Shift work: Weight change and lifestyle factors

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Thesis for the degree of Philosophiae Doctor (PhD)
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SCIENTIFIC ENVIRONMENT

I have been employed at the Department of Global Public Health and Primary Care, Faculty of Medicine, University Bergen, Norway, as a PhD student from 2015 to 2019. From 2017 to 2019, I have also been affiliated with the Norwegian Research School in General Practice (NAFALM). This PhD project was financed by The Norwegian Research Fund for General Practice.

My main supervisor has been Professor Bjørn Bjorvatn at the Department of Global Public Health and Primary Care, Faculty of Medicine, University Bergen. My first co-supervisor has been Professor Ståle Pallesen at the Department of Psychosocial Science, Faculty of Psychology, University Bergen. My second co-supervisor has been Post-doctor Siri Waage at the Department of Global Public Health and Primary Care, Faculty of Medicine, University Bergen. Bjørn Bjorvatn, Siri Waage, and Ståle Pallesen are also affiliated with the Norwegian Competence Center for Sleep Disorders at Haukeland University Hospital.

ACKNOWLEDGEMENTS

All talk of circadian rhythm
I see today with a newsprint fray
My night is colored headache gray
Daysleeper, Daysleeper, Daysleeper
REM – Daysleeper

Completing a PhD is a challenging endeavor. The road to earning a PhD degree can be long and winding for all those who embark on such a tough task. On a personal level, I believe this project encompasses the whole range of emotions: joy, mastery, anger, fear, despair, and even pain. Now that the work is almost completed, I feel proud and exhausted.

This project would never have been possible if I had not been standing on the shoulders of giants. The shoulders that I have leaned on the most are those of my main supervisor professor **Bjørn Bjorvatn**. You are a patient man, because at times I believe I have tested your patience to the full extent. I apologize for this, but at the same time offer my gratitude for your guidance and advice along the way. Your clear insights, experience, and strong analytical skills have challenged me repeatedly. Because you have always been constructive in your critiques, I have never doubted that your feedback was grounded in a sole desire to help me succeed in this project. Without you this would not have been possible.

The sleep research milieu in Bergen has excellent academic standards and hosts the Norwegian Competence Center for Sleep Disorders. I extend a special thanks to my co-supervisors **Ståle Pallesen** and **Siri Waage** for being available, generous with good advice, and always quick to respond when called upon. In this regard, I also wish to extend my gratitude to the additional co-authors on the papers in this thesis: **Bente Elisabeth Moen** and **Nicolas M. F. Øyane**. Beyond academic merits, the sleep research milieu in Bergen is one of the most socially inclusive and supportive groups I have encountered. I have so many great memories and encounters: **Kjersti, Eirunn, Kristine, Tom, Ingvild, Anette**, and **Øystein**, thank you! I had the privilege of attending NAFALM. Being a NAFALM student was a great opportunity to learn from other Norwegian general practitioners from all over the country. These meetings broadened my perspective and enabled me to build relationships beyond the University of Bergen.

Doing a PhD project and being a general practitioner are challenging. The last few years have been a trilemma for me—a constant struggle between being a father, a primary care doctor, and a PhD candidate. Difficult tasks cannot be solved without support. **Henrik** and **Marit**, my parents in law, thank you for your support. I am especially grateful for the support from my mother, **Magda**, and father, **Sigurd**, for all the help during this project. Thanks for the effort and support you have put in throughout the years. My upbringing was a perfect blend of joy, challenges, support, and individual responsibility. I thank my father for his continuous effort to incorporate a positive self-belief in me and for showing me the power of a strong work ethic perhaps best paraphrased in the quote: ”Happy are those who dream dreams and are ready to pay the price to make them come through.” I thank my mother for her self-sacrifice and support, and, thus, laying the foundation for meaningful work and private lives for me and my brother.

I am especially thankful to my wife, **Johanne**, just for putting up with me and always being there. So far our relationship has been characterized by growth when life’s adversities have faced us. I hope this is our common trajectory. I am also thankful to my kids, **Bertine** and **Henrik,** for being two wonderful kids who enjoy spending time with their father and mother. When time comes, I hope they also have the opportunity to dream dreams and have the work ethic to see them through.

ABSTRACT

Our society is dependent on 24hour services: healthcare, transportation, law enforcement, and fire services, as well as an ever-expanding service sector. The employees who contribute to these 24hour services, collectively called *shift workers*, suffer the cost of working outside regular daytime hours. Beyond acute health effects such as disturbed sleep and disrupted circadian rhythms, research has unveiled adverse long-term health consequences of shift work, for example, in terms of cardiometabolic health.

In this thesis, we examine possible effects of shift work on body-weight related outcomes and lifestyle factors: smoking habits, alcohol consumption, caffeine consumption, and exercise habits. The data used in all three papers stems from The SUrvey of Shift work, Sleep and Health (SUSSH). SUSSH is a large cohort of Norwegian nurses that was initiated in late 2008. The overall aim of SUSSH was to examine possible adverse health consequences of shift work.

In paper 1, we investigated possible associations between cumulative night shift exposure and adverse consequences to body weight and lifestyle factors. The cross-sectional data, consisting of 2059 nurses, was extracted from the first wave of SUSSH. The number of self-reported night shifts worked last year (NNL) was used as an operationalization of night work load. Body Mass Index (BMI), obesity (BMI>30), smoking habits, alcohol consumption (Alcohol Use Disorders Identification Test Consumption (AUDIT-C)), caffeine consumption and exercise habits were used as outcome variables and analyzed separately. NNL was found to be significantly and positively associated with BMI, both when evaluated against BMI as a continuous parameter (β =0.055, $p<0.05$), and when evaluated against obesity (OR=1.01(1.00-1.01)). The AUDIT-C score was found to be significantly and positively associated with hours worked per week, but not with NNL.

In paper 2, we build on the main finding from paper 1 and investigated prospective changes in BMI between nurses in different work schedules and changes in BMI and differences in cumulative night shift exposure over a four-year follow-up period.

Nurses (n=1244) who reported their work schedules at both baseline and follow-up were included; pregnant nurses at baseline or follow-up were excluded. The shift schedules included were: day-only, two-shift rotation (day and evening shifts), three-shift rotation (day, evening and night shifts), night-only, those who changed to schedule containing night shifts, and those who changed away from schedules containing night shifts. We found that night-only workers, two-shift workers, three-shift workers, and those who changed work schedule away from- or towards night work all had significant BMI gain during the follow-up period. Day-only workers had a non-significant BMI gain. In our multiple linear regression model, we found that night-only workers had significantly larger BMI gain compared to day-only workers (β=0.89 (0.06-1.72)), $p<0.05$). We did not find any significant association between average yearly number of night shifts (NNs) and BMI using our regression model. Overall, we concluded that night-only workers had significantly larger weight gain than day-only workers.

Paper 3 builds on paper 1 in terms of lifestyle factors. In paper 3, we addressed the relationship between shift work and lifestyle factors using a prospective design with six-year follow-up. This subcohort of nurses consisted of 1371 nurses. Different work schedule groups (day workers, night workers, workers starting- and stopping working night shifts), quick returns (≤11h between consecutive shifts; QRs), and NNs were evaluated for their possible effects on changes in caffeine consumption, smoking habits, alcohol (AUDIT-C), and exercise habits. Day workers and the groups with the lowest exposure to QRs (<5) and NNs (<1) were used as contrasts in the respective analyses. A significant increase in caffeine consumption was found across all work schedule groups. Furthermore, declines in smoking prevalence were found among all groups, although they were not significant for those who changed work schedules towards- or away from night shifts. Day workers had a significant increase in the AUDIT-C score. No work schedules were associated with changes in exercise habits. However, our main finding was negative: we did not find any significant between-group differences regarding work schedules, QRs, or NNs on any of the lifestyle factor trajectories.

In conclusion, we investigated different characteristics of shift work and changes to body-weight in paper 1 and paper 2. Our findings suggest that night work contributes to weight gain. However, paper 2 failed to replicate paper 1 in terms of a clear dose-response relationship between cumulative night shift exposure and weight gain. The overall conclusion from paper 1 and paper 3, contrary to our a priori hypothesis, is that we did not find any large differences between different lifestyle factors and particular shift work characteristics. Our findings challenge the hypothesis often supported by models trying to elucidate causal pathways between shift work and adverse health consequences. These models often incorporate lifestyle and behavioral factors along a potential causal pathway in conjunction with circadian disruption and insufficient sleep.

LIST OF PUBLICATIONS

1. Buchvold, H.V., Pallesen, S., Øyane, N.M., Bjorvatn, B. Associations between night work and BMI, alcohol, smoking, caffeine and exercise - a cross-sectional study. BMC Public Health 2015;15:1112. https://doi.org/10.1186/s12889-015-2470-2.

2. Buchvold, H.V., Pallesen, S., Waage, S., Bjorvatn, B. Shift work schedule and night work load: Effects on body mass index - a four-year longitudinal study. Scand J Work Environ Health 2018;44(3):251–257. https://doi.org/10.5271/sjweh.3702.

3. Buchvold, H.V., Pallesen, S., Waage, S., Moen, B.E., Bjorvatn, B. Shift Work and Lifestyle factors: A 6-Year Follow-Up Study Among Nurses. Front. Public Health. 2019;7:281. https://doi.org/10.3389/fpubh.2019.00281.

The publications will be referred to with their corresponding numbers: **Study 1**, **Study 2**, and **Study 3**.

LIST OF TABLES AND FIGURES

LIST OF ABBREVIATIONS

AASM: American Academy of Sleep Medicine

ANOVA: Analysis of Variance

AUDIT-C: Short Form of the Alcohol Use Disorders Identification

BMI: Body mass index

CHD: Chronic heart disease

CVD: Cardiovascular disease

EEG: Electroencephalogram

EWTD:The European Working Time Directive

GEE: General estimating equations

GMT: Greenwich Middle Time

HPA-axis: Hypothalmic-pituitary-axis

IARC: International Agency for Research on Cancer

MD: Mean difference

MET: Metabolic equivalent task

NAFALM: The Norwegian Research School in General Practice

NNL Average number of night shifts worked in the previous year

NNs: Number of night shifts (based on a proxy for yearly average exposure)

NREM sleep: Non-rapid eye movement sleep

OR: Odds ratio

PA: Physical activity

PhD: Philosophiae doctor

Process C: Circadian Process

Process S: Homeostatic Process

PSG: Polysomnography

QRs: Quick returns (less than 11 hours between shifts)

REM sleep: rapid eye movement sleep

RR: Relative risk

SUSSH: The SUrvey of Shift work, Sleep and Health

SWD: Shift Work Disorder

VLPO: Ventrolateral Preoptic Nucleus

CONTENTS

1. INTRODUCTION

And so it goes goes goes tick tock tick tock tick tock
and one day we no longer let time serve us,
we serve time, and we are slaves passing,
bound into a life predicated on restrictions
because the system will not function
if we don't keep the schedule tight
Harlan Ellison - Repent Harlequin

In 1879, Thomas Alva Edison invented the light bulb and helped conquer the night. In 1882 he opened the first power plant in Manhattan, and artificial lightning spread fast throughout the Manhattan Peninsula and, shortly after, the industrialized world. At the same time as an effort to approximate for a changing and more interconnected world the Greenwich Middle Time (GMT) was established as a time reference in October 1884 and the world was divided into timezones. Thus, local customs and natural lighting conditions were officially replaced as timekeepers with standardized time. These technological and subsequent societal changes exemplify the large changes in the last centuries, and modern society's subsequent, increasing reliance on 24hour services. However, the slow evolutionary pace of adaptation has not kept up. Humans have adopted their sleep-wake and rest-activity rhythms to local lightning conditions given by the earth's 24hour rotation.

The conflict between modern society's reliance on 24hour services and our individual sleep-wake cycle is best personified by shift workers; workers who, as a group, are defined by their irregular working hours. According to the European Working Conditions Survey, 21% of the workforce participated in shift work in 2015, which was up from 17% in 2010 (1). As shown by the trends in the European Working Conditions Survey and other research, modern society and our 24/7 economy are growing increasingly reliant on jobs with non-standard working hours (2). The adverse health consequences are illustrated by the growing body of evidence on the acute and chronic health consequences of shift work (3,4). For example, shift work has been associated with an increased risk of metabolic and cardiovascular disease, certain types of cancers, and increased overall mortality rate (3–5).

While Harlan Ellison's short story refers to the toll of clocks and standardization of time on individual freedom, shift work research may be seen as a narrative on the adverse health consequences of conflicting internal and external clocks. This thesis humbly aims to illuminate the possible effects of shift work on weight gain and lifestyle factors. Specifically, this thesis examines body weight change when exposed to different characteristics of shift work, and, in the same manner, addresses possible adverse changes to various lifestyle factors: smoking, alcohol, caffeine, and exercise.

1.1 Sleep

We're better when we're fast asleep
When you raise me from my fragrant sheets
It's that innocence I want to keep
Oh wake me not, oh wake me not
Sivert Høyem - Sleepwalking man

Sleep remains an enigma; it is essential and universal, but far from fully understood. For the human species, evolution donated about one-third of our lifespans to sleep. Given its share of the human lifespan and its essential nature, it is a paradox that we are still not able to answer the most fundamental question: why do we sleep? The most frequent hypotheses trying to answer the enigmatic question include energy conservation, tissue repair, the removal of neurotoxic waste products, and memory consolidation (6–8).

From a descriptive perspective, our knowledge of sleep is extensive. Most adults sleep for an average 6 and 8 hours per night (9). Sleep duration and sleep structure changes throughout one's lifespan and differs between genders, and substantial interindividual differences exist (10,11). Despite our society often being currently labeled as sleep-deprived there is still controversy regarding the secular trends in sleep length among adults, but sleep curtailment seems to be the case for children and adolescents (12,13). Sleep is susceptible to disruption by a range of influences beyond aging and other obvious physiological parameters. For example, from a sociological perspective, sleep may be affected by the country in which one lives in, occupation, lifestyle factors, and domestic demands (14–18). From an environmental perspective, noise, local temperature, and light conditions may affect sleep length and quality (19). Lastly, from a medical perspective, insufficient sleep, and sleep problems are associated with a range of comorbidities such as neurodegenerative disease, psychiatric disorders, pain-related conditions, and obesity (20,21). Insufficient sleep, in the long run, affects mortality and increases the risk of a range of morbidities (4,22–24). Sleep curtailments negative impacts on mortality may, at least partly, be mediated through adverse impact on cardiovascular health (25). It should also be noted that several reviews have pointed out a U-shaped risk curve between sleep length and mortality. Regarding sleep length, an optimal middle way seems to be the most favorable option (22,23,25).

Recommendations for optimal sleep length are based on our current knowledge of the adverse health consequences of insufficient sleep and sleep curtailment. Official guidelines recommend between 7 and 9 hours of sleep for adults, in addition, more age-specific recommendations exist (26,27). However, sleep is not a static measure, an American survey revealed that adults slept for 6.9 hours on workdays, and 7.5 hours on weekends, signaling that occupational demands interfere with individual sleep needs (28). Occupational strain, concerning insufficient sleep, is probably most felt by shift workers where night workers experience the most sleep curtailment (29). The difference in sleep length between work and free days is an example of social jet lag and is most salient in late chronotypes (evening persons) (30).

1.2 Sleep definition and regulation

> *You know the day destroys the night*
> *Night divides the day*
> ***The Doors – Break on through***

Although the underlying functional aspects of sleep are still largely unknown, sleep is defined by its electrophysiological properties as measured by polysomnography (PSG). PSG divides sleep into two main stages: rapid eye movement sleep (REM) and nonrapid eye movement sleep (NREM). NREM is further categorized into three categories: N1-N3 (31). Electrophysiologically, the higher the NREM stage, the more low-frequent and high-amplitude waves there are. Clinically, low-frequent and high-amplitude waves correlate with deep sleep and a high threshold for awakening. N3 is also called slow-wave sleep and is electrophysiologically characterized by the most low-frequent and high-amplitude oscillations. The great majority of deep sleep is obtained in the first half of the sleep period. REM sleep (Stage R) is polysomnographically characterized by mixed frequency, low-amplitude waves that mimic those of the waking state, low muscle tone, and the presence of rapid eye movements (31).

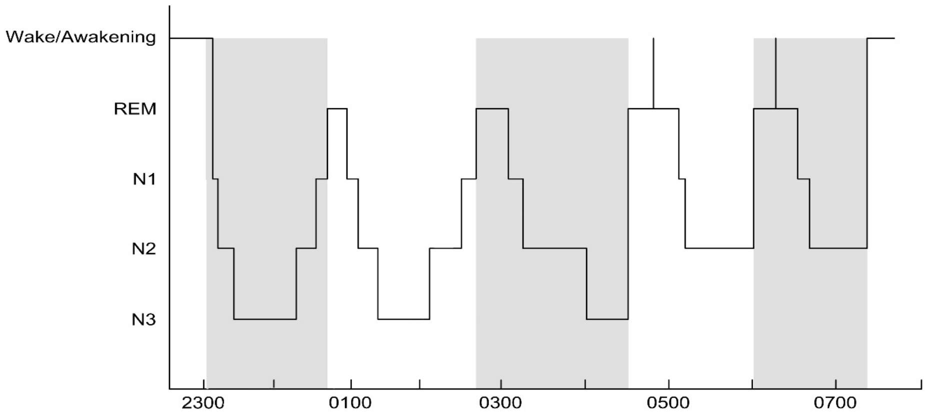

Figure 1. A schematic example of a hypnogram: The visualization of the absolute and temporal distribution of different sleep stages throughout the night.

During sleep, we alternate between NREM and REM sleep, and the cycle between REM and NREM alternates approximately every 90–120 minutes. The visualization of the sleep cycles is called a hypnogram (Figure 1). With average sleep length, the cycle loops 4-5 times during a night's sleep. Throughout the night NREM sleep accounts for 75–80% (N2: 50%, N3:12,5-20%, and N1 the remaining) of sleep, while short episodes of wakefulness (<5%) and REM sleep (20–25%) account for the rest (32). However, the relative distribution between sleep stages changes throughout the night: deep sleep dominates in the first half, while REM sleep predominates in the last third of the night (32). The predominance of NREM sleep, and especially N3 sleep in the first half of the night is believed to be a result of relief from sleep pressure and evidence of the homeostatic function of sleep. The amount of slow-wave sleep (stage N3) that one gets positively correlates with prior time spent awake (32).

However, prior time spent awake is not the sole determinant of sleep length and structure. The 24hour sleep–wakefulness rhythm is believed to governed by two oscillatory processes: Process S and Process C (33). Process S is defined as a homeostatic factor that builds up over the time spent awake: a proxy for built-up sleep pressure. Processes C, a circadian (from the Latin words, circa diem, about a day) factor, is a 24hour (24.18h on average) cycling process that remains relatively constant (34). Process C can be understood as a rest–activity rhythm that optimizes the functional periods of activity and rest during the 24hour light–dark cycle. In addition to the sleep–wakefulness rhythm, Process C governs a range of behavioral, physiological, endocrine and metabolic functions (35). An example is body temperature which follows the circadian sinusoid. Process C can be altered by changing lightning or environmental conditions; an example being the adaptation to new light conditions that occurs when traveling over several time zones (34). The process of changing Process C to new conditions is called entrainment, and a time-cue, such as light, is called a zeitgeber (time-giver). The circadian rhythm is influenced by lighting conditions during waking hours, including lights wavelength, duration, temporal timing, strength(lux), and the person's history of exposure (36–38). Social interactions and meals, formerly believed to be of great importance, have been shown to be of less significance as zeitgebers (36). The interplay between the Process S and Process C and their effects on sleep are illustrated in the theoretical framework of the two–process model, whereby these two processes interact to determine both sleep length and structure (33).

