallis test of any difference between seasons

IQR: Interquartile range

Table 3. Relative differences (%) in serum 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) concentrations in plasma between 425 outdoor, rotating night, permanent night and indoor workers

		Model 1[1]		Model 2[2]	
Job group	N	% difference	95% CI	% difference	95% CI
25OHD					
Indoor workers	162	0.0	Reference	0.0	Reference
Outdoor workers	112	-4.5	-14.1 ; 6.1	2.0	-7.9 ; 13.0
Rotating night workers	118	-1.9	-11.8 ; 9.1	-4.8	-14.1 ; 5.4
Permanent night workers	33	-28.4	-39.2 ; -15.7	-24.6	-36.1 ; -11.1
PTH					
Indoor workers	161	0.0	Reference	0.0	Reference
Outdoor workers	112	-7.1	-14.2 ; 0.6	-7.3	-14.7 ; 0.7
Rotating night workers	118	-1.3	-8.9 ; 7.0	0.4	-7.6 ; 9.1
Permanent night workers	33	23.6	9.2 ; 39.8	14.2	-0.2 ; 30.6

[1] Adjusted for season

[2] Adjusted for season, sex, age, SES, use of vitamin D supplements, BMI, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to freezing.

Table 4. Risk of vitamin D insufficiency (< 50nmol/L) or hyperparathyroidism (> 6.9 pmol/L) in outdoor and night workers relative to indoor workers among 425 workers.

		Model 1[1]		Model 2[2]	
Job group	N	OR	95% CI	OR	95% CI
Vitamin D insufficiency					
Indoor workers	162	1.00	Reference	1.00	Reference
Outdoor workers	112	1.15	0.66 ; 1.99	0.85	0.43 ; 1.70
Rotating night workers	118	1.11	0.63 ; 1.95	1.15	0.57 ; 2.35
Permanent night workers	33	3.61	1.59 ; 8.20	4.16	1.29 ; 13.33
Hyperparathyroidism					
Indoor workers	161	1.00	Reference	1.00	Reference
Outdoor workers	112	0.39	0.12 ; 1.21	0.29	0.08 ; 1.04
Rotating night workers	118	1.06	0.45 ; 2.51	1.26	0.47 ; 3.36
Permanent night workers	33	2.37	0.83 ; 6.81	2.20	0.60 ; 8.06

[1] Adjusted for season

[2] Adjusted for season, sex, age, SES, use of vitamin D supplements, BMI, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to freezing.

Table 5. Relative difference (%) in 25-hydroxyvitamin D concentrations with and without adjustment for hours spent outdoor/day[1] among 186 workers participating from April throughout September

		Model with job group only [2]		Model with outdoor hours only[2]		Model with job group and outdoor hours[2]	
Variables (% difference)	N	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Job group							
Indoor worker	81	0.0	Reference	-	-	0.0	Reference
Outdoor worker	44	7.8	-6.0; 22.4	-	-	-1.2	-15.0; 14.5
Rotating night worker	46	-7.6	-18.6; 4.9	-	-	-5.3	-17.4; 8.7
Permanent night worker	15	-15.3	-32.1; 5.7	-	-	-9.3	-28.2; 15.6
Outdoor hours[1]/day (% difference per hour/day)							
Work days	186	-	-	5.3	1.8; 9.1	4.9	0.7; 9.2
Days off	186	-	-	1.2	-1.9; 4.3	1.3	-1.8; 4.5

[1] Defined as light measurements above 1000 lux

[2] Adjusted for month, sex, age, socio-economic status, use of vitamin D supplements, BMI, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to storage.

Paper III

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Declaration of co-authorship

Full name of the PhD student: Stine Daugaard Pederseb

This declaration concerns the following article/manuscript:

Title:	Night work, light exposure and melatonin on work days and days off
Authors:	Stine Daugaard, Anne Helene Garde, Jens Peter Ellekilde Bonde, Jens Christoffersen, Åse Marie Hansen, Jakob Markvart, Vivi Schlünssen, Debra J. Skene, Helene Tilma Vistisen, Henrik A. Kolstad

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If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. No or little contribution
B. Has contributed (10-30 %)
C. Has contributed considerably (40-60 %)
D. Has done most of the work (70-90 %)
E. Has essentially done all the work

Element	Extent (A-E)
1. Formulation/identification of the scientific problem	D
2. Planning of the experiments and methodology design and development	B
3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	D
5. Writing of the first draft of the manuscript	E
6. Finalization of the manuscript and submission	D

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3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	D
5. Writing of the first draft of the manuscript	E
6. Finalization of the manuscript and submission	D

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Full name of the PhD student: Stine Daugaard Pederseb

This declaration concerns the following article/manuscript:

Title:	Night work, light exposure and melatonin on work days and days off
Authors:	Stine Daugaard, Anne Helene Garde, Jens Peter Ellekilde Bonde, Jens Christoffersen, Åse Marie Hansen, Jakob Markvart, Vivi Schlünssen, Debra J. Skene, Helene Tilma Vistisen, Henrik A. Kolstad

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C. Has contributed considerably (40-60 %)
D. Has done most of the work (70-90 %)
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4. Interpretation of the results	D
5. Writing of the first draft of the manuscript	E
6. Finalization of the manuscript and submission	D

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Full name of the PhD student: Stine Daugaard Pedersen

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14/8 17	LARS REJNMARK	
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E. Has essentially done all the work

Element	Extent (A-E)
1. Formulation/identification of the scientific problem	D
2. Planning of the experiments and methodology design and development	B
3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	D
5. Writing of the first draft of the manuscript	E
6. Finalization of the manuscript and submission	D

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Signatures of the co-authors

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Date: 24/8-17

Signature of the PhD student