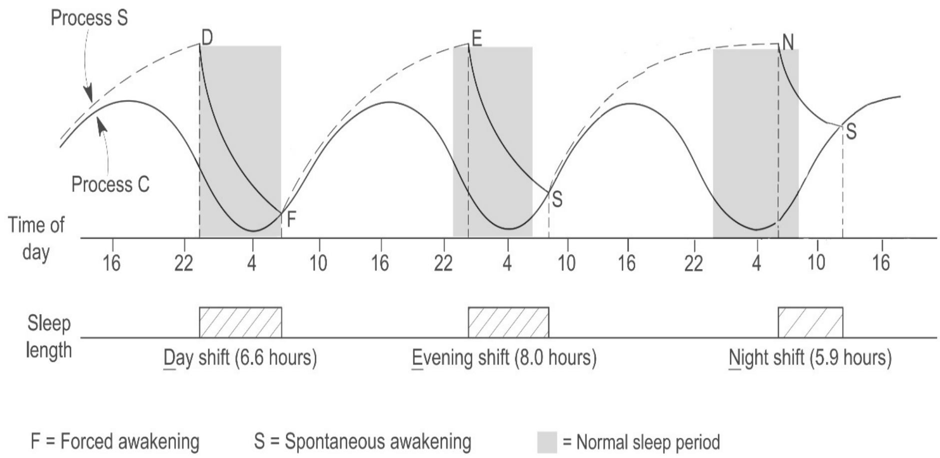

Figure 2. A schematic illustration of the two–process model for a forward rotating shift worker. Sleep before morning/day shift, and after evening shift and after night shift (29,33).

The duration of sleep is mainly dependent on sleep onset relative to the circadian phase (39). Sleep outside this optimal circadian window, which for healthy individuals will be between their habitual bed and wake-up times, results in shortened sleep length and incomplete recovery. From an occupational perspective, the two–process model explains why shift workers have the longest sleep length after evening shifts and the shortest after night shifts (29). As illustrated in Figure 2, day workers will, in the absence of a preceding evening shift, go to bed habitually and wake-up early, often by an alarm clock. The forced early awakening can give rise to sleep curtailment: the earlier the start of the morning shift, the more sleep will be curtailed (40). Sleep after an evening shift is often the longest; evening shift workers go to bed late but can wake up spontaneously later in the morning. Night workers experience sleep curtailment after night shifts. During the night shift, the shift worker must simultaneously fight increasing sleep pressure (Process S) and a decreasing activity rhythm (Process C). Both of these processes promote sleep during the night. After the night shift an increasing Process S is opposed by an increasing Process C, the net result being severely truncated sleep (29,41). Sleep structure is also altered when sleep is truncated and occurs outside of the normal circadian sleep window: when sleep is truncated it is the sleep in the latter part of the normal sleep period that is sacrificed—REM sleep and stages N1 and N2 (42). It should also be noted that there are large individual differences with regards to chronotype: an individual's preferred timing of sleep in the 24hour period (43). Different chronotypes will have differences in habitual sleep and wake up times: this is often exemplified by being characterized as a morning- or an evening person. From an occupational perspective, a morning person may experience more sleep curtailment after a night shift than an evening person, while the opposite may be true for their respective sleep length before an early morning shift (44). Beyond the two–process model, it should also be emphasized that behavioral factors and changing environmental demands can override both Process S and Process S; an example being the night worker fighting increasing sleepiness during the night shift as mentioned above.

In summary, with a normal diurnal rhythm and in the absences of altered functional demands, such as shift work, Process S and Process C act in opposition during the day and maintain a long period of wakefulness, and during the night, they act synergistically, consolidating a long bout of sleep. While the two-process model gives a conceptual framework for sleep regulation, it fails to account for the sleep to wake transition. From a safety and performance perspective, it is worth noting that a modification of the two–process model has been suggested: a third process, Process W, accounting for sleep inertia and decreased neurobehavioral performance during the sleep to wake transition period has been suggested (45). Regarding neurobehavioral performance, experimental research has shown performance and alertness to correlate with body temperature; the worst performance is found at the body temperature nadir corresponding to the nadir of the circadian rhythm which is found approximately two hours before habitual wake-time (46,47). In the afternoon, there may also be a period of increased sleepiness and decreased performance due to a slight mismatch between Process S and Process C. This phenomenon has been called the "post-lunch dip" and for individuals with a larger mismatch between Process S and Process C it could explain the habit of taking a siesta in the afternoon (48).

Anatomically, the circadian system adjusts to local and temporal lightning conditions by signaling pathways from the retina to a collection of neurons in the *Suprachiasmatic Nucleus* (SCN). In SCN, local neurons display a stable 24-hour rhythm that is maintained by a negative transcription feedback loop involving several clock genes, and influence their rhythmic oscillations to many endocrine and metabolic systems throughout the body (49). The SCN serves as a master clock for maintaining a stable 24-hour circadian rhythm, but circadian oscillations are found throughout the body. These peripheral clocks are believed to play a significant role in metabolism (50). While SCN orchestras circadian functions, the anatomical basis for sleep regulation is more complex and not fully understood. An arousal system with several activating pathways and neurotransmitter systems in the brain stem, hypothalamus, and basal forebrain is believed to be central to wakefulness (51). These interacting neurotransmitter systems that control wakefulness are collectively called the ascending arousal system (52,53). Other neuroanatomical sites, such as VLPO (ventrolateral preoptic nucleus) area which uses GABA as its neurotransmitter are central to inducing and maintaining sleep and, thus, the inhibition of the ascending arousal system. Sleep and wakefulness, being all or nothing process, are believed to work through reciprocal inhibition, giving rise to a "flip-flop" switch between sleep and wakefulness (54).

1.3 The metabolic consequences of insufficient sleep and circadian disruption

> *The total entropy of an isolated system*
> *can never decrease over time*
> ***Second Law of Thermodynamics***

Sleep is an active state: a range of functions are being performed during sleep to maintain homeostasis (55). Endocrine and metabolic functions follow a circadian rhythm. For example, while corticosteroids, insulin, and catecholamines are secreted mainly during the biological day, melatonin, growth hormone, and prolactin concentrations peak during the night (35). With circadian disruption, as is experienced frequently by shift workers, acute and chronic alternations in these endocrine systems are common (56–59). Disruptions of these hormonal systems have been suggested to be possible causal mediators between shift work and cardiovascular disease (60,61).

Experimentally, it has been shown that circadian disruption and night work can lead to insulin resistance (58,62). One study found that healthy adults who slept and ate at all circadian phases developed postprandial glucose increase similar to those in a prediabetic state (63). In addition to circadian disruption, sleep debt is also likely to decrease glucose tolerance (64). The experimental findings corroborate the epidemiological research and give biological plausibility for a causal relationship between the observed association between shift work and diabetes (65,66). Leptin and ghrelin, hormones involved in appetite regulation, have been shown to be affected by sleep curtailment (67). As for glucose metabolism, the leptin-ghrelin system may also be affected by circadian misalignment in addition to sleep curtailment (68). The dysregulation of these two hormonal systems could contribute to the increased risk of weight gain seen among shift workers (69). Cortisol, a stress hormone under strong circadian influence, has been shown to be affected by sleep curtailment (64). Upregulation of neuroendocrine stress systems such as the hypothalamic–pituitary–adrenal-axis (HPA-axis) and increased activation of the sympathetic nervous system are also believed to contribute to increased cardiovascular risk (70). In addition to the hormonal systems involved in cardiometabolic health, melatonin, a hormone secreted during darkness, has been suggested to have a protective role in oncogenesis. Several studies have proposed that circadian disruption and the suppression of melatonin could contribute to possible increased cancer risk (71,72). Regarding the possible chronobiological pathways that link shift work and obesity three main pathways have been suggested: disruption of circadian rhythms, altered feeding behavior, and changed lipid and carbohydrate metabolism (57). These pathways share clear commonalities with those suggested for the metabolic toll of sleep deprivation: alterations in glucose metabolism (decreased glucose sensitivity and insulin resistance), upregulation of appetite (possibly through changes in leptin and ghrelin–hormones regulating appetite), and reduced energy expenditure (73).

1.4 Shift work

I get up in the evening and
I ain't got nothing to say
I come home in the morning
I go to bed feeling the same way
I ain't nothing but tired
Bruce Springsteen - Dancing in the dark

Shift work can be defined as work outside the normal day working window, involving irregular or unusual hours compared to a normal daytime work schedule (3,74). The vague definitions of shift work encompass the large heterogeneities between different shift schedules and working arrangements across different occupations and countries. According to the sixth European Working Conditions Survey, 21% of workers are engaged in some kind of shift work (1). Many sectors, such as the health care- and transportation services are critical to public safety and operations and, thus, by categorical necessity, operate around the clock.

Due to the conflict between the health and safety of the individual worker and the economic and societal demands for 24hour services, working time has been regulated to protect workers' health and safety, as well as the safety of operations. The European Working Time Directive (EWTD) is an example of a legislative framework with such intentions. EWTD limits working hours per week, length of working time per day and work hours per night, and determines adequate periods of rest (75). Paralleling the EWTD, The Working Environment Act in Norway has the same functions. Within these legislative frameworks, shift lengths and cycles vary within and between different occupational groups (76). However, exemptions to these regulations can be negotiated between unions and employers.

From an occupational health perspective, it is paramount to try to deconstruct shift work into its' constituents and identify which of them are detrimental to health and safety. New evidence-based knowledge could give rise to recommendations that could, ultimately, lay ground for legislative changes. The below-outlined characteristics of shift work could, in different ways, contribute to circadian disruption, insufficient sleep, impaired work–life balance, and, ultimately, diminished health. From an organizational perspective, the same constituents could limit operational performance and safety. From a health and safety perspective, examples of important parameters of shift work are outlined below (71,76).

i. *Shift types*: start and end time, duration of shifts (8, 10, 12 hours), combinations of two shift- (morning and evening), or three shifts systems (morning, evening, night)
ii. *Night work*: with or without night work
iii. *Duration*: years of exposure
iv. *Intensity*: for example, number of night work shifts/month, night shifts/year, number of consecutive night shifts and days off after these consecutive nights
v. *Cumulative exposure*: interaction between intensity and duration
vi. *Permanent* or *rotating:* number of consecutive nights in permanent rotations
vii. *Speed and direction of rotation*: daily or weekly changes between shift types, forward or backward rotation (clockwise or counterclockwise rotation)
viii. *Rest periods between shifts:* minimum number of hours between two consecutive shifts. Quick returns (<11h between shifts) being an example

These specific features of shift work could, in different ways, contribute to insufficient sleep and circadian disruption. Sleep length is most compromised after or between night shifts and before early-morning shifts (40,77). Night shift workers, even in permanent night shift workers, seldom show full circadian adaption (78). Sleep debt accumulates over number of consecutive nights and could affect personal and operational safety (79). Long work weeks are shown to be related to a higher incidence of a range of sleep disturbances, and long individual work shifts (>12 hours) also raise the issue of personal and operational safety (79,80). Short rest periods between shifts, QRs (≤11h between consecutive shifts), are common and curtail sleep (76,77,81). The most frequent example of QRs is the transition from evening shift to day shift the following day. For those with rotating schedules, both two- and three shift schedules, this could be a potential source of insufficient sleep. Still, if insufficient sleep is the major mediator between shift work and adverse health consequences, then the major disruptor is probably night work. It curtails sleep the most, and adaption is seldom reached, not even for permanent night workers (4,41,78).

Breaking shift work down and focusing on the most detrimental characteristics of shift work, such as quick returns and cumulative nightwork exposure, may lead to an increase in the accuracy of risk estimates and have policy implications regarding optimized shift systems. In addition, it may help identify workers with demanding work schedules that may require more frequent surveillance. An isolated focus on crude measurements of different working schedules may not be sensitive enough to detect adverse health consequences. Optimal shift schedules must be a compromise between sound sleep and circadian principles, operational demands, and workers' preferences, regarding work–life balance (42,82). However, most recommendations share common characteristics that focus on minimizing circadian disruption and sleep debt: the use of forward rotations systems, a maximum of 3 consecutive night shifts, a minimum of 11 hours of rest between shifts, and a maximum duration of 8 to 12 hours per shift (82,83).

It should be noted that optimal shift scheduling on group level can never fully account for the large interindividual differences concerning shift work tolerance. Important factors concerning individual differences are age, circadian type, gender, and personality traits (84). Concerning age, research suggests that the critical age for shift work tolerance is between 40 and 50 years (85). This may be due to increased sensitivity to sleep loss and circadian effects. The reduced tolerance to shift work with age may be underestimated due to selection effects, such as the healthy worker effect, whereby only those workers who cope with a demanding work schedule tend to stay. Regarding gender differences, the evidence remains equivocal: a review on shift work tolerance suggested that male shift workers sleep better and may have a healthier lifestyle than their female counterparts (84). Another review has problematized the potential double burden for female shift workers; demanding work and domestic responsibilities may interfere with shift work tolerance (86). The authors of the latter review focus on the social dimensions that may affect a person's tolerance to shift work. Familial relationships, the presence of children in the household, and domestic obligations may all contribute to problems coping with shift work.

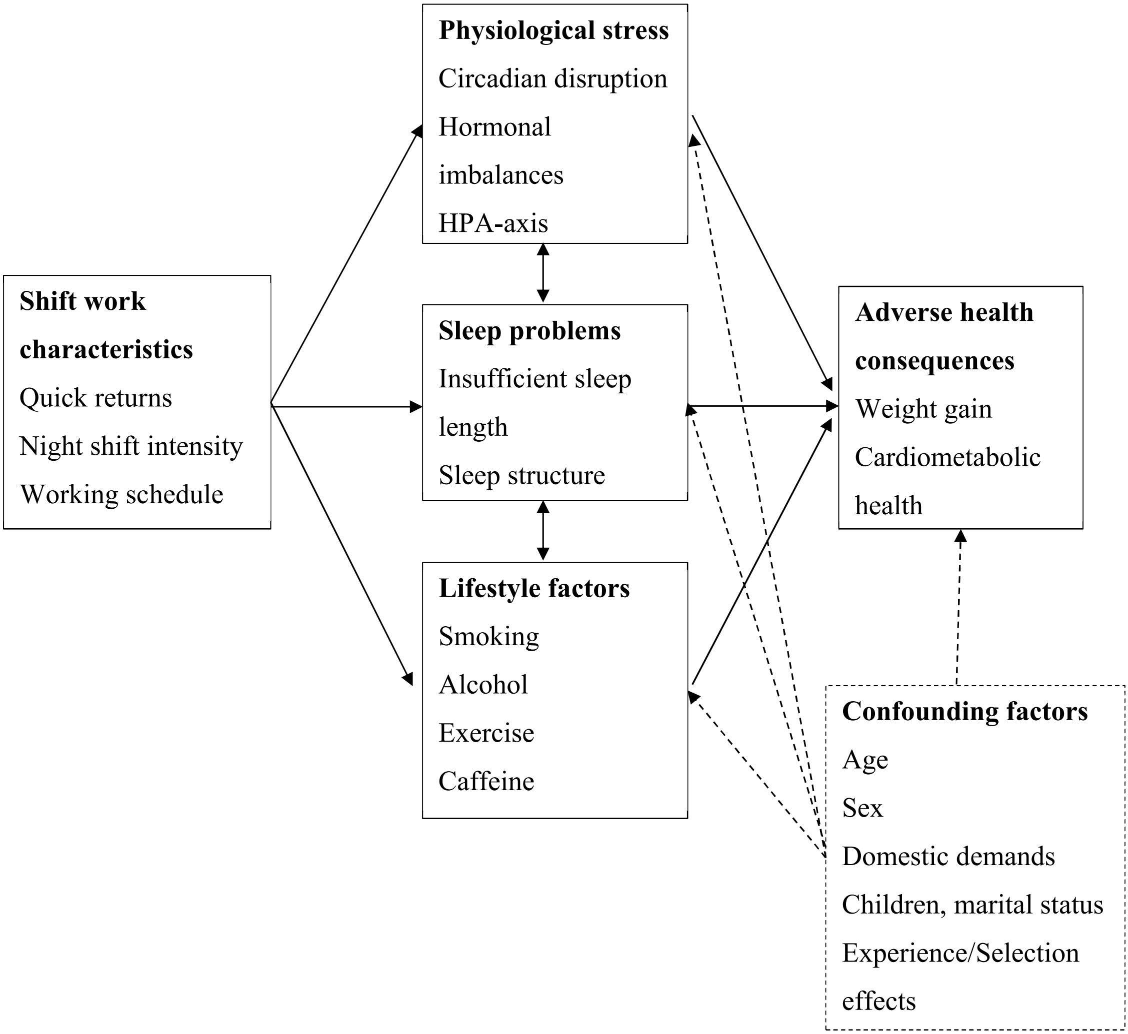

Figure 3. An overview of important shift work characteristics addressed in this thesis, and how these characteristics through mediating mechanisms (sleep -, physiological -, and lifestyle related) may lead to adverse health consequences, especially in terms of cardiometabolic health.

1.5 Shift work and health

The night is the hardest time to be alive
and 4 am knows all my secrets
Poppy Z. Brite

As a result of sleep curtailment and circadian disruption, fatigue, sleepiness, and sleep-related problems are frequently reported by shift workers (41,42). Experimental evidence corroborates epidemiological data that accumulated sleep debt causes increasing fatigue and lowers alertness (87,88). One review estimated that the risk of an accident was 30% higher during the night shift compared to the day shift (79). Wagstaff et al. extrapolate on this in their review, suggesting that rotating shift work carries a higher risk than permanent night work due to lack of adaptation, and that the risk of accidents at 12 hours of work is twice the risk after 8 hours (89). The safety issues related to very long working hours and the interaction between long working hours and night work have been verified in several other studies, along with the increased risk of attention failures and accidents (90,91). Reduced alertness and performance during the night could help explain the high proportional incidence of massive industrial catastrophes during the very early morning (92). In the very early morning, coinciding with the temperature nadir, the circadian system and the large built-up sleep pressure interact and create a perfect storm; the two systems contribute to a considerable decrease in performance and cognitive function (41,93). However, in a sleep-deprived state after long working hours, the risk of accidents and failures extends beyond the circadian nadir, as exemplified by the increased risk of car accidents when commuting home after a night shift (94).

The acute problems of sleep disturbances and fatigue could translate into chronic problems, an example being shift work disorder (SWD). SWD is a condition characterized by excessive sleepiness and difficulty sleeping caused by the conflict between an individual's working schedule and their sleep–wake rhythm (95). From a mental health perspective, shift work has also been associated with chronic impairments of cognition and increased risk of dementia (96,97). Shift work and disruption of sleep and circadian rhythms may impact immune function: studies have found shift workers to be more susceptible to common viral infections (98–100). These associations have not translated into clear patterns of increased sick leave. The evidence regarding sick leave and shift work remains undetermined (101). An increased risk of all-cause mortality has been found among shift workers; specifically increased CVD (cardiovascular disease) mortality among shift workers has been suggested to account for some of this observed association (5,102). An increased risk of gastrointestinal problems have been found among shift workers: for example, peptic ulcer disease (103). The International Agency for Research on Cancer group (IARC) classified shift work that includes circadian disruption as probably carcinogenic to humans in 2007; they restated and refined their statement in 2019 when they classified night shift work as probably carcinogenic to humans (104,105). Reviewing the data about different cancers and shift work, Kolstad concluded in 2008 that there was limited evidence for breast cancer, and insufficient evidence for prostate cancer, colon cancer, and overall cancer (106). However, more recent meta-analyses on breast cancer, prostate cancer, and colon cancer argue in favor of an association between night shift work and the respective cancers and also find evidence of a dose-response relationship between night shift work and the respective cancers (107–109). Furthermore, possible mechanisms have been suggested for the association between night shift work and cancer: melatonin suppression, reduced vitamin D levels, circadian disruption affecting cell-cycle regulation, sleep deprivation affecting the immune system, and adverse changes to lifestyle factors (110,111). Reproductive health may also be affected by shift work, especially preterm birth or late miscarriage (112,113).

Models for explaining the pathways through which shift work leads to chronic disease often focus on three themes, insufficient sleep, circadian disruption, and adverse effects on behavioral factors (4,57,114). A recent review also incorporates the need for sufficient recovery in their model of shift work and adverse health outcomes (115). From a metabolic and cardiovascular perspective, additional emphasis has been placed on the disruption of endocrine and hormonal systems, glucose metabolism, the ghrelin/leptin system, HPA-axis dysregulation, and increased sympathetic tone (57,60,116,117). A narrative review of shift work and cardiovascular disease also suggests psychosocial stress as a potential pathway toward cardiovascular disease in addition to the aforementioned possible pathways (60).

1.5.1 Shift work and cardiovascular disease

The authors behind an older review concluded that shift workers have a 40% increased risk of CVD compared to day workers (117). The authors behind later reviews, almost chronologically over a 10-year span, by Frost et al. and later Torquati et al., have modified this conclusion and the original risk estimates (61,118). Frost et al. concluded in 2009 that there was limited evidence for a causal relationship between shift work and chronic heart disease(CHD) (118). In contrast, in 2017 Torquati et al. concluded that the risk of any CVD event was 17% higher among shift workers compared to day workers, and that CHD morbidity was 26% higher among shift workers compared to day workers. Moreover, the authors concluded that the increased CVD risk among shift workers is non-linear and appears only after five years of exposure. Beyond five years of exposure, there was a dose-response relationship with a 7.1% increase of CVD events for every additional five years of shift work exposure (61). Another systematic review and meta-analysis by Vyas et al. found shift work to be associated with both increased risk of myocardial infarction (risk ratio 1.23 (1.15-1.31)) and of ischemic stroke (risk ratio 1.05 (1.01-1.09)) (119).

The relationship between shift work and CVD could be addressed in terms of the prevalence of individual risk factors. Metabolic syndrome is a cluster of risk factors that contribute to a high risk of a CVD event: hypertension, insulin resistance, dyslipidemia, and obesity (120). While several studies had found the prevalence of the metabolic syndrome to be higher among shift workers than day workers, the research is equivocal: the authors behind a systematic review concluded that there was insufficient evidence for an association between shift work and metabolic syndrome when confounders were adjusted for(121–123). Evaluating hypertension, Manohar et al. estimated the pooled OR to be 1.31 (1.07-1.60) for shift workers compared to day workers when combining both cross-sectional and cohort studies (124). Diabetes, a disease defined by the chronic dysregulation of glucose metabolism, is associated with shift work. A systematic review concluded that there was moderate evidence of an association between shift work and Type-2 Diabetes (66). Supporting this conclusion, a recent meta-analysis found a pooled adjusted OR for the association between ever vs never exposure to shift work and diabetes to be 1.09 (1.05-1.12) (65).

1.5.2 Shift work and weight change

There is an increasing amount of evidence that suggests that shift work increases the risk of weight gain (69,125). A recent review from 2018 concluded with a pooled OR of 1.23 (1.17-1.29) for the association between night shift work and obesity/overweight (69). Moreover, through subgroup analysis, fixed-night workers were also found to have a higher risk of obesity/overweight than rotational shift workers. The strength of their conclusion differs from that of an older review from 2011 in which the authors more cautiously concluded that there was strong evidence of a crude association between shift work and body weight increase, but insufficient evidence to conclude that there was a confounder-adjusted relationship (126).

Addressing individual studies deemed to be of high quality in the aforementioned reviews, these studies corroborate the claim of a relationship between shift work and weight gain. In their 14 years follow-up study, Suwanzono et al. concluded that alternating shift work was an independent risk factor for weight gain among Japanese workers (127). A few studies have also addressed workers changing toward- or away from shift work during the follow-up period. In addition to comparing day and shift workers, Zhao et al. addressed those who changed toward or away from shift work. Interestingly, those who changed toward day work had a BMI decrease while shift work maintainers and those who changed from day to shift work underwent BMI increases in the follow-up period (128). Similarly, in their ten years follow-up study of male Japanese workers, Morikawa et al. found that those who maintained shift work (shift-shift workers) and those who changed from day to shift work during follow-up (day-shift workers) had a significant BMI increase compared to those who worked day shifts only in the follow-up period (129).

In their large study of over 50000 nurses, Ramin et al. found support of a dose-response relationship in terms of number of night shifts/month and obesity(BMI≥30) (130). This finding was echoed by Peplonska et al. in their study of Polish nurses. They found an association between the frequency of night shifts and increased risk of obesity (131). A third study by Kim et al. found a dose-response relationship regarding years of exposure to shift work and being overweight (BMI≥25) (132). It is worth noting that these studies have methodological weaknesses due to their cross-sectional designs and can, thus, not establish directionality.

The findings of a prospective relationship between shift work and weight gain, a possible dose-response relationship between shift work and BMI increase, along with a reversal of outcome when exposure is withdrawn is suggestive of a causal relationship (133). However, it should be noted that the evidence is not conclusive and fully consistent. For example, the researchers behind one study found a decrease in BMI among shift workers and an increase in BMI among day time workers in a one-year follow-up study among workers starting a new job (134).

1.6 Shift work and lifestyle factors

The strain between work and domestic demand can be especially challenging for shift workers. Shift work can create work–life imbalances and potentially affect lifestyle factors adversely (135). Models trying to elucidate the relationship between shift work and adverse health consequences often include lifestyle factors, in addition to insufficient sleep and circadian disruption, as possible casual mediators (4,60).

1.6.1 Smoking

Smoking is probably the lifestyle factor that is most extensively studied in relation to shift work, and perhaps, the most important modifiable risk factor for CVD (136). Bøggild and Knutsson found in their review on shift work and cardiovascular disease that 6 of 13 cross-sectional studies reported significantly higher smoking prevalence among shift workers than day workers, one study found that shift workers smoked less than day workers, and the rest of the studies did not find any differences (117). This issue is elaborated upon by van Amelsvoort et al. in their two-year longitudinal study in which they find shift workers to be significantly more prone to start smoking (137). Given their findings, the authors argue that smoking might be an agent along the causal pathway and, thus, should not be solely treated as a confounding factor. Similarly, the researchers behind a Danish cohort study of newly-educated health care assistants found that when comparing different shift systems, fixed-night work was associated with higher odds of smoking relapse, and lower odds of smoking cessation compared to fixed-day workers (138). Together, these two studies take a different approach to smoking and shift work beyond that of treating smoking as a sole confounder between shift work and CVD. The argument about also treating smoking as a mediating variable, and not only a confounding factor, has also been advocated in a review on methodological aspects of shift work research (139).

1.6.2 Alcohol

While studies have found an association between alcohol consumption and long working hours, there is still inconsistent evidence between shift work and increased alcohol consumption (140–142). Comparison between studies is also difficult due to large heterogeneity in outcome measures regarding alcohol consumption: changes in biochemical markers, cut off value (units per week or gram alcohol) or the use of validated instruments (142–144). Although caution is warranted due to heterogeneity in both exposure and outcome measures, several studies report not finding any significant differences between shift and day workers regarding alcohol consumption (141,142). Some studies have looked beyond the simple association between shift work and alcohol consumption. One study reported an interaction between night work and long working hours (>8h) on increased alcohol consumption (144). The authors behind another study found that only night workers with poor sleep quality had higher alcohol consumption levels compared to day workers, suggesting that alcohol might be used as a therapeutic tool to induce sleep (143). Dorrian et al. did not find any differences in total alcohol consumption. However, when evaluating the drinking patterns of shift workers, they were found to be more likely to binge drink (145,146).

1.6.3 Caffeine

In contrast to alcohol and smoking, caffeine use may have positive health effects in the short and long run. Caffeine's acute mechanism of action is its antagonistic effect on the adenosine receptors in the brain. Adenosine is a potent sleep inducer, and adenosine concentration builds up with increasing sleep pressure (32). Corroborated by experimental evidence and its mechanism of action caffeine has been suggested as a therapeutic tool to mitigate sleepiness and decreased alertness (147,148). In line with these suggestions, a Cochrane review summarizing possible short term cognitive benefits and harms concluded that caffeine might be an effective intervention among shift workers for improving performance (149). Recent research also suggests that there are positive long term effects of caffeine consumption: reduction in all-cause mortality, cardiovascular disease and cancer incidence (150). A few studies have compared caffeine consumption between different subgroups of shift workers with inconclusive results. Drake et al. found no difference in caffeine consumption between day and night workers when evaluating SWD (151). Another study comparing those who had always worked night shifts to those who had never worked night shifts found that night workers had a significantly higher caffeine consumption (130).

1.6.4 Exercise

Increased exercise might be advocated among shift workers to counteract the observed increase in cardiovascular risk. Exercise has also been suggested to mitigate the negative effects of shift work and to increase shift work tolerance (85). However, the actual situation may be the opposite; due to work–life imbalances shift workers may exercise less than others. Studies examining the relationship between exercise and shift work have yielded inconclusive results. In their cross-sectional study, Peplonska et al. reported that rotating night shift workers, when compared to day workers, were found to be associated with higher occupational physical activity (PA) and lower leisure time activity (152). The researchers behind another study using actigraphy to record PA among hospital shift workers and non-shift workers reported the same findings; no large difference between the two groups was found regarding leisure time PA, but shift workers were found to be more physically active during work (153). The results are not conclusive. One study found the opposite: shift workers were more sedentary at work than day workers (154). As paralleled by their findings concerning smoking, Nabe-Nielsen et al. reported that fixed-night workers had lower odds of becoming physically active than fixed-day workers (138). These findings concerning smoking and exercise could suggest that changing or initiating positive health behaviors might be extra difficult when working a demanding shift schedule including night shifts. A recent systematic review of physical activity interventions among shift workers found that while the interventions in general were effective on outcome measures during the intervention, more research were needed to address if the interventions led to permanent changes in physical behaviour and how to best reach shift workers with such interventions (155). Another important notable distinction between working time PA and leisure time PA is their opposite impact on health. A review suggested that while leisure time PA has positive effects on cardiometabolic health, working time PA may be a result of a stressful environment and have the opposite effect (156).

1.6.5 Diet

In their paper on shift work and diet Lowden et al. review the role of diet among shift workers from both physiological and behavioral perspectives (157). One concern raised by the authors is that the timing of meals and nocturnal eating may disrupt both glucose metabolism and satiety hormones. From this perspective, working night shift may be the most dangerous. Another issue, that may worsen the situation of nocturnal eating is the possibility that the quality of diet may be worse. An increased use of snacks and unhealthy foods among night workers compared to day workers have been reported (158,159). Corroborating these findings, a recent review on night working and nutrition patterns also found quite consistent findings of lower fruit and vegetable consumption among night workers (160). Interestingly, Lowden et al. conclude that total energy intake over 24 hours probably does not differ between day and shift workers. The conclusion that total energy intake does not differ between shift– and day workers is also supported by other reviews (159,161). Despite no differences in total energy intake, Lowden et al. still conclude that dietary differences could contribute to metabolic disturbances due to differences in the temporal distribution of energy intake and the quality of diet between shift workers and their day working counterparts (157)

1.7 Methodological issues in shift work research

Everything is vague to a degree you do not realize
till you have tried to make it precise
Bertrand Russell

The authors behind a recent editorial in Scandinavian Journal of Work, Environment & Health paraphrase the consequences of methodological issues related to research on shift work and cardiometabolic health when they ask: “if new studies on shift work and cardiovascular risk add to the knowledge base? Or if they have the same biases and limitations as earlier studies and thus are not expanding the knowledge base” (162). These methodological concerns are reiterated in most reviews on shift work and chronic disease (69,71,125,126,139,162). The major methodological concerns are study design, classification and the assessment of exposure, assessment of outcome, lack of adequate control for confounding factors, and various kinds of potential biases.

For acute effects of shift work on performance measures, for example, an available option is to conduct experimental studies. In theory, experimental designs can elucidate temporal directionality and adjust for possible known and unknown confounders due to the randomization process. However, such experiments are difficult to carry out when looking at long time exposure as is often needed in shift work research, and when it is difficult to standardize and isolate the exposure, as is the case for work schedules. Most studies within shift work research have had a cross-sectional or prospective design. The weakness of the cross-sectional design is that is measured only at one-time point and can thus not elucidate any directionality between exposure and outcome (163). A minimum, but not sufficient, requirement for causal inference is the establishment of temporal directionality. Another weakness, shared by prospective designs, is the possibility of inadequate control for confounding, if both exposure and outcome are related to a third variable, and this third variable is not adjusted for, then the calculated effect sizes might not be valid (163).

Another issue with epidemiological studies within shift work research is the difficulty of classifying, isolating, and deconstructing the exposure adequately. The definition of shift work is very broad and this translates into very different measures of shift work exposures in the literature. This makes a comparison between studies and conducting meta-analysis and knowledge synopsis difficult. Working time arrangements can differ between occupations and countries; an accurate assessment of exposure may, thus, have limited generalizability. This heterogeneity in exposure was exemplified by a Danish study in which the researchers reviewed eight different definitions of night shifts. Fortunately, the authors concluded that most definitions gave the same exposure classification when the definitions included a work period during the night (164). Quantifying the amount of night work is an example of isolating and identifying constitutes of shift work that may be detrimental to health. In line with this, the IARC group has identified domains of shift work that lead to circadian disruption and should be addressed in epidemiological studies: working-time, duration, intensity, rotation type, and direction of rotation (71). Similarly, Härmä et al. lists a total of 29 working time variables that should be addressed in working-time research (165). The 29 items are categorized into four dimensions: length of working hours, time of day, shift intensity, and social aspect of working hours. Regarding body weight-related outcomes and various lifestyle factors, the definition of the particular outcome can also make comparisons between studies and knowledge synopsis difficult.

Beyond deconstructing shift work and accurately evaluating its constitutes, sound shift work research relies on an accurate assessment of exposure. The use of questionnaires and self-reported data is common. Such data are prone to recall bias and misclassification bias. The authors behind a study evaluating the validity of self-reported shift work found that many nurses who categorized themselves as day workers did, in fact, when self-reported data were compared to objective pay-roll data, work some night shifts resulting in misclassification (166). The highest validity of self-reported data was found among night workers. Objective payroll data has been suggested as a potential resource for accurate exposure assessment. Many nurses seem to opt-out of demanding schedules, especially night work. This selection effect has been called the healthy worker effect; only those who are healthy choose and tend to stay in demanding work schedules (167). Interestingly, both selection- and misclassification biases are believed to skew the results toward the null, which could lead to an underestimation of the true risk estimate or, in extreme cases, a statistical type 2 error—the failure to correctly reject the null hypothesis (139,166). As mentioned above, controlling for possible confounding is important in non-experimental designs. The choice of confounders might be controversial in itself, but within shift work research, it may be the case that the parameter is not a confounder but a mediator, an aforementioned example being smoking. This issue has been addressed in several papers (137,139,162). Adjusting for this could lead to an underestimation of the actual effect.

2. RATIONALE AND RESEARCH AIMS

Several studies have reported a relationship between weight gain and night work. However, many studies are based on cross-sectional data and often a crude assessment of shift work exposure. Consequently, additional prospective studies that address different characteristics of shift work are needed. Lifestyle factors are often mentioned as possible intermediaries between shift work and adverse effects on cardiometabolic health. However, the evidence remains inconclusive, and additional research is needed to assess differences in lifestyle factors between various shift work characteristics.

2.1 The overall aim of the thesis

The overall aim of the thesis was to evaluate how different characteristics of shift work could contribute to adverse consequences on body weight-related outcomes and lifestyle factors.

2.1.1 Aims of study 1

The main aim of the first study was to address the association between night work, body weight outcomes, and lifestyle factors beyond a conventional dichotomous approach evaluating differences between day and night workers. Specifically, we investigated our data for possible associations between night work intensity (number of night shifts worked the previous year (NNL) and the outcome measures: BMI, obesity, smoking, alcohol (AUDIT-C), caffeine consumption and exercise habits.

2.1.2 Aims of Study 2

Building on the findings from Study 1, we wanted to address body weight changes with a prospective design evaluating different shift work characteristics such as whether different work schedules and changes toward- or away from schedules containing night work could give rise to differences in weight gain in the follow-up period of four years. Furthermore, we wanted to address whether cumulative night shift exposure gave rise to differences in weight gain.

2.1.3 Aims of Study 3

Building on the findings of study 1 and study 2 we wanted to investigate how different characteristics of shift work could affect lifestyle factors using a prospective design. Specifically, we evaluated different work schedule groups, quick returns, and cumulative night shift exposure for possible adverse effects on the following lifestyle factors: smoking, alcohol (AUDIT-C), caffeine consumption, and exercise habits.

3. METHODS

3.1 Participants and procedures

The data for all three studies in this thesis stemmed from the SUSSH cohort. The overall aim of the project was to investigate sleep, well-being, and health among Norwegian Nurses over a period of ten years. Major areas of investigation have been shift work characteristics and possible impact on different health outcomes: for example, sleep and sleep disturbances, mental health, metabolic health, and sick leave.

The first wave was conducted from December 2008 to March 2009. The population consisted of registered members of the Norwegian Nurses Organization (NNO), which includes most of the nurses who work in Norway. A stratified sample (N=6000) comprising a total of five strata; each containing 1200 nurses holding at least a 50% work position, was randomly selected from the member registry of the NNO. The criteria for the different strata were time elapsed since graduation: <12 months (stratum 1), 1–3 years (stratum 2), >3–6 years (stratum 3), >6–9 years (stratum 4) and >9–12 years (stratum 5). The stratification toward a young cohort was done to ensure that the cohort could be followed for the planned 10-year period. However, nurses were not excluded based on age. Each nurse in the sample received a questionnaire by postal mail. A total of 6000 letters were sent: 600 letters were returned due to wrong addresses thus leaving a cohort of 5400 nurses. After completing the questionnaire, the respondents could return them in a pre-paid envelope. Two reminders were sent to those who did not respond.

After the initial wave (wave 1a), the cohort consisted of 2059 nurses, yielding a response rate of 38.1%. In addition, 906 newly-educated nurses were recruited to this cohort during the fall of 2009 (wave 1b). The response rate in this additional sample was 33.1% (906/2741). The cohort in the later waves consisted of those nurses (n=2965) who responded to the first survey (wave 1a or wave 1b). Annual follow-up waves were conducted. The response rates from the main waves used in this thesis are given in table 1.

Table 1. Response rates from the main waves of the SUSSH cohort used in this thesis.

Year	2008/09	2009	2013	2015
Wave	1a	1b	5	7
Response rate	38.1%	33.1%	69.4%	67.5%
N=	2059	906	1923	1892

From wave 4 the original sample (1a) and the additional sample (1b) were merged. Those who participated in the first wave (1a+1b) constituted those who were asked again in the consecutive waves.

Table 2. Important baseline characteristics of the SUSSH cohort (wave 1a+1b) (N=2965).

Working Schedule (n=2914)	
Day only	5.7%
Evening only	0.2%
2-shift rotation (day and evening)	29.7%
Night only	8.6%
3-shift rotation (day, evening night)	52.4%
Other schedules including night work	3.3%
Equivalent of full-time position (n=2936)	
<50%	4.8%
50–75%	31.0%
76–90%	13.9%
>90%	50.3%
Number of nights worked the previous year (n=2917)	23.1(29.0)
Number of quick returns worked the previous year (n=2800)	31.7(29.5)
Average working hours per week (n=2897)	33.7(7.1)
Age (n=2956)	31.8(8.2)
Gender (%female) (n=2952)	90.7%
Children living at home (%yes) (n=2832)	43.8%
In a relationship (%yes) (n=2935)	70.0%
BMI (n=2933)	24.4(4.1)
Obesity prevalence (BMI ≥30)	9.5%
Smoking prevalence (n=2827)	11.9%
Caffeine (units/day) (n=2944)	3.0(2.7)
Exercise (≥1h per week) (n=2846)	67.0%

Proportions given as percentages and continuous variables as means with the standard deviation in parenthesis.

3.1.1 Samples and procedures of study 1

The data used in Study 1 was from the first wave (1a) of respondents, which consisted of 2059 nurses.

3.1.2 Samples and procedures of study 2

The data used in Study 2 was from the first Wave (1a+1b) and the fifth wave. For NNs (number of night shifts) we also used data from wave 2. The total sample in the first wave was 2965. The total sample in the fifth wave was 1923. We excluded nurses who reported to be pregnant at the time of measurements (n=284) and those who did not report their working schedules or did not work any of the investigated work schedules in both Wave 1 and Wave 5 (n=395). The sample used in study 2, thus, consisted of 1244 nurses.

3.1.3 Samples and procedures of study 3

The data used in study 3 came from the first wave (1a+1b) and the seventh wave. The total sample in the first wave was 2965, and the total sample in the seventh wave was 1892. We excluded nurses who were pregnant at the time of measurement (n=287) and those who did not report their working schedules in both Wave 1 and Wave 7 (n=234). The sample used in study 3, thus, counted 1371 nurses. For the questions on AUDIT-C, we only had a comparable dataset from Wave 1b and Wave 7. As a result, the data on alcohol consumption and habits consisted only of the cohort of newly educated nurses.

3.2 Instruments

3.2.1 Predictor variables

Work Schedule: The nurses were asked for their working schedule: day only, evening only, two-shift rotation (day and evening), three-shift rotation (day, evening and night), night only, or other schedules including night work. In Study 2, the most common shift work schedules were included, excluding evening only and other schedules including night work. Thus, we used the following schedules in Study 2: day only, two-shift rotation, three-shift rotation, and night only.

The most common schedules were also analyzed in Study 3, but with a different approach. In study 3 we grouped those who had day only, evening only, and day and evening work in the follow-up period into one group of day workers and those who had a schedule that included night work into another subgroup of night workers (night only, three-shift rotation, and those who reported having another schedule including night work). We classified those who changed from a schedule containing night work into a schedule with day and/or evening work into one subgroup. Furthermore, we classified those who changed toward a schedule containing night work from a schedule containing only day and/or evening shifts into another subgroup. In addition, we analyzed the original work schedule as described above for Study 2.

Typical work hours for Norwegian nurses in rotational work schedules in Norway are 07:00-15:00 (day shift), 14:30-22:00 (evening shift), and 22:00-07:00 (night shift). There may be local variations, especially among day only workers in outpatient clinics, where, for example, 08:00-16:00 shifts are quite frequent. Shift workers in full-time positions in Norway most often have 35.5 hour work weeks, whereas day only workers in full-time position have 37.5 hours-work weeks.

Night Shift Intensity: In Study 1, the number of night shifts worked the previous year (NNL) was used as a continuous parameter. In Study 2 and Study 3 an average of this parameter was calculated and used. In Study 2, this parameter was calculated as the average of nurses' estimations of number of night shifts in waves 2-5, because wave 2 reflected exposure in the previous year (the first year). In study 3, wave 1 and wave 7 were used to calculate average nightwork exposure. This was done to increase power, and under the assumption that this estimation would, as in study 2, still serve as good proxy for average nightwork exposure in the follow-up period.

In both study 2 and Study 3, we categorized this continuous variable, average number of night shifts (NNs), into three subgroups where the lowest exposure group was chosen as contrast in the analysis. The cut-offs were made in order to minimize exposure in the contrast group while also keeping a sufficient group size: <1 NNs, 1-

20 NNs, and >20 NNs. In Study 2, we analyzed day only and night workers(night only and three-shift workers combined) regarding these exposure groups. Furthermore, in Study 2 we did a subgroup analysis among night workers: <20 NNs, 20-40 NNs, >40 NNs. In Study 3, we also investigated change from baseline to follow-up for NNs: ±10 difference in number of NNs between baseline and follow-up (contrast), >10 decreases in NNs, and >10 increases in NNs.

Quick Returns (QR): This parameter was only analyzed in Study 3. At both baseline (wave 1a+1b) and follow-up (wave 7), the nurses were asked about their number of QRs in the last year. We used this data to calculate an average from the two time points. This average was used in the statistical analyses as a proxy for average number of yearly QRs in the follow-up period. The continuous variable was categorized into three subgroups, where the lowest group was chosen as contrast: <5 QRs, 5-30 QRs, >30 QRs. As for NNs, we tried to minimize the exposure in the reference group while maintaining sufficient group size. In addition, in Study 3, as for night shift intensity, we made a change score using workers with the lowest change scores as contrast: ±10 difference in number of QRs between baseline and follow-up(contrast), >10 decreases in number of QRs, and >10 increases in number of QRs.

Covariates/Confounders: In all three studies, we adjusted for gender and age in our multivariable analyses. A review on shift work tolerance suggested that male shift workers may experience less sleep-related problems and may adhere to a healthier lifestyle compared to female shift workers (84). Age is believed to be inversely related to shift work tolerance, especially concerning night work. A critical age between 40 and 50 years has been suggested before many start to experience lower shift work tolerance: for example, more sleep-related problems (85,168). However, it should be noted that selection effects, such as the healthy worker effect, and experience may attenuate the age-related effects (84). Thus, in Study 1, a cross-sectional study, we adjusted for night work experience (+/- 5 years)*:* A study among Norwegian intensive care nurses revealed that while increasing age in general reduced shift work tolerance, experience tended to attenuate sleep-related problems which suggests increased coping with experience (168). To accommodate for experience, we adjusted for years since graduation (as an experience-proxy) in Study 2 and Study 3. Hours worked per week were adjusted for in Study 1 and Study 2 as this could serve as a potential stressor in addition to shift work itself.

Shift work tolerance can be affected by social factors. Several domestic demands may affect shift work tolerance adversely. A review suggests that a partner may be a source of social support, but they could also be someone who has to be taken care of (86). The authors argue that female shift workers assume the role as caretakers more often than their male counterparts. Furthermore, having children at home can increase work-life imbalance and make coping with shift work difficult (86). To accommodate for these possible imbalances between work and domestic demands, we adjusted for marital status and whether the nurses had children living at home.

3.2.2 Outcome variables

Body Weight Related Outcomes: Body Mass Index was calculated conventionally using weight over the square of height in meters (weight(kg))/(height(m)^2). The nurses self-reported height and weight in the questionnaire. Obesity was defined as BMI>30 in Study 1.

Short Form of the Alcohol Use Disorders Identification (AUDIT-C): Alcohol consumption was evaluated using the AUDIT-C. AUDIT-C is a self-report instrument with three items measuring alcohol use. The questions were 1) How often do you have a drink containing alcohol? 2) How many drinks containing alcohol do you have on a typical day when you are drinking? 3) How often do you have six or more drinks on one occasion? The total score ranges from 0 to 12. The instrument appears to be a practical, valid primary screening test for heavy drinking and/or active alcohol abuse or dependence (169). A score of 3 or higher points on the AUDIT-C may indicate potential alcohol misuse. In a primary-care setting, a threshold score of 3 or higher in females, and 4 or higher in males simultaneous maximized sensitivity and specificity for potential misuse (170). In our analysis, we used both the composite AUDIT-C score and the dichotomous AUDIT-C score (cut off: ≥3 for females and ≥4 for males).

Smoking: The nurses were asked if they smoked daily (yes/no) to get an estimate of the prevalence of daily smokers. Furthermore, those who smoked were further asked to provide an estimate of the number of cigarettes they smoke daily.

Exercise: Exercise was measured by an item asking for hours of sweaty exercise per week (0, <1h, 1–2h, ≥3hours). We collapsed exercise data into two groups (<1h and ≥1h per week). The question concerning exercise used in the present study has been compared to $V02_{max}$ and activity sensor and was found to be a reasonably valid measure of vigorous activity (171). Regarding the cut-off, one study reported that at least one hour walking per week predicted lower cardiovascular risk. And, in addition, that vigorous activity predicted the lowest risk (comparing highest to lowest categories) (172).

Caffeine consumption: Nurses were asked for the average number of caffeine-containing units they consumed per day. In addition, caffeine consumption was evaluated as a dichotomous parameter (drinking three or more caffeine-containing units vs. drinking fewer than three units per day). Regarding the cut-off, an umbrella review of meta-analyses suggested that the optimal risk reduction for various health outcomes was found for intake of 3-4 cups of coffee per day (150). Another large epidemiological study found that lower mortality was observed for all groups of those consuming coffee compared to non-drinkers (173). A significant trend was found for both male and female coffee drinkers: those consuming 2-3 cups of coffee per day or more had reduced mortality than those with lower consumption (173).

3.3 Statistical Analyses

3.3.1 Study 1

SPSS version 22 was used for the analyses. To evaluate possible associations between NNL and the outcome variables, a multiple hierarchical regression model was constructed to evaluate the different outcome variables when adjusting for possible confounders using a stepwise approach. Step 1 in the regression model adjusted for age and sex. Step 2 adjusted for hours worked per week and the duration of experience of night work (≤5 or >5years). Lastly, in step 3, our main predictor, NNL, was entered into the model. This model was analyzed separately against the different continuous outcomes: BMI, number of cigarettes smoked daily, and AUDIT-C. Dichotomous outcome variables, smoking prevalence, AUDIT-C (under over threshold), caffeine consumption (score ≥3 units/day), and exercise (<1h and ≥1h per week) were evaluated using logistic regression. Both crude and adjusted logistic regression analyses were conducted for each of the outcome variables using the same covariates as in the multiple hierarchical regression model. The significance level for all analyses was $p<0.05$.

3.3.2 Study 2

SPSS version 24 was used for the analyses. Regarding descriptive analysis, Chi-Square and Fischers' exact test were used to compare proportions, and one-way ANOVA (Analysis of Variance) was used for comparison between continuous variables across groups. For our analysis of BMI, we analyzed within-group differences using paired t-tests comparing baseline and follow-up measurements of BMI. The effect size in a paired t-test is the arithmetic difference between the two measurements (mean difference (md)). Within-group analysis was conducted for different work schedules, different numbers of NNs (<1, 1-20, >20), a subgroup analysis of day only and night workers (NNs:<1, 1-20, >20), and among night workers (NNs; (<20, 20-40, >40).

For the between-group analysis of different subgroups of work schedules and NNs, we analyzed the data using multiple linear regression. Adjustment for BMI at baseline was made to correct for any baseline imbalances in BMI. A crude model only correcting for BMI at baseline was analyzed first. Then a model adjusting for age, sex, children living at home, marital status, and years since graduation was used. Day workers and those with the lowest exposure to NNs were used as contrasts in the respective analysis. Significance level for all analyses was $p<0.05$.

3.3.3 Study 3

SPSS version 25 was used for the analyses. Regarding descriptive analysis, Chi-Square tests were used to compare proportions, and one-way ANOVA (Analysis of Variance) and Kruskal-Wallis Test were used for comparison between continuous variables (means/medians). The lifestyle factors were evaluated for both within- and between-group changes. To evaluate within-group changes for different work schedules, we used paired t-tests for continuous variables and McNemar's test for paired proportions. For analyses between groups, we used a logistic regression model using the dichotomized lifestyle factors variables of smoking(yes/no), AUDIT-C score (above/under threshold), caffeine consumption (≥ 3 units/day), and exercise habits (≥1 hour/week). We analyzed working schedules (day workers as contrast), NNs (lowest exposure groups as contrast), and QRs (lowest exposure groups as contrast). In our crude analyses, we only adjusted for the baseline value of the respective lifestyle factor. In our adjusted analyses, we adjusted for baseline values of the respective lifestyle factors, age, sex, years since graduation, and children living at home. The significance level for all analyses was $p<0.05$.

3.4 Ethics

The project was approved by the Regional Committee for Medical and Health Research of Western Norway, Region West (case number NO. 088.88). Together with the first questionnaire wave, the nurses received an information letter about the aims of the study and an informed consent form that they signed and returned with the completed questionnaire. In all consecutive waves, and in addition to the questionnaire, the nurses received a letter ensuring the confidentiality of their data and the option to withdraw from the study at any time. This letter also informed the nurses that by participating in the specific wave of research they were eligible to participate in a lottery where 25 of the responders would receive a gift card of 500NOK.

4. RESULTS

Below follows a summary of the main findings from studies 1–3.

4.1 Study 1

In our multiple hierarchical regression model, BMI, AUDIT-C score, smoking, caffeine, and exercise were analyzed separately in the regression model. When evaluating BMI, we found NNL to be significantly and positively related to BMI ($\beta=0.055$, $p<0.05$). In our logistic regression model, NNL was found to be positively and significantly associated with obesity (OR 1.01 (1.00–1.01)).

Our other main finding was that hours worked per week was significantly and positively related to the composite AUDIT-C score ($\beta=0.075$, $p<0.05$) and the dichotomized AUDIT-C score (OR 1.03 (1.01–1.05)). Those who had worked schedules including night work for over 5 years had lower alcohol consumption compared to those with less than 5 years for both the composite AUDIT-C score ($\beta=-0.052$, $p<0.05$) and the dichotomized AUDIT-C score (OR=0.75 (0.59-0.95)). NNL was not found to be significantly related to the continuous AUDIT-C score or dichotomized AUDIT-C score.

We found no association between NNL and smoking prevalence. NNL was found to have no significant association with cigarettes smoked daily among smokers. Regarding caffeine consumption, we found that NNL was significantly and positively related to caffeine consumption (OR 1.00 (1.00–1.01)). NNL was found not to be associated with exercise habits in our logistic regression model.

4.2 Study 2

We evaluated the within-group difference in BMI between baseline and follow-up using a paired t-test for each of the five working schedule related groups. All groups except day workers had significant within-group increases in BMI: day-only (md=0.33 (-0.17–0.84)), two-shift rotation (md=0.48 (0.20–0.75)), three-shift rotation (md=0.46 (0.30–0.62)), night-only (md=1.30 (0.70–1.90)), stopped working nights (md=0.57(0.17–0.84)), and started working nights (md=0.63 (0.20–1.05)). Furthermore, within-group changes for average yearly number of night shifts were first evaluated for the whole cohort: <1NNs (md= 0.34 (0.05–0.63)) ,1-20 NNs (md=0.56 (0.27–0.85)), >20NNs (md=0.57 (0.34–0.79)). A subgroup analyses of night workers only was also done: <20NNs (md=0.44 (0.02–0.86)), 20-40NNs (md=0.34 (-0.03–0.71)), >40NNs (md=0.80 (0.50–1.11)). In this subgroup analysis, only the group with middle exposure of NNs was found to be not significant.

Evaluating between-group differences in BMI in both our crude and adjusted linear regression models with day only workers as contrast, we found that night-only workers underwent significantly larger weight gains than day-only workers (contrast). The effect sizes in the crude and adjusted models were; β=0.95 (0.15–1.76) and β=0.89 (0.06–1.72), respectively. Furthermore, none of the other working schedules significantly differed from day-only workers in the follow-up period. We did not find any significant differences in NNs, not for the whole cohort or the sub-cohorts of 1) night workers and 2) day only and night workers that were analyzed.

4.3 Study 3

When evaluating smoking habits in the cohort we did find a significant within-group decline for day workers (17%→11%, p=0.03), and night workers (11%→7%, p=0.03). For those who started working a schedule with night shifts (7%→5%, p=0.31) and stopped working a schedule with night shifts (11→5%, p=0.07) there was a non-significant decline in smoking prevalence. Among smokers, there was a significant decline in cigarettes smoked per day for the day workers, night workers, and those who stopped working a schedule with night shifts. We did not find any significant between-group changes concerning smoking prevalence for the different work schedules, QRs, and NNs in the between-group analyses.

Regarding alcohol consumption, day workers were the only group with a significant increase in their AUDIT-C score in the follow-up period (2.8→3.2, p=0.04). We did not find any significant between-group changes concerning alcohol consumption for the different work schedules, QRs, and NNs in the between-group analyses.

For all four work schedule groups, there was a significant within-group increase in caffeine consumption (units/day): day workers (3.2→3.8, $p<0.001$), night workers (3.1→3.7, $p<0.001$), stopped working nights (2.8→3.5, $p<0.001$) and started working nights (2.6→3.4, $p<0.001$). The increase in caffeine consumption from baseline to follow-up was also significant for all groups when caffeine consumption was measured as a dichotomous parameter (≥3units/day). We did not find any significant differences in caffeine consumption in our crude or adjusted logistic regression models between the different work schedules, QRs or NNs groups.

We did not find any significant differences when analyzing the four defined work schedule groups and exercise for within-group changes in the follow-up period. I addition, we did not find any between-group differences regarding the shift work characteristics (work schedule, QRs, and NNs) and exercise habits.

5. DISCUSSION

5.1 Shift work and weight gain

Recent systematic reviews and meta-analyses summarizing the current body of evidence on the association between shift work and weight gain argue in favor of a significant relationship (69,125,174). Still, as mentioned, comparing shift work research is often difficult due to heterogeneities in design, exposure, and outcome. As a result, reviews have addressed the need for future studies to untangle what characteristics of shift work that are detrimental for health in general, as well as cardiometabolic health. In other words, additional studies that move beyond shift work as a single construct are necessary (71).

The novelty of Study 1 in this regard, is that it focused on night shift intensity. Specifically, the number of night shift worked in the previous year was used as an exposure parameter. For both BMI and obesity, we found a significant association between NNL and these two body-weight related outcomes. Other studies have revealed a similar dose–response relationship. Ramin et al. compared ever- versus never night workers and found night work to be associated with increased odds of obesity (130). Among night workers, high levels of average night shifts per month were significantly associated with an increased risk of obesity: the association was dose-dependent. Similarly, other studies have found a dose–response relationship between night shift intensity and body–weight related outcomes (131,132). While a dose–response relationship could be suggestive of a causal relationship between night work and weight gain, all studies mentioned in this paragraph have cross-sectional designs. Directionality is a prerequisite for causal inference, and these studies exemplify the need for prospective studies.

Study 2 is, thus, a natural extension of our findings from Study 1. Former prospective studies on the association between shift work and body-weight related outcomes have often taken a dichotomous approach: comparing day workers with shift- or night workers(128,129). We aimed to address shift work beyond that of a single construct prospectively. We addressed working schedules, changes of schedules, and cumulative night work exposure (NNs). We found all work schedule groups except day-only workers to have significant weight gain during follow-up. Our main finding in Study 2 was that night-only workers had significantly larger weight gains compared to day-only workers. The relationship was also upheld in our adjusted model.

By investigating those who changed towards- or away from a schedule containing night work, we tried to address the question of introduction or withdrawal of the exposure to night work and changes in body weight. Former studies have found an association between BMI change and withdrawal from- or introduction of night work exposure, which from an epidemiological perspective further strengthen the argument of a causal relationship between shift work and weight gain (128,129,133). However, we did not replicate these findings. A limitation in our study is the disproportionately large selection out of schedules containing night work compared to the selection into schedules containing night work. Nurses may opt-out of night work for many reasons unrelated to coping, while those choosing a demanding schedule with night work may be especially prone to cope with night work. Such selection biases may have distorted our results. Unfortunately, we do not have any information about why these nurses quit; if one was able to stratify on such qualitative aspects, then the result may have been more nuanced. These issues could further be confounded by possible preselection effects before our baseline assessment. No significant differences were found between day workers and 3-shift workers (rotational shift workers), even though such differences have been found in other studies (121,127). However, regarding rotational shift work a Danish study found two and three shift schedules with nightwork to be associated with lower odds of weight gain compared to fixed-day work (138). In this regard, the evidence on rotational shift work and weight gains remains equivocal to some degree. One could argue that rotational work allows for day-time activities. This could be of particular importance in households with children and high domestic demands.

Study 2 failed to replicate the dose–response relationship suggested by the cross-sectional findings from Study 1. Shift work exposure can be difficult to monitor, especially self-reported data of dynamic exposure variables such as NNs. However, we addressed NNs among the cohort as a whole, and in subgroup analyses for night workers, and day-only vs. night workers. We did not find any patterns of a dose-response relationship between the graded exposure groups. When evaluating within-group differences among night workers, all groups had significant weight gain, except for the middle exposure group (20-40NNs/year). An American study investigating rotating night shift work, job strain, and changes in BMI found that duration (number of months) of night work exposure during the 4-year follow-up period and BMI change reported an inverted u-shaped relationship (175). While these findings are not comparable due to the differences in assessment of night work exposure, both findings raise a fundamental question about the nature of the relationship between cumulative night work exposure and weight gain. The assumption of a linear dose–response relationship may not hold. Obviously these findings need to be replicated by prospective studies to determine the nature of the relationship. Theoretically, one could argue for both a u-shaped and an inverted u-shaped relationship between cumulative night work exposure and weight gain. Those with low exposure may be struggling shift workers who have reduced their night workload, and those with high exposure may also be struggling due to high workload, circadian disruption and sleep curtailment. On the other hand, those with low exposure may be the only group with sufficient recovery, the middle exposure group may suffer from sleep curtailment and circadian disruption, while the nurses with the highest night shift exposure may be a selected group as a result of survivor effects– only those who cope over time stay in such a schedule. The latter concern underlines the importance of future studies to account for preselection effects, and ideally follow cohorts of workers from their entry into the workforce.

Statistical significance does not always equal clinical significance, and a critical reader will probably try to translate our findings into a clinical context. One can try to elaborate: one may argue that, despite the statistically significant associations, the effect sizes in terms of β-values and OR are small and, thus, may not be clinically relevant. If one addresses this questions in terms of the OR of 1.01 for the association between numbers of nights worked the last year and the odds of being obese, the OR of 1.01 suggests that the odds of being obese may substantially differ among those with low and high levels of exposure to night shifts; one extra night shift per year will increase the odds of being obese by 1%. Evaluating our main finding in Study 2, the significant difference between day-only and night-only workers in weight gain during the four-year follow-up period, the difference between working day-only and working night-only would translate into a 0.89 change in BMI all else being equal. We consider this to be of clinical significance.

5.2 Shift work and lifestyle factors

5.2.1 General considerations

Lifestyle factors have been suggested to act as both confounders and mediators in models trying to elucidate the association between shift work and adverse consequences on cardiometabolic health (60,137,139). Still, while theoretical models often incorporate lifestyle factors as mediators, the epidemiological evidence remains equivocal (141,176). Below follows a more thorough discussion of our findings in relation to the current body of evidence for each of the respective lifestyle factors addressed in this thesis. The SUSSH cohort does not include dietary data, and subsequently, this thesis does not address this issue. However, as suggested in previous studies, dietary differences regarding the composition of nutrients, increased snacking during night shifts, and of the temporal distribution of energy intake may differ for workers in various working arrangements and contribute to the observed differences in cardiometabolic health (157,159,177).

5.2.2 Smoking

Smoking prevalence has declined during the last two decades. In Norway, the smoking prevalence in the population was 12% in 2018, which is down from 32% in 1998 (178). This secular trend makes the comparison to older studies difficult. Furthermore, the present-day validity of these older studies is challenged by a changing working environment and a growing service sector. Many former studies were based on male blue-collar workers. A review from 1999 on risk factors and cardiovascular disease revealed that many studies reported increased smoking prevalence among shift workers compared to their day-working counterparts (117).

Our young, female-dominated cohort differs somewhat from many earlier studies in this respect. In both Study 1 and Study 3, we did not find any significant differences between our examined shift work characteristics and smoking prevalence. Study 3 addresses shift work in terms of NNs, QRs, and compares different working schedule groups; no between-group differences regarding smoking were found. When evaluating within-group differences among day workers and night workers a clear trajectory emerges for both groups—a major decline in smoking prevalence. Furthermore, we see a similar trajectory for those who changed towards or away from night work. Here the findings are not significant, probably due to group size and low baseline prevalence. Overall, our findings are consistent general smoking trends in Norway (179). This secular trend is probably a combination of increased health awareness and successful legislative changes. Since 1998, there has been legal protection from exposure to smoking in workplaces in Norway, smoking being allowed only in separate smoking rooms (180). It should also be noted that the decline in smoking prevalence has been accompanied by a rise in the consumption of snus – a moist tobacco product placed under the upper lip (179).

Some studies of nurse cohorts have reported higher smoking prevalence among night workers than day workers. Comparing ever and never night shift workers among nurses, Ramin et al. found ever night-shift workers to have a higher smoking prevalence than never night-shift workers (OR 1.30 (1.19–1.42)) (130). Another large study evaluating only females and comparing ever night workers with never night workers found a significantly higher odds of being a current smoker among ever night workers (OR 1.37 (1.19–1.58)) (181). Evaluating difference in smoking habits, Kivimäki et al. found ever shift workers to smoke more compared to never shift workers (141). In Study 1, we found that cigarettes smoked per day among smokers were higher among those with >5 years of night work experience than those with less. However, these studies are cross-sectional and, thus, cannot say anything about trajectories. One objection to our study could be that inaccuracies in the exposure assessment make it difficult to detect any differences. Still, the fundamental difference, making comparison difficult, is the large secular trend with falling smoking prevalence in Norway and this secular trend could also diminish the differences among day and night workers earlier observed.

Several studies have argued that smoking is a possible mediating factor and not just a confounder in the relationship between shift work and cardiovascular disease (60,137,139). In a Danish study evaluating newly-educated health care assistants' health behaviors before entering the workforce and one year after they had entered the workforce, the researchers found that fixed-night workers had higher odds of smoking relapse and lower odds of smoking cessation than fixed-day workers (138). These findings are echoed by the authors of another study comparing shift and day workers; the number of cigarettes smoked per day increased significantly more among shift workers compared to day workers (137). Smoking is known to have alerting effects that may be beneficial during night shifts (182). While these findings have not been investigated directly in this thesis, one may still speculate about whether initiating positive changes to lifestyle factors may be more challenging for shift workers than those with less demanding schedules, especially concerning lifestyle factors with possible altering effects. While we addressed changes both in terms of working schedules and change scores in NNs and QRs, we did not find any significant changes supporting this. However, the general, secular decline in smoking prevalence in Norway as observed in this cohort may make it very difficult to detect such nuances.

5.2.3 Alcohol

While evaluating different aspects of shift work exposure and AUDIT-C score, both as a continuous and as a dichotomous parameter, we did not find any significant between-group differences in Study 1 or Study 3. In Study 1, we found a significant association between working hours and AUDIT-C score, which corroborates earlier findings of a positive relationship between alcohol and long working hours (140). An association between long working hours, night work and alcohol has also been found:

in an American study the researchers identified a significant interaction between long working hours (>8hours) and night work on alcohol consumption (144).

Our prospective data from Study 3 did not reveal any between-group significant differences for any of the shift work characteristics addressed and AUDIT-C score. As addressed in general terms earlier in this thesis, caution is needed when interpreting negative findings in shift work research. Still, our results are supported by other findings regarding total alcohol consumption across different working time arrangements (141,143). It should be mentioned that significant heterogeneities in terms of both measurements of exposure to shift work and the assessment of alcohol consumption make comparison difficult (141,142). Beyond alcohol consumption, a few studies have examined both drinking patterns and reasons for consuming alcohol. Dorrian et al. evaluated the drinking patterns between shift and day workers. They found evidence of increased risk of binge-drinking behaviour among shift workers (145,146). Another study revealed that night-shift workers with poor sleep quality had higher alcohol consumption than the others workers in the cohort, suggesting that alcohol may be used as a therapeutic tool to improve sleep-related problems (143). One review even draws the opposite conclusion; night shift workers were found to have lower alcohol consumption compared to day workers, and the duration of night work tended to be associated with lower alcohol consumption (160).

In line with this, Study 1 found night work experience over 5 years to be associated with lower AUDIT-C score compared to those with less night work experience. An interesting finding by other authors from the SUSSH cohort is that the AUDIT-C score was higher among nurses new to night work compared to those with experience above 6 years of night work (183). A limitation was that it was just a crude assessment, not adjusting for age. In Study 3, except within-group changes among day workers toward the cohort mean, we found no significant changes in AUDIT-C score. However, when looking at the absolute figures and trajectories in Study 3 for the work schedule groups, we found that those who stopped night work reduced their AUDIT-C scores, while those who started night work increased their AUDIT-C scores. Great caution must be taken when evaluating non-significant directionalities, but it is interesting to compare these findings with the other findings mentioned above from the SUSSH cohort where experience seems to give rise to lower AUDIT-C score. One possible explanation is that experience and the accumulating selection effects –only those who cope with night work stay– account for these findings. However, we did not find any differences when evaluating changes in NNs and QRs exposure and AUDIT-C score. Similarly, a Korean study investigating shift working nurses found an inverse relationship between shift work experience and regular alcohol consumption (132). This could also be part of the reason why the above mentioned review concluded that night workers when compared to day workers seemed to be associated with lower alcohol consumption (160).

Evaluating our findings and those from other studies one may speculate if entering into demanding schedules, including night work, may be a crucial period where the likelihood of changing lifestyle factors in negative direction increases. One example being alcohol consumption, another the above-mentioned findings by other researchers on smoking cessation and relapse. In Study 3, we only found non-significant changes in AUDIT-C score for those who opted in or out of schedules containing night work. A reason for that these findings did not reach statistical significance is that these changes may attenuate over time. Following this line of reasoning our long follow-up time of six-years may be a limitation concerning this particular issue.

5.2.4 Caffeine

In addition to its positive long-term health effects, caffeine has been suggested to have therapeutic use in mitigating sleepiness and enhancing performance during night shifts (147,149,150). Study 1 found a significant, but small, association between NNL and caffeine consumption (OR 1.00 (1.00–1.01)). However, this finding was not replicated in Study 3. In Study 3, we found a significant within-group increase in caffeine consumption among all the different work schedule groups. This increase could be because a large part of the cohort had just entered the workforce and, thus, could be changing their caffeine consumption habits with their transition into the workforce. Another paper from the SUSSH cohort found experienced night working nurses to consume more coffee than those new to night work (183).

While addressing the between-group difference in Study 3 for workings schedules, NNs, or QRs, we found no significant differences between our investigated shift work characteristics and caffeine consumption. Our findings are consistent with those of Drake et al. who did not find any significant difference between day workers, permanent night workers, or rotating shift workers concerning caffeine intake in a cross-sectional study (151). In contrast, Ramin et al. found a significantly higher caffeine intake among night workers in their cross-sectional study when comparing those who had always worked night shifts to those who had never worked night shifts (130). A recent review on night work and nutritional patterns found relatively consistent higher use of caffeine among night working nurses (160). Still, one could argue that both early-morning shifts and night shifts may be challenging for nurses because both shift-types may interfere with the nurses' circadian rhythms and, thus, result in high levels of sleepiness. Caffeine may be used by both groups to mitigate sleepiness. Similarly, nurses with different work schedules, may all have high exposure to QRs, NNs, or both which could leave the shift worker in constant circadian misalignment, sleep deficient, and challenged by conflicting work and domestic demands. Thus, one could argue for a high consumption across all shift work characteristics, which could explain our findings of no differences between the different exposure groups

5.2.5 Exercise

A lack of adequate exercise has been proposed to be one mediating mechanism between shift work and increased body weight, for example, as a result of impaired work–life balance (4,60). One argument is that shift workers have less opportunity for leisure-time activity than those with less demanding schedules (161). The proposed associations, although sound in theory, are not corroborated by the current body of evidence. Exercise habits or activity can be difficult to measure, but the majority of studies conclude that there are no significant differences between shift workers and their day working counterparts despite heterogeneity in the outcome measure. Study 1 and Study 3 draw the same conclusion concerning exercise habits: no differences were found across our different exposure assessments.

Our operationalization of exercise may not have been sensitive enough to detect minor differences in the investigated shift work characteristics and exercise habits, but concerning leisure-time activity, both self-reported measures and objective measures of activity, report the same results: no large differences are found between day and shift workers (153,154,184). Interestingly, while not finding any differences between leisure-time activity, Hulsegge et al. found shift workers to be more sedentary at work. The findings are not consistent; other studies have revealed shift workers to be more active during work (152,153). Although leisure-time exercise is generally believed to be beneficial, increased work-related activity can be a symptom of a stressful working environment and may, thus, not be beneficial (156). In terms of cardiovascular risk, psychosocial stress due to high occupational demands may, in fact, contribute to increased cardiovascular risk (185).

5.3 Countermeasures

There is no single antidote for the negative health consequences of shift work. Countermeasures must be taken on the individual and the organizational level. Increased knowledge about sleep and circadian rhythms on both levels could help mitigate the negative effects of shift work.

The individual shift worker feels the strain from circadian disruption and insufficient sleep on a day-to-day basis: sleepiness, fatigue, and sleep-related problems (41,42). Possible options to mitigate excessive sleepiness during night work include optimized illumination, naps, and correctly scheduled caffeine intake (186). After work measures to minimize circadian disruption and promote enough sleep should be emphasized. Increased knowledge about circadian principles and sleep hygiene could decrease sleep deficits: for example, correctly scheduled bright light treatment or melatonin treatment, and the importance of immediate sleep after night shifts (186). Furthermore, knowledge about additional treatment options and where to seek help should be made known and available to struggling shift workers. The protective role of adherence to a healthy lifestyle to counteract the negative long-term effects of shift work should be made explicitly known. For example, exercise increases shift work tolerance and promotes cardiometabolic health (85). Age seems to be inversely related to shift work tolerance. Older shift workers could, for example, get exemptions from demanding night shifts (187). Sound self-help literature exists and should be made known to shift workers (74,188).

On the organizational level, optimal scheduling based on sound circadian and sleep principles should be the norm. Nonetheless, many working-time arrangements violate these principles, an example being the frequent use of quick returns among nurses or the long night shifts of Norwegian doctors extending half-way into the next working day, thus placing the whole sleep period in the wrong period of the circadian rhythm; the result being severely truncated sleep. Most reviews focus on the same themes for optimal scheduling: the provision of forward-rotating shift schedules, a maximum of three consecutive night shifts, a minimum of 11 hours of rest between shifts, the avoidance of very early morning shifts, limitation of shifts to 8 or 12 hours, the provision of an adequate number of rest days, especially after demanding shift spells, and the allowance for flexible working time arrangements if possible (82,83,186,189). Occupational physicians are needed on both the individual and organizational levels (190). Health examinations for shift workers should be tailored to this group and go beyond changes in anthropometric measures and basic screening examinations. Examples of tailored advice could include the provision of nutritional advice, emphasis on the importance of regular exercise, and dissemination of knowledge about the importance of adherence to circadian principles and sleep hygiene. Health promoting interventions in the workplace regarding weight related outcomes have been found effective, but it is uncertain to what degree such interventions reach those with night and evening work (191,192). Workers changing from day- to night work and night- to day work should receive special attention. For those starting night work, baseline assessments and sound advice as mentioned above should be given; for those opting out of night work, assessment should be made about why they quit, and to see if they need additional future follow-up. Furthermore, occupational physicians should be available for managerial staff for recommendations on optimal scheduling.

5.4 Methodological considerations

The strength of the SUSSH cohort is its relatively large, homogenous population and prospective design. An advantage of conducting a study on a homogenous population is that possible confounding factors related to occupation are avoided, for example, socioeconomic status. Another strength is that the cohort is relatively young and newly-educated, which should help minimize preselection effects. We also believe that when addressing lifestyle factors and BMI, as was done in this thesis, it is important to exclude pregnant women, as we did in Study 2 and Study 3, especially in a female-dominated cohort. Still, many studies have not accounted or adjusted for pregnancies in their analyses. This thesis addresses the exposure, shift work, beyond the simple approach of comparing different work schedules with different outcome measures. We tried to deconstruct shift work into important constituents such as cumulative night shift exposure and cumulative QRs exposure. In both Study 2 and Study 3, we utilized the data longitudinally, which constitutes a methodological improvement compared to cross-sectional data, which has often been used in shift work research.

As a corollary to the last argument, an obvious limitation of Study 1 is the reliance on cross-sectional data. Measurement taking place only once at only, as in a cross-sectional study, cannot provide information about temporality and thus not directionality. The result being that no causal inferences can be made about significant associations found in cross-sectional studies. From this perspective, Study 2 and Study 3 are extensions of Study 1, and represent substantial improvements by utilizing prospective designs.

Among the general limitations of this cohort study is the initial response rate of 38.1% in wave 1a and of 33.1% in wave 1b. This raises the question about the representativeness of the SUSSH cohort. A limitation, in this regard, is that we have no information about the non-responders, which makes attrition analysis impossible. A possibility, thus, exists, that the non-responders differ significantly from the responding and final cohort investigated. However, low initial response rates are not unique to the SUSSH cohort: a study by Baruch et al. suggested that most study populations have a response rate of around 53%±20% (1 standard deviation from the mean response rate) (193). The initial response rates are within this range, and it should also be emphasized that the later waves had high and stable response rates, where the lowest response of the consecutive waves was in wave 7 with 67.5%.

Possible misclassification bias and selection bias are common issues within shift work research. The selection effects are collectively called the healthy worker effect; only those who are healthy and can cope with a demanding work schedule tend to choose and stay in such a schedule (139,167,194). One study found former shift workers to have more morbidities than shift workers for each age strata, furthermore, among shift workers the oldest workers were found to show remarkable adaptability and resilience to the 12hour night shift (195). These findings exemplify the selection out of shift work for those workers who for various reasons do not cope with night work, and the survival bias of the workers who remain. Another issue is that of the misclassification of exposure. One study revealed that when comparing self-reported data to objective registry data among those who reported working shift work without night work there was a low sensitivity to correct classification due to the fact that many of these nurses did not report their night shifts (166). Both the misclassification of exposure toward the non-exposed and selection away from night work share a common theme: both biases will most likely skew the results toward the null. The underestimation will be problematic for all results, but the tendency of these biases to skew the results toward the null may be especially problematic with negative results, as exemplified by the results in this thesis on shift work and lifestyle factors. The probability of a false negative result may, thus, be higher than that expected by randomness, the result being an increased probability of committing a type 2 error when we conclude that no difference exists. Due to this important limitation, extra caution is needed when interpreting the negative results in this thesis and to emphasize the importance of replication of the results with large and sensitive studies. Study 2 and Study 3 do, to some degree, account for the selection effects that occurred during the follow-up period and address those who changed toward– and away from schedules containing night work. A possible collective problem for all three studies in this thesis is the risk of preselection effects, that is, accounting for nurses who selected out of demanding schedules prior to the collection of the first wave. Some cross-sectional studies have used ever vs. never shift workers for comparison to avoid the methodological issue regarding preselection effects (130,141). However, as mentioned, we believe that the young age of this cohort may mitigate the problem of preselection effects to some extent.

The generalizability of a large homogenous, female-dominated cohort may be questioned, and occupational and gender differences could exist. May the male blue-collar shift workers differ more from their day working counterparts than the nurses in this cohort? Regarding the external validity of this study, another concern is that the results may not apply to other countries: large secular trends in, for example, smoking prevalence, and legislative changes to reduce smoking prevalence in Norway may not be applicable to other countries (180). Scandinavian countries are known for their well-regulated working-time arrangements, solid welfare programs, and equality between genders. These societal and cultural traits may have influenced the results, an earlier mentioned example being that the double burden and strain between work and domestic demands felt by many female workers may be less troublesome in the egalitarian Scandinavian countries than other countries.

The study relies on self-reported data and there are uncertainties in terms of how well the data reflects objective realities, a relevant example being the tendency to overestimate height and underestimate weight compared to objectively collected data (196). The data was collected annually, and this probably helps minimize the risk of recall bias (197). We have tried to assess exposure to shift work beyond working schedules. Still, even with regular working schedules, the accuracy of nurses' own reports may not be entirely accurate (166). For example, some nurses work extra shifts beyond their regular working schedules. We have argued that one of the strengths of this thesis is that shift work was assessed beyond working schedules.

Nonetheless, the use of NNL/NNs and QRs is not without methodological issues. One could easily argue that nurses' estimations of NNL/NNs and QRs may be uncertain. These variables may fluctuate, but most nurses work regular, repeating schedules, and should be able to make good estimations of these parameters on a yearly basis. All nurses who were included in the SUSSH cohort should have had at least a 50% work position; this helped to minimize the share of very small working positions. Still, there will be variations in their weekly hours. This could be a limitation, especially for working schedules which do not account for this. Contrarily, it should also be noted that many nurses with smaller permanent positions work extra shifts which are not accounted for in the data. Concerning NNL/NNs and QRs exposure, these parameters are reported as a continuous parameter and should thus reflect the nurses' actual exposure. Another methodological concern is whether the use of an average is a good approximation of the actual exposure to QRs or NNL/NNs. In study 3, we used the average of the baseline and follow-up measurements, we could, thus, not account for large fluctuations between these two measurements. However, we tried to adjust for those who made permanent changes by using a change score in addition to an average score. Still, the results remained the same. Nonetheless, there can be large variations in the follow-up period, due to maternal or sick leave, for example, which were not accounted for in Study 2 and Study 3 which had a prospective design.

One always tries to address the research hypothesis in the best possible manner when using a collected dataset. Still, the choice of variables, the structuring of these variables, and the use of statistical methods always involves choice and, hopefully, sound judgment. In Study 3, we faced a tough decision due to the small group size for some of the working schedule groups, should we proceed with the original groups or collapse the groups into day and night workers? For our primary analyses, we chose the latter, but we also analyzed the original working schedules in our models. The justification for grouping night workers together into one group is based on the premise that night work is the most detrimental aspect of shift work (114). However, the validity of this argument could be questioned regarding lifestyle factors; for example, evening work may interfere with social life and opportunities to exercise more than night work. Still, no difference was found between the different original working schedules and the respective lifestyle factors in our additional analyses. However, the small group size, lack of statistical power, and the possibility of the aforementioned biases warrant caution when interpreting a negative result. Another potential concern regarding the working schedule groups is the monitoring of those who changed toward or away from night work in the follow-up period: A limitation here is that we did not account for at what time in the follow-up period they changed schedule.

Our choice and structuring of lifestyle factors in this thesis deserve justification. Regarding BMI, we used this in a conventional way. In Study 1, we also used obesity as an outcome measure: We used a broader definition of BMI>30.00 as our definition of obesity, which differs marginally from the more conventional approach (BMI≥30.00). Still, we reexamined the data, and no nurses reported having BMI exactly of 30.00 so the small differences in obesity definition did not affect the results in Study 1. The data was analyzed with two decimals, making the difference between the two definitions miniature.

Ideally, validated instruments or objective measurements should be used for both exposure and outcome measures. Structuring and analyzing self-reported data will always be open to judgment and involve the need to balance competing arguments and concerns. In this regard, exercise habits were evaluated with a dichotomized parameter (<1hour exercise/week or ≥1h) in Study 1. Caution is needed when interpreting such a crude measure, because it may fail to detect nuances among different groups. In Study 3, we tried to elaborate on this by analyzing exercise as in Study 1 and, in addition, we compared those who exercised least (contrast) to those who exercised most. Still, our data may reflect realities to a lesser extent than objective data, such as actigraphy data or conversions of different forms of self-reported physical activity to standard units such as the metabolic equivalent of task (MET) (198). AUDIT-C is a well-known, validated instrument, but limitations in our data set may raise concerns. In Study 1, we used AUDIT-C as both a continuous parameter and as a gender-adjusted dichotomized parameter to assess a threshold for potential misuse. We used the same approach in Study 3. However, due to a change in wording in the AUDIT-C questions between the first wave (1a) and consecutive waves, we felt uncertain about the comparison between this wave and later waves. Our solution was to compare only the latter part of the first wave (1b). This solution was not without cost; it reduced the statistical power of the analyses and, in addition, one could question the representativeness of the cohort of newly-educated nurses making up the 1b wave. Another potential limitation concerning the use of the AUDIT-C is that while the two first questions address frequency and volume, we do not have exact information about daily or weekly alcohol consumption, for example, units/week. The data may, thus, fail to detect nuances and changes in lighter or normal alcohol consumption habits which could be of importance.

We approached the two prospective studies in this thesis using two data points. The main reasons for doing this was that we do not have complete datasets for all questions in each annual wave. Another reason is that some nurses failed to address all the questions in the questionnaire. The latter would thus reduce the power of the study. Still, as the cohort progresses and we have more additional time-points it would be natural for future studies to rely on more sophisticated statistical analyses such as Mixed Models or General Estimating Equations (GEE) (199). Examples of the advantages of such techniques would be in their handling of missing data and corrections for within-subject dependencies between multiple observations. From a statistical perspective, our multiple testing in Study 2 and a single between-group significant finding could raise a concern about the risk of committing a type 1 error—falsely concluding that a difference exists. We did not account for multiple testing in our analysis. Corrections such as Bonferroni's are considered conservative, and the use of corrections are controversial because there will always be a trade-off between reducing the rate of a type 1 errors and increasing the rate of a type 2 errors) (200). Other studies with similar designs have also chosen not to correct for multiple testing (128,129).

5.5 Implications and suggestions for future research

There is a crack, a crack in everything
That's how the light gets in
Leonard Cohen – Anthem

Our findings from Study 1 and Study 2 suggest a significant positive relationship between night work and weight gain. Study 2 had a large cohort with a prospective design which improved the methodological quality beyond the cross-sectional assessments in Study 1. Future studies should go even further in enhancing methodological quality. Beyond sufficient cohort size and prospective designs with adequate follow-up periods, examples of methodological improvements include an objective assessment of exposure and outcomes, as well as the deconstruction of shift work into its constituents. Scandinavian countries have good registry data: payroll registries may be a source of objective and accurate exposure data. While there large differences in working time across occupations and countries, great effort should be taken to use standardized or consensus-based definitions of shift work and its' constituents, and working time patterns in general. This would reduce heterogeneity in exposure assessment and facilitate knowledge synopsis.

Studies with negative results are difficult to interpret, especially when they rely on self-reported data and there is a risk of residual confounding. Our findings from Study 3, where we found no difference among different shift work exposure parameters and lifestyle factors need to be replicated concerning such methodological improvements mentioned above. Future studies should be large and sensitive in their exposure assessments. This will minimize the risk of committing a statistical type 2 error—falsely concluding that no difference exists.

There is a large selection out of demanding work schedules among the nurses in our cohort, especially out of schedules containing night work. Study 2 and Study 3 corroborate this. The SUSSH data stems from a relatively young cohort, which should minimize preselection effects. Ideally, future cohort studies should follow newly-educated workers from the start to avoid uncertainties regarding preselection effects. Increased attention should also be directed toward those who experience negative consequences and quit shift work, what characterizes this group, and what preventive measures are efficacious. Thus, there is a need for qualitative and intervention studies.

In both Study 2 and Study 3, we evaluated shift work beyond that of a single construct. Both QRs and night shift intensity were addressed. This approach should be used more widely to identify the especially hazardous aspects of shift work, both in terms of adverse health consequences and operational safety. Regarding outcome measures, there are, as documented, large heterogeneities in how lifestyle factors are measured. Effort should be taken to use standardized, validated outcome measures. Regarding body-weight related outcome measures, future studies should use both BMI and obesity as outcome variables. A single focus on a dichotomous parameter like obesity may lead to a failure to detect important nuances with possible substantial long-term implications regarding weight gain.

6. CONCLUSION

Every culture has its own unique set of temporal fingerprints.
To know a people is to know the time values they live by.
Jeremy Rifkin - Time Wars

In this thesis, we have examined different shift work characteristics for possible adverse effects on body-weight related outcomes. Furthermore, we examined the same shift work characteristics for their potential impact on lifestyle factors.

For body-weight related outcomes, our findings contribute to the current body of evidence suggesting that night work leads to increased body weight. The result of Study 1 suggested a dose-response relationship between number of night shifts and weight increase. Study 2 corroborates this finding to some degree because we found that night-only workers underwent significantly larger weight gains than day-only workers. However, we did not find evidence of a clear dose-response relationship between cumulative night work exposure and larger weight gain in our prospective assessment.

Study 1 and Study 3 addressed shift work and lifestyle factors. Overall, we found no difference concerning different working schedules, differences in cumulative exposure to night shifts, or differences in cumulative exposure to QRs and lifestyle factors. Our conclusion corroborates other investigations on shift work and lifestyle factors and challenges the notion that shift workers differ fundamentally from their day working colleagues regarding lifestyle factors.

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Associations between night work and BMI, alcohol, smoking, caffeine and exercise - a cross-sectional study

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Abstract

Background: Shift work is associated with negative health effects. Increased prevalence of several cardiovascular risk factors among shift workers/night workers compared with day workers have been shown resulting in increased risk of cardiovascular events among shift workers and night workers. Previous studies have taken a dichotomous approach to the comparison between day and night workers. The present study uses a continuous approach and provides such a new perspective to the negative effects of night work load as a possible risk factor for undesirable health effects.

Methods: This cross sectional study (The SUrvey of Shift work, Sleep and Health (SUSSH)) uses data collected from December 2008 to March 2009. The study population consists of Norwegian nurses. The study collected information about demographic and lifestyle factors: Body Mass Index (BMI), smoking habits, alcohol consumption, caffeine consumption and exercise habits. The lifestyle parameters were evaluated using multiple hierarchical regression and binary logistic regression. Number of night shifts worked last year (NNL) was used as operationalization of night work load. Adjustment for possible confounders were made. Obesity was defined as BMI > 30. Alcohol Consumption was evaluated using the short form of the Alcohol Use Disorders Identification Test Consumption (AUDIT-C). Data were analyzed using SPSS version 22.

Results: We had data from 2059 nurses. NNL was significantly and positively associated with BMI, both when evaluated against BMI as a continuous parameter (*Beta* = .055, $p < .05$), and against obesity (OR = 1.01, 95 % CI = 1.00-1.01). The AUDIT-C score was significantly and positively associated with hours worked per week (OR = 1.03, 95 % CI = 1.01-1.05).

Conclusions: We found a positive significant association between night work load and BMI. This suggests that workers with a heavy night work load might need special attention and frequent health checks due to higher risk of undesirable health effects.

Keywords: Shift work, Night work, BMI, Obesity, Alcohol, Caffeine, Smoking, Exercise

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Background

Shift work is consistently shown to be associated with adverse health effects, i.e. gastrointestinal complaints, sleep difficulties, cancer, cardiovascular and metabolic diseases, and mental health problems [1–4]. In industrialized countries many sectors rely on 24 hours services, for instance the health care sector. With increasing evidence in terms of adverse effects on health, more attention and research has been directed to this field. In particular, much emphasis has been put on the possible increased risk of cardiovascular disease among shift workers, although a causal relationship remains unclear [5–8].

Cardiovascular disease is one of the leading causes of death in industrialized countries. Over the years several cardiovascular risk factors for have been identified, and much effort has been devoted in order to reduce or eliminate the impact from these. Especially among sub-populations/high risk groups, risk stratification and primary prevention has been advocated, such as smoking cessation, increased physical activity, moderate alcohol intake, and weight management [9].

Several studies have focused on relative differences in prevalence of cardiovascular risk factors of shift workers/night workers compared to day workers. Shift and night workers have higher prevalence of risk factors such as smoking, dyslipidemia, and weight gain when comparing to day workers [5, 6]. Biggi et al. found that the cluster of independent risk factors collectively termed metabolic syndrome was increased among night workers compared to day workers [7]. Bøggild et al. concluded in a metaanalysis that shift work represented a 40 % increase in the risk of cardiovascular disease [8].

As a result of the increasing evidence supporting negative health effects of shift work, newly published studies suggest that countermeasures are needed to reverse this. Different measures for primary prevention have been proposed to counteract the negative effects of shift work: for instance, proper work scheduling, exercise, and dietary guidelines [10, 11]. In addition to longitudinal studies addressing possible causal relationship between shift work and cardiovascular disease, more studies are needed to investigate possible sub-populations among shift workers who have an elevated risk for developing cardiovascular disease.

Most previous studies have taken a dichotomous approach to the comparison of night and day workers in terms of possible cardiovascular risk factors such as weight gain and elevated BMI. The present study instead evaluates the night shift work load effect on BMI, alcohol consumption, smoking habits, caffeine consumption, and exercise habits using the number of night shifts worked the last year as a predictor. Our design may help to investigate further whether workers with a heavy night shift work load might need more frequent health checks or more direct countermeasures due to increased risk of undesirable health effects and habits.

Methods

Design

The data were stemmed from “The SUrvey of Shift work, Sleep and Health” (SUSSH). This cross-sectional study was conducted from December 2008 to March 2009. The population consisted of registered members of the Norwegian Nurses Organization (NNO), which include most of the nurses working in Norway today. In January 2009 there were 87083 registered members of NNO. A stratified sample ($N = 6000$) comprising a total of five strata; each containing 1200 nurses holding at least a 50 % work position, was randomly selected from the member registry of the NNO. The criteria for the different strata were time elapsed since graduation: less than 12 months (stratum 1), 1–3 years (stratum 2), >3-6 years (stratum 3), >6-9 years (stratum 4) and >9-12 years (stratum 5). Each nurse in the sample received a questionnaire by postal mail. After completing the questionnaire, the respondents could return them in a pre-paid envelope. Two reminders were sent to those who did not respond. An internet version of the questionnaire was available for those who preferred to complete the questionnaire online. A total of 600 letters were returned due to wrong addresses. As a result the final sample consisted of 5400 nurses, of which 2059 participated in the survey, yielding a response rate of 38.1 %.

Data

The questionnaire covered demographic factors in terms of sex and age, marital status, and whether the responders had children living at home. Responders were also asked for their working schedule: day only, evening only, day and evening, three shift rotation, night only, or another schedule including night work. The questionnaire also covered how long they had been working this schedule, and how long they had worked as a nurse. The nurses were asked to indicate the number of night shifts they had worked the last year (NNL). Furthermore they were asked to report average work hours per week, and their percentage of a full time equivalent work position (50-75 %, 76-90 % and above 90 %).

BMI

Body Mass Index was calculated conventionally using weight over the square of height in meters. The nurses self-reported height and weight in the questionnaire. We had data on weight and height for a total of 2038 nurses. Obesity was defined as BMI > 30.

Smoking habits

The nurses were asked if they smoked daily (yes/no). Those who smoked were further asked to provide number of cigarettes smoked daily. In our cohort 214 nurses were daily smokers. Number of cigarettes smoked daily comprised the dependent variable in the linear regression analysis wheras daily smoking (yes/no) was used as dependent variable in a logistic regression model.

Alcohol consumption

Alcohol Consumption was evaluated using the short form of the Alcohol Use Disorders Identification Test Consumption (AUDIT-C). AUDIT-C is a self report instrument with three items measuring alcohol consumption. The instrument appears to be a practical, valid primary screening test for heavy drinking and/or active alcohol abuse or dependence [12]. A score of 3 or higher points on the AUDIT-C might indicate potential alcohol misuse. In a primary care setting a threshold score of 3 or higher in females, and 4 or higher in males simultaneous maximized sensitivity and specificity [13]. We had data for 2021 nurses. In our analysis we used the composite AUDIT-C score as a parameter for potential alcohol misuse in a hierarchical regression analysis, and the dichotomous AUDIT C score (cut off: ≥3 for females and ≥4 for males) as dependent variables in logistic regression analyses. The Cronbach's alpha for AUDIT C was 0.68 in the present study.

Caffeine consumption

Nurses were asked to indicate average number of caffeine containing units consumed per day. The questionnaire did not differentiate between drinks with different total caffeine content. For example, one unit would be one cup of coffee or a glass of coca cola. 2050 nurses responded to this question. Caffeine consumption was evaluated as a dichotomous parameter (drinking 3 or more caffeine containing units vs. less than 3 units per day).

Exercise habits

Exercise was measured by an item asking for hours of sweaty exercise per week (0, <1 h, 1-2 h, ≥3 hours), and was answered by 1971 nurses. We collapsed exercise data into two groups (<1 h and ≥1 h per week). In a large female cohort study at least one hour walking per week predicted lower risk for cardiovascular disease [14].

Statistical analyses

SPSS version 22 was used for the analyses. In the linear multiple hierarchical regression models we wanted to investigate what kind of effect number of nights worked the last year (NNL) had on: BMI, alcohol consumption, smoking habits, when adjusting for possible confounding factors. Caffeine consumption was excluded from the multiple hierarchical regression model due to violation of normality assumption. Each of the lifestyle parameters were analyzed separately, using the same type of multiple hierarchical regression model. Step 1 included demographic factors: sex and age. Step 2 included hours worked per week and the duration of experience with night work (more or less than five years). In step 3. children living at home, and NNL were included in the model.

Furthermore, binary logistic regression analyses were used to investigate whether NNL was significantly related to the dichotomized (based on cut-offs) lifestyle parameters. Both crude and adjusted analyses were undertaken for all dependent parameters. Caffeine consumption and exercise habits were included as dependent variables in these models in addition to obesity, AUDIT-C, and

Table 1 Demographic characteristics of nurses with different kinds of night work load

	Number of nights worked last year		
	0 (*n* = 568)	1-30 (*n* = 860)	>30 (*n* = 631)
Age (*n* = 2057)	34.9 (34.2-35.6)	32.4 (31.8-32.9)	32.4 (31.8-33.0)
Gender (% female) (*n* = 2049)	92.6 % (90.4-94.7)	92.5 % (90.7-94.3)	86.3 % (83.6-89.0)
Hours Worked Per Week (*n* = 2017)	34.0 (33.4-34.6)	33.7 (33.2-34.1)	34.2 (33.6-34.7)
Average hours Sleep per Night (*n* = 2048)	6.9 (6.8-7.0)	6.9 (6.8-7.0)	7.0 (6.9-7.0)
Worked Schedule including Night Work (% > 5 years) (*n* = 1750)	26.7 % (21.8-31.5)	29.5 % (26.4-32.7)	43.5 % (39.6-47.5)
Sweaty Excercise (% > 1 hour per week) (*n* = 1971)	64.1 %(60.0-68.1)	67.4 % (64.2-70.1)	65.7 % (61.2-69.5)
BMI (*n* = 2038)	24.4 (24.0-24.7)	24.1 (23.9-24.4)	24.8 (24.4-25.1)
Obesity (*n* = 2038)	10.0 % (7.6-12.6)	6.6 % (4.9-8.3)	11.7 % (9.2-14.3)
AUDIT-C (*n* = 2021)	3.3 (3.2-3.5)	3.7 (3.6-3.8)	3.8 (3.7-4.0)
Caffeine Containing Drinks per Day (*n* = 2050)	3.2 (3.0-3.5)	2.8 (2.7-3.0)	3.2 (3.0-3.4)
Daily Smokers (*n* = 1956)	12.9 % (10.1-15.7)	9.7 % (7.7-11.7)	10.7 % (8.8-13.2)
Cigarettes per day among daily smokers (*n* = 214)	10.0 (8.6-11.4)	9.0 (7.9-10.1)	9.1 (7.9-10.3)

Confidence Intervals 95 % in parenthesis. *BMI* body mass index. Obesity defined as BMI >30. AUDIT-C = The *AUDIT* alcohol consumption questions smoking. The adjusted logistic regression models controlled for the same possible confounders as in the linear multiple hierarchical regression models described above. There is variation in the number of participants in the different models due to missing data, as indicated in the tables and data section. In the adjusted analyses, n will naturally be lower, since only participants who have answered all questions in the model will be included in the analysis.

Ethics

The Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West) approved the study.

Results

Demographics

The mean age was 33.1 years (SD 8.2), range 21 to 63 years. The study population consisted predominately of females (90.6 %). The nurses worked on average 33.9 hours per week (SD 6.5), 55.8 % of the nurses reported holding a working position that exceeded 90 %. They had worked on average 5.2 years as nurses (SD 4.3). In all 76.0 % worked in medical-surgical hospital departments, 13.8 % worked in psychiatric departments, 3.6 % in nursing homes, and 3.7 % worked in home care services, and 2.9 % in others respectively. Three shift rotation was most common (56.2 %), followed by two shift (24.8 %), night shift only (8.2 %), day shift only (7.5 %), other schedules with day and night 2.8 %, and evening shift only 0.2 %. For number of nights worked the last year a mean of 25.0 (SD 28.9) night shifts, with range from 0 to 206 were reported. A total of 66.1 % had schedules which included night work for less than five years, 33.9 % for more than five years. Sweaty exercise for ≥1 hour per week on average was reported by 28.2 % of the nurses reported. Demographic characteristics are shown in Table 1.

BMI

Mean BMI was 24.4 (SD 4.0). Using BMI as the dependent variable in the hierarchical regression analysis we found that step 1 (age and sex) explained 4.5 % of the variance (Table 2). Step 2 and 3 did not explain significant proportions of the variance. After step 3 the model as whole explained 4.9 % of the variance F(6,1668) = 14.18, $p < .05$. Evaluating each of the independent variables separately, number of nights worked the last year (NNL) was statistically significant and positively related to BMI ($\beta = .055$, $p < .05$). NNL was also significant and positively associated to BMI when adding exercise as an independent predictor to the same model (($\beta = .057$, $p < 0.05$). Data not shown. Age was positively related to BMI ($\beta = .145$, $p < 0.05$). Sex was positively and significantly related to BMI: females had lower BMI than males ($\beta = -.147$ $p < 0.05$). In our logistic regression model, NNL was positively associated (OR = 1.01, 95 % CI = 1.00-1.01) with obesity (BMI > 30) (Table 3).

Alcohol consumption

Mean score for AUDIT-C was 3.7 (SD 2.0). Using the same hierarchical regression model, we found that after step 3 the model as a whole explained 12.5 % of the

Table 2 Multiple hierarchical regression analyses with BMI, AUDIT-C, and number of cigarettes daily as dependent variable

	BMI (*n* = 1674)		AUDIT-C (*n* = 1622)		Number of cigarettes smoked daily (*n* = 184)	
	β	ΔR^2	β	ΔR^2	β	ΔR^2
Step 1		0.045*		0.063*		0.113*
Age	0.140*		−0.203*		0.288*	
Gender (1 = females)	−0.153*		−0.158*		−0.157*	
Step 2		0.0002		0.018*		0.016
Age	0.137*		−0.179*		0.246*	
Gender	−0.154*		−0.141*		−0.152*	
Average hours worked per week	−0.009		0.120*		0.002	
Schedule with Night Work >5 years	0.009		−0.067*		0.134	
Step 3		0.003		0.047*		0.010
Age	0.145*		−0.113*		0.267*	
Gender	−0.147*		−0.132*		−0.157*	
Average hours worked per week	−0.003		0.075*		−0.020	
Schedule with Night Work >5 years	0.001		−0.052*		0.152*	
Children living at Home no/yes	−0.009		−0.229*		−0.097	
NNL	0.055*		0.032		- 0.057	

* Significant finding $p < .05$. β Beta coefficient, $\Delta R2$ R square change, *BMI* body mass index, *AUDIT C* the *AUDIT* alcohol consumption questions, *NNL* number of night shifts worked last year

Table 3 Logistic regression analyses predicting effects on lifestyle variables

Independent Variable	Obesity (BMI > 30)				AUDIT-C (Score ≥3 female ≥4 males)				Smoking (yes/no)				Caffeine Consumption (Score ≥ 3)				Exercise Habits (≥1 hour per week)			
	Crude (n = 1730-2038)		Adjusted (n = 1622)		Crude (n = 1711-2011)		Adjusted (n = 1612)		Crude (n = 1658-1956)		Adjusted (n = 1557)		Crude (n = 1741-2050)		Adjusted (n = 1631)		Crude (n = 1678-1971)		Adjusted (n = 1575)	
	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI	OR	95 % CI
Age	1.02* n = 2036	1.00-1.04	1.02	0.99-1.04	0.95* n = 2010	0.94-0.97	0.97*	0.95-0.98	0.97* n = 1955	0.95-0.99	0.96*	0.94-0.97	1.10* n = 2048	1.08-1.11	1.10*	1.09-1.14	1.00 n = 1969	0.99-1.01	1.01	0.99-1.02
Gender																				
Female	1.00 n = 1836		1.00		1.00 n = 1821		1.00		1.00 n = 1737		1.00		1.00 n = 1849		1.00		1.00 n = 1774		1.00	
Male	1.83* n = 192	1.18-2.82	1.45	0.88-2.47	0.82 n = 190	0.60-1.13	0.78	0.53-1.15	1.15 n = 210	0.69-1.91	1.05	0.59-1.85	3.25* n = 191	2.30-4.58	3.17*	2.10-4.81	1.83* n = 187	1.34-2.50	1.65*	1.15-2.36
Average hours worked /week	1.00 n = 1996	0.98-1.02	0.99	0.97-1.02	1.03* n = 1971	1.02-1.05	1.03*	1.01-1.05	0.99 n = 1915	0.97-1.02	1.00	0.98-1.03	1.02* n = 2008	1.01-1.03	1.01	1.00-1.03	1.02* n = 1932	1.01-1.04	1.01	0.99-1.03
Schedule with night work																				
<5 years	1.00 n = 1141		1.00		1.00 n = 1130		1.00		1.00 n = 1097		1.00		1.00 n = 1150		1.00		1.00 n = 1115		1.00	
>5 years	1.31 n = 589	0.94-1.82	1.07	0.74-1.54	0.59* n = 581	0.47-0.73	0.75*	0.59-0.95	0.92 n = 561	0.66-1.28	1.15	0.80-1.65	1.70* n = 591	1.39-2.08	0.95	0.75-1.21	1.03 n = 563	0.83-1.28	1.10	0.86-1.41
Children living at Home																				
No	1.00 n = 982		1.00		1.00 n = 971		1.00		1.00 n = 941		1.00		1.00 n = 989		1.00		1.00 n = 944		1.00	
Yes	1.11 n = 966	0.82-1.51	1.08	0.75-1.54	0.48* n = 953	0.40-0.59	0.60*	0.47-0.76	1.05 n = 932	0.78-1.40	1.12	0.84-1.68	0.75* n = 969	0.63-0.90	0.83	0.65-1.00	0.61* n = 941	0.50-0.75	0.59*	0.47-0.75
NNL	1.01* n = 2038	1.00-1.01	1.01*	1.00-1.01	1.00 n = 2011	1.00-1.01	1.00	1.00-1.01	1.00 n = 1956	1.00-1.01	1.00	0.99-1.00	1.00* n = 2050	1.00-1.01	1.00*	1.00-1.01	1.00 n = 1971	1.00-1.01	1.00	1.00-1.00

* Significant finding, $p < .05$. *NNL* number of night shifts worked last year

variance $F(6,1668) = 40.8$ $p < .05$ (Table 2). Age was negatively associated with alcohol consumption ($\beta = -.113$, $p < .05$). Females reported a significantly lower alcohol consumption than males ($\beta = -.132$, $p < .05$). Hours worked per week was significant and positively associated to alcohol consumption ($\beta = .075$, $p < .05$). Those who have had worked schedules including night work for over 5 years had lower consumption ($\beta = -.052$ $p < .05$) than those with less night work experience. Those who had children living at home had a lower AUDIT-C score compared to nurses without children living at home ($\beta = -.229$ $p < .05$). NNL was not significantly related to the AUDIT-C composite score ($\beta = .032$ $p = .167$). In our logistic regression model we found no significant association with NNL, however there was a significant positive relationship (OR = 1.03, 95 % CI = 1.01-1.05) between average working hours per week and the AUDIT-C score. Children living at home were inversely related to the AUDIT C score (OR = 0.60, 95 % CI = 0.47-0.76). Age was inversely related to the AUDIT-C score (OR = 0.97 CI = 0.95-0.98). Those who have had worked schedules including night work for over 5 years had significantly lower AUDIT-C score (OR = 0.75 CI = 0.59-0.95) (Table 3).

Smoking

Mean cigarettes smoked daily were 9.4 (SD 5.2) among daily smokers. Using the same hierarchical regression model, we found that after step 3 the model as a whole explained 13.9 % of the variance $F(6,178) = 4.8$ $p < .05$ (Table 2). Age was positively associated with cigarettes smoked ($\beta = .267$ $p < 0.5$). Males were smoking more than females ($\beta = .-157$ $p < .05$). Those who have had worked schedules including night work for over 5 years smoked significantly more ($\beta = .152$ $p < 0.5$). Evaluating smoking using logistic regression we did not find any significant associations except age (OR = 0.96, 95 % CI = 0.94-0.97) (Table 3).

Caffeine consumption

Mean caffeine containing drinks per day were 3.0 (SD 2.7). Evaluating caffeine consumption using logistic regression we found age (OR = 1.10, 95 % CI = 1.09-1.14), male gender (OR = 3.17, 95 % CI = 2.10-4.81) and NNL (OR = 1.00, 95 % CI = 1.00-1.01) to all be significantly and positively associated with caffeine consumption (≥3 drinks per day).

Exercise habits

We found males to be exercising significantly more (OR = 1.65 95 % CI = 1.15-2.36) than females, and that those with children living at home exercised significantly less (OR = 0.59 95 % CI = 0.47-0.75) than those without children living at home. NNL was not associated with exercise habits.

Discussion

Our findings suggest that there is a positive association between night work load and BMI, even when controlling for several relevant confounders. The association was significant both when using BMI as a continuous parameter, and when evaluated as obesity (BMI >30). Ramin et al. found that higher levels of average night shifts per month in American nurses were significantly associated with increased risk of obesity [15]. This is consistent with our finding. Other studies have taken a dichotomous approach and shown a significant difference in BMI or weight gain between night and day workers. For instance, Biggi et al. found that night workers had significantly higher BMI than day workers [7]. Metabolic syndrome is being defined as a cluster of cardiovascular risk factors: obesity, dyslipidemia, hypertension, and impaired glucose tolerance. Bacquer et al. found in a longitudinal study that rotating shift work increased the risk of metabolic syndrome. The risk was graded with respect to the number of years with shift work [16]. Furthermore several studies have looked directly at cardiovascular risk and found that shift workers are at higher risk [8, 17]. There is, however, some controversy regarding increased incidence among shift workers for ischemic heart disease [18].

Due to the cross sectional design of the current study, no causual relationship can be established. Still, some notions about possible processes involved seem warranted. One possible underlying mechanism explaining our results is disruption of the circadian rhythm, which may impair glucse metabolism and lipid homeostasis [19]. Another possible explanation is irregular sleep-wake cycle or short sleep duration which is associated with heavy night work load. Bjorvatn et al. have previously reported a clear association between short sleep duration and elevated BMI and obesity [20]. Short sleep duration has been shown to influence hormones related to appetite regulation [19]. Altered eating behavior is another proposed mechanism; Wong et al. found that among nurses shift work was positively associated with abnormal eating behavior [21]. Studies indicate that the total energy intake in night and day workers does not differ significantly, but the quality of diet and distribution of energy intake might explain the observed differences [11]. In summary, both biological and behavioral mechanisms are believed to contribute to the increased BMI observed among those with altered sleep-wake cycle [11, 22].

We did not find any significant association between alcohol consumption and night work load. Hermanson et al. examined 990 subjects working day, two-shift or three shifts schedules with AUDIT and biochemical parameters indicating potential misuse: carbohydrate-deficient transferrin (CDT) and Gamma-glutamyl transferase (GGT). Using these three parameters they did not find a higher level of risky alcohol consumption among shift workers compared to day workers: however, two shift-workers appeared to drink less [23]. Ohida et al. found that among Japanese female nurses there was an positive association between working night shift and using alcohol as sleep aid [24]. We found that hours worked per week were positively correlated with alcohol consumption, suggesting that high work load might lead to higher alcohol consumption, which is consistent findings from a large systematic review by Virtanen et al. [25]. Wong et al. did not find a significant difference in alcohol consumption between ever and never night workers in a large female cohort [26].

We did not find any significant association between night work load and smoking. However, many studies repeat elevated levels of smoking among shift workers [7, 27]. In a large cohort of nurses, Ramin et al. found that night workers were more likely to smoke and consumed more caffeine than those who had never worked night shift [15]. We found a significant positive association between NNL and daily caffeine consumption, which might suggest that caffeine is being used as a stimulant during night work. Shy et al. report that 89 % of emergency residents consumed caffeine during night shifts, with 52 % using it every shift [28].

We did not find any association between night work load and exercise habits. Our dichotomized parameter for exercise habits might not be sensitive enough to unveil any association. An association could theoretically go both ways. A positive association might be explained by increased lifestyle awareness to counteract known negative health effects of night work. A negative association might be due to social and practical constraints and disruption of daily rhythm. Schneider et al. did not find an association between leisure time physical activity and shift work when adjusting for possible confounders [29].

The strengths of the present study are its homogeneous population and size. All variables except caffeine and exercise habits were evaluated using both multiple linear hierarchical regression and binary logistic regression. To further evaluate the possible association between night work load and BMI more studies with prospective designs are warranted [30]. The limitations regarding this study concern its cross-sectional design, and uncertainties regarding data based on subjective reports. The low response rate in this study is unfortunately a part of an increasing problem in epidemiological research. A review by Baruch et al. suggested that most study populations have a response rate around 53 % ± 20 % (1 standard deviation from the mean response rate in this review) [31]. Our response rate (38,1 %) is within this range. Unfortunately, we have no information about the non-responders, making comparative analysis not possible. The low response rate and other methodological issues warrants caution in interpreting results, and exemplifies the need for prospective studies in this research area. There will be some uncertainties regarding nurses own estimation of number of nights worked the last year (NNL). However, many nurses have regular schedules that should make them able to make good estimates of NNL. A potential problem with our study is the "healthy worker effect": i.e. only those with a tolerance for night work tend to stay in this type of work. Hence, this might have led to an underestimation of the true negative effects of night work.

Conclusions

This study adds to the growing evidence of the effect of night work on BMI. We also found a consistently higher AUDIT-C score across our models for those with a higher work load which might contribute further to undesirable health effects. Some sub-populations among shift workers, for example those with a heavy night work load, certain chronotypes, and those with high cardiovascular risk at baseline might need special attention and frequent health checks up due to higher risk of undesirable health effects. Earlier introduction of possible counter-measures; for example exercise or, if possible, changes in shift schedule may be needed for those vulnerable to the negative impact of night work.

Competing interests

No competing interests.

Authors' contribution

HVB: design of the study, data analysis, interpretation of the results, drafting the paper. SP: collecting the data, design of the study, interpretation of the results, critical review of the paper, NMFØ: interpretation of the results, critical review of the paper, BB: collecting the data, design of the study, interpretation of the results, critical review of the paper, All authors have approved the final manuscript.

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II

Original article

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Shift work schedule and night work load: Effects on body mass index – a four-year longitudinal study

by Buchvold HV, Pallesen S, Waage S, Bjorvatn B

There are few prospective studies exploring the effects of different shift schedules and night work exposure on weight gain. In this study, we found that night workers gained significantly more weight than day workers over a four-year period. Night workers seem to be a subgroup of shift workers who need special attention due to higher risk of weight.

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Key terms: BMI; body mass index; body mass index; cardiovascular disease; CVD; longitudinal study; night shift; night work; night work load; night worker; obesity; shift work; shift work schedule; shift worker

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Shift work schedule and night work load: Effects on body mass index – a four-year longitudinal study

by Hogne Vikanes Buchvold, MD,[1] Ståle Pallesen, PhD,[2] Siri Waage, PhD,[1, 2] Bjørn Bjorvatn, PhD, MD [1, 2]

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Objectives The aim of this study was to investigate changes in body mass index (BMI) between different work schedules and different average number of yearly night shifts over a four-year follow-up period.

Methods A prospective study of Norwegian nurses (N=2965) with different work schedules was conducted: day only, two-shift rotation (day and evening shifts), three-shift rotation (day, evening and night shifts), night only, those who changed towards night shifts, and those who changed away from schedules containing night shifts. Paired student's t-tests were used to evaluate within subgroup changes in BMI. Multiple linear regression analysis was used to evaluate between groups effects on BMI when adjusting for BMI at baseline, sex, age, marital status, children living at home, and years since graduation. The same regression model was used to evaluate the effect of average number of yearly night shifts on BMI change.

Results We found that night workers [mean difference (MD) 1.30 (95% CI 0.70–1.90)], two shift workers [MD 0.48 (95% CI 0.20–0.75)], three shift workers [MD 0.46 (95% CI 0.30–0.62)], and those who changed work schedule away from [MD 0.57 (95% CI 0.17–0.84)] or towards night work [MD 0.63 (95% CI 0.20–1.05)] all had significant BMI gain (P<0.01) during the follow-up period. However, day workers had a non-significant BMI gain. Using adjusted multiple linear regressions, we found that night workers had significantly larger BMI gain compared to day workers [B=0.89 (95% CI 0.06–1.72), P<0.05]. We did not find any significant association between average number of yearly night shifts and BMI change using our multiple linear regression model.

Conclusions After adjusting for possible confounders, we found that BMI increased significantly more among night workers compared to day workers.

Key terms BMI; cardiovascular disease; CVD; night shift; night worker; obesity; shift worker.

Shift work has been shown to be associated with many different health consequences such as sleep difficulties, gastrointestinal disease, cancer, metabolic disease, and increased risk of cardiovascular disease (CVD) (1–5). According to the last European Working Conditions Survey, 21% of the workforce participates in some type of shift work (6). Accordingly, the health of the shift worker is a major public health concern.

Lately, much attention has been directed towards the possible increased risk of metabolic and cardiovascular disease among shift workers, as well as the pathways and mechanisms that may mediate the effects of shift work on CVD (2, 7, 8). Obesity is a well-recognized cardiovascular risk factor. Notably, increased prevalence of body weight related outcomes, such as increased body mass index (BMI) and obesity has been found among shift workers (8, 9). In addition to constituting a metabolic and cardiovascular risk factor, obesity has also been identified as a risk factor for several types of cancer, musculoskeletal disorders and poor health in general. In addition, obesity is also linked to increased mortality (10–14). As the prevalence of obesity is rising worldwide, both the Organization for Economic Co-operation and Development and the World Health Organization have expressed concern about obesity reaching global epidemic proportions (15, 16).

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Several cross-sectional studies have shown that shift workers are at increased risk of having higher BMI compared to day workers (17–21). A few longitudinal studies have also reported larger weight gain among shift and night workers compared to day workers (22–24). However, several systematic reviews have consistently pointed to several major methodological limitations in the majority of previous studies within this field of research, such as lack of large prospective studies and heterogeneities in study designs, especially related to different work schedules and exposure variables (3, 8, 9, 25, 26).

Taking these issues into account, the aim of this study was to investigate how different work schedules and average number of yearly night shifts were associated with changes in BMI over a four-year follow-up period in a large sample of nurses.

Methods

Design

The data stemmed from an ongoing project "The Survey of Shiftwork, Sleep and Health" (SUSSH). The project was initiated in December 2008. In the present study, we analyzed data from the first five annual waves. The population consisted of registered members of the Norwegian Nurses Organisation (NNO), which include most of the working nurses in Norway. The survey population (N=6000) comprised a total of five strata, each containing 1200 nurses holding at least a 50% work position, and was randomly drawn from the member registry of the NNO. The criteria for the different strata were time elapsed since graduation: <12 months (stratum 1), 1–3 years (stratum 2), >3–6 years (stratum 3), >6–9 years (stratum 4) and >9–12 years (stratum 5). The stratification towards a young cohort was done in order to ensure that the cohort could be followed for the planned ten-year period. However, nurses were not excluded based on age. Figure 1 provides an overview of the selection process for the nurses involved in this SUSSH sub cohort.

Data

Data used in this study were extracted from (i) baseline: sex, age, body weight, height, marital status, and whether the responders had children living at home, years since graduation, and work schedule, (ii) wave 2–5: number of night shifts previous year, and (iii) wave 5: body weight and work schedule. BMI was calculated conventionally using weight (kg) over the square of height in meters.

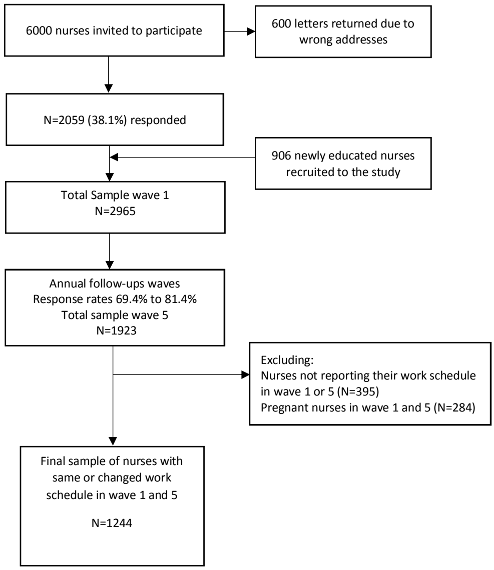

Figure 1. Flow chart visualizing the selection process for the analysis of the nurses in this study.

Work schedule

Responders were asked about their work schedule: day only, evening only, two-shift rotation (day and evening), three-shift rotation (day, evening and night), night only, or another schedule including night work. We studied workers who reported working the same schedule in wave 1 and wave 5 and included those involved in the most frequently reported work schedules: Day only (N=65), two-shift rotation (N=300), three-shift rotation (N=445), and night only (N=43). We also included those who in the follow-up period had stopped working night shifts (N=302), and those who had started working night shifts (N=89). Thus, we had a total of six subgroups. The most common work hours in rotational work schedules are 07:00–15:00 (day shifts), 14:30–22:00 (evening shifts), and 22:00–07:00 (night shifts). There may be local variations, especially among day-only workers working in outpatient clinics, where for example 08:00–16:00 shifts are quite frequent. Shift workers in full position have a 35.5 hours work-week, while day-only workers have a 37.5 hours-work week.

Average number of yearly night shifts

In each wave, the nurses were asked to report the number of night shifts they had worked last year. Thus, in wave 2 this reflected the number of nights worked the year after the first BMI measurement. As a result of this, we calculated a sum score from wave 2–5 which comprised the years with night work between the two BMI measurements. By dividing the sum score by number of waves we created a continuous exposure which represented the average number of night shifts per year. Only those who answered the question in all 4 waves were included. The nurses who reported working day only throughout the follow-up period were included with 0 night shifts in the sum score. We further categorized this continuous variable into three subgroups with respect to average number of yearly night shifts: <1, 1–20, and >20. Regarding average number of yearly night shifts, we did a subgroup analysis including only day and night workers (night and three shift workers combined). We analyzed the latter subgroup with respect to the categorized average number of yearly night shifts variable. In addition, for the night workers (night and three-shift workers), we also conducted a sub-categorization with respect to average number of yearly night shifts reflecting their night shift exposure: <20, 20–40, and >40.

Statistical analysis

SPSS version 24 (IBM, Armonk, NY, USA) was used for the analyses. Continuous variables were expressed as means (±SD) and categorical variables as proportions (%). For demographic data and different work schedules, ANOVA analyses were used to compare means and chi-square tests were used to compare proportions. To evaluate within-subgroup differences (BMI change from wave 1 to 5) for work schedule, we used paired t-tests. Further, we used hierarchical linear regression analyses to adjust for the following confounders when evaluating the outcome variable (BMI in wave 5): BMI at baseline, sex, age, children living at home (baseline), marital status (baseline), and years since graduation (baseline). When adjusting for BMI at baseline in our model and using BMI in wave 5 as our outcome variable, we used the residual change scores to evaluate changes in BMI in the follow-up period (27). Children living at home and marital status were chosen as confounders because of their potential for non-work related disruption of life balance and sleep. Years since graduation was included as a possible confounder to adjust for potential work related effects (eg, experience) beyond our follow-up period. Regarding the choice of confounders, we did not include exercise habits and lifestyle behaviors. We will argue that lifestyle factors might entail one of the mechanisms driving the larger weight gain among shift workers due to disruption of work-life balance. Adjusting for these factors could thus lead to an underestimation of the effects of night work on BMI change. Work schedule was dummy coded using day workers as contrast in the model. For average number of yearly night shifts, we used those workers with lowest average number of yearly night shifts as contrasts. For both work schedule and average number of yearly night shifts, we used the same linear regression model with BMI in wave 5 as the outcome variable. The unstandardized regression coefficients (B) reflect the magnitude of change observed in the dependent variable (in this case change in BMI) when the predictor/independent variable changes with one unit when controlling for the influence of the other predictors/independent variables included in the regression analysis. Significance level was set to $P<0.05$.

Ethics

The Regional Committee for Medical and Health Research of Western Norway (REK-WEST) (NO. 088.88) approved the project.

Results

Demographics

In this sub-cohort of the SUSSH, the mean age of the study population at baseline was 32.9 (SD 8.6) years, range 21–63 years. In wave 1, the nurses worked on average 33.7 (SD 6.9) hours per week and 51.6% reported working a position exceeding 90%. At baseline, three-shift rotation was most common (57.0%, N=709), followed by two-shift rotation (30.7%, N=379), night only (6.5%, N=81), and lastly day only (6.0%, N=75). Mean BMI in wave 1 was 24.6 (SD 4.2) kg/m^2 and 25.1 (SD 4.7) kg/m^2 in wave 5. Prevalence of obesity was 11.0% (N=134) and 13.0% (N=159) in wave 1 and 5, respectively (table 1).

Work schedule

Day workers did not change BMI significantly during the follow-up period. However, all the other groups – two-shift rotation, three-shift rotation, night only, and those who stopped and started with night work in the four year period – increased in BMI (table 2). The linear regression models showed that night workers had significantly larger BMI gain compared to day only workers, even when adjusting for all confounders (table 2).

Average number of yearly night shifts.

A total of 810 nurses reported yearly number of night

Table 1. Demographics at baseline for the shift work population consisting of Norwegian nurses. **BOLD indicates significance (P<0.05).**

	Day workers (N=65)				2-shift workers (N=300)				3-shift workers (N=445)				Night-only workers (N=43)				Stopped working nights (N=302)				Started working nights (N=89)				P-value
	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD	N	%	Mean	SD	
Female	57	89.1			273	91.3			393	88.7			36	85.7			273	91.1			82	92.1			0.65 [a]
Age [b]	65		37.6	7.8	298		34.6	9.8	445		31.5	7.8	43		35.9	8.7	301		32.3	8.1	89		30.3	8.0	**<0.0001** [c]
Children living at home [b]	44	71.0			135	46.7			171	39.5			27	64.3			144	49.3			20	35.7			**<0.0001** [a]
In relationship [a]	55	84.6			208	69.6			287	64.9			35	81.4			206	68.2			54	60.7			**0.006** [a]
Average work hours per week [a]	63		35.7	5.7	300		33.8	6.1	430		34.1	6.3	42		27.9	10.4	294		33.0	7.2	84		33.3	7.9	**<0.001** [c]
Years since graduation [b]	64		8.2	3.1	299		2.8	3.7	444		3.9	3.9	43		5.9	5.0	301		3.9	3.8	89		2.6	3.9	**<0.0001** [c]
BMI [b]	64		24.3	3.6	293		24.8	4.6	441		24.2	3.8	43		25.9	3.9	300		24.8	4.6	89		24.9	4.3	**0.0497** [c]
Obese	4	6.3			35	12.0			37	8.4			6	14.0			40	13.3			13	14.6			0.133 [d]
Average yearly night shifts [e]									249		33.3	18.5	26		116.1	36.3	163		15.9	12.7	34		34.4	40.5	**<0.0001** [c]

[a] Evaluated using Pearson Chi-square.
[b] Data recorded at baseline.
[c] Evaluated using one-way ANOVA.
[d] Evaluated using Fisher's exact test due to expected cell count <5.
[e] Average number of yearly night shifts in the follow-up period.

shifts in each wave. The mean was 24.6 night shifts/year (range 0–195, SD 30.9). Using the same hierarchical regression model, we did not find any significant relationship between night shift exposure (average number of yearly night shifts) and BMI change (table 2). In our subgroup analysis of only day and night workers with respect to average number of yearly night shifts, we did not find any significant differences between groups in terms of BMI (data not shown). Similarly, in the subgroup analyses of nurses working nights (<20, 20–40, >40) higher number of night shifts was not significantly related to BMI change (table 2).

Discussion

In the present study, we found that those working nights only gained more weight (higher BMI gain) during the four-year follow-up period compared to day-only workers, even when adjusting for relevant confounders. However, the average number of yearly night shifts in the follow-up period was not significantly associated with BMI gain.

Increased attention has recently been directed towards the possible causal relationship between shift work and weight increase. There is however large heterogeneity across studies within this field when it comes to study design, choice of exposure variable (type of shift work schedule and total night work exposure) and choice of outcome variables (BMI increase, weight increase, prevalence of overweight or obesity). Two systematic reviews on this topic emphasize the need for more longitudinal studies including analyses of different shift schedules and cumulative night work exposure (8, 9). Van Drongelen et al (9) concluded in 2011 that there was strong evidence for a crude association between shift work exposure and weight increase, but also noted that there was insufficient evidence for a confounder-adjusted relationship between shift work and weight increase. However, in a more recent systematic review, Proper et al (8) concluded that there was a strong evidence for a relation between shift work and increased body weight.

The present study addressed some of the methodological concerns that have been raised in previous reviews. We investigated both work schedules and average number of yearly night shifts using a prospective design (3, 8, 9). In our study, night only workers had the largest BMI gain in the follow-up period, which also turned out to be significantly larger compared to day workers, even after adjusting for possible confounders. This result is consistent with other longitudinal studies (22–24). A few studies have looked at BMI and shift work with respect to metabolic syndrome (a cluster of independent risk factors for CVD: central obesity, dyslipidemia, hypertension, and glucose intolerance) (28). In a 20-year follow-up study on night workers (working 210–230 nights per year), Biggi et al found that night workers, compared to day workers, had elevated BMI and obesity rates, which is in line with our findings (29). Zhao et al found in a two year follow-up study of nurses and midwives that shift work maintainers and those who changed from day to shift work significantly increased

Table 2. Paired t-test evaluating within group effects and linear regression model analyzing respective body mass index (BMI, kg/m²) changes in the follow-up period. [CI=confidence interval; SD=standard deviation]

	Paired t-test						Linear regression model (BMI at year four as dependent variable)			
	N	BMI at baseline		BMI at year four		Mean difference (95% CI)	Model 1 [a] (N=1225/ N=792/N=271) [c]		Model 2 [b] (N=1172/ N=754/N=260) [c]	
		Mean	SD	Mean	SD		BMI_{diff} [d]	95% CI	BMI_{diff} [d]	95% CI
Work schedule										
Day only (contrast)	64	24.25	3.52	24.59	3.66	0.33 (-0.17–0.84)				
2-shift rotation	288	24.88	4.53	25.36	4.79	0.48 (0.20–0.75) [e]	0.11	-0.43–0.66	0.15	-0.43–0.73
3-shift rotation	436	24.17	3.72	24.63	3.94	0.46 (0.30–0.62) [e]	0.08	-0.45–0.60	0.03	-0.52–0.58
Night only	43	25.95	3.87	27.25	4.52	1.30 (0.70–1.90) [e]	0.95	0.15–1.76 [f]	0.89	0.06–1.72 [f]
Stopped working nights	296	24.82	4.57	25.40	5.39	0.57 (0.17–0.84) [e]	0.20	-0.47–0.75	0.14	-0.43–0.71
Started working nights	87	24.69	4.14	25.32	4.96	0.63 (0.20–1.05) [e]	0.26	-0.45–0.40	0.22	-0.49–0.92
Average number yearly night shifts, whole cohort										
<1(contrast)	189	24.29	3.40	24.63	3.78	0.34 (0.54–0.63) [f]				
1–20	277	24.68	4.49	25.24	5.30	0.56 (0.27–0.85) [e]	0.22	-0.19–0.63	0.17	-0.26–0.60
>20	326	24.88	4.07	25.44	4.34	0.57 (0.34–0.79) [e]	0.23	-0.16–0.63	0.27	-0.15–0.68
Average number yearly night shifts, night workers										
<20 (contrast)	64	24.25	3.91	24.69	4.36	0.44 (0.02–0.86) [f]				
20–40	109	24.45	3.89	24.79	4.89	0.34 (-0.03–0.71)	0.10	-0.64–0.44	0.09	-0.49–0.66
>40	98	24.76	3.68	25.56	3.88	0.80 (0.50–1.11) [e]	0.37	-0.18–0.92	0.56	-0.03–1.15

[a] Model 1: Adjusted for BMI_{year1}.
[b] Model 2: Adjusted for BMI_{year1}, sex, age, children living at home, marital status, and years since graduation at baseline. BMI at baseline was significant among the adjusting variables in both models. Children living at home was significant in the adjusted model with night only workers.
[c] Number on individuals included in the linear regression models (n=) for work schedule and average number of yearly night shifts, respectively.
[d] Unstandardized coefficients (B) values (units BMI change/units change in predictor variable).
[e] P<0.001.
[f] P<0.05.

BMI, while those who changed from shift work to day work did not (24). When analyzing data of those who changed schedule during the follow-up period in the present study, we found that they had significant within-group BMI gain, but compared to day workers they did not have a significant larger BMI gain. The interpretation of this finding is difficult because we do not have information on why they changed work schedule. However, it is interesting that so many nurses stopped working nights. One may speculate that there is a "healthy worker effect" or a "survivor effect", meaning that only those with a tolerance for night work tend to maintain this kind of work schedule (30). This could potentially underestimate the effect of shift and night work on BMI in the present study. One could also argue that increased salary may attract some nurses to work nights, and night work may be less physically demanding than day and evening work. Thus, there may also be a selection into shift and night work. We did not find a significant difference between the three shift rotation workers and day workers with regards to BMI. This could possibly reflect that the average exposure to night work in this group might not have been large enough, or that the follow-up period might not have been sufficiently long. In our subgroup analysis of the night workers (night-only workers and three-shift workers), we found that those with highest number of night shifts had the largest BMI gain (table 2). Interestingly the group with a medium number of yearly night shifts (20–40 night shift/year) did not have a significant BMI gain in the follow-up period. One may speculate that even though no linear relationship between night work and BMI gain was detected, a very heavy night work load (above a certain number of night shifts) may lead to increased BMI gain at a group level. This might be the result of both failure to adapt biologically and increased social constraints and restricted opportunities to adhere to a healthy lifestyle. In a study of Korean nurses, Kim et al (20) found a higher prevalence of obesity and overweight (odds ratio 1.63) among those with the longest exposure to shift work when adjusting for confounders. However, that study was based on a cross-sectional design, thus conclusions regarding overweight and obesity trajectories based on that are not possible.

As previously stated, different exposure variables regarding shift work schedules have been used in different studies making comparisons difficult. Some studies have reported that those changing from day to night shifts and permanent night shift workers are those at highest risk of weight gain (17, 31). A few studies have investigated if there is a graded effect of cumulative night work exposure on weight gain in addition to the effects of years exposed to shift work. Peplonska et al (19) concluded that there was a graded association both between cumulative night shifts and cumulative night shift hours and obesity. Similarly, Ramin et al (32) found for example that higher levels of night shifts per month were associated with increased risk of obesity. The risk was graded with respect to the number of night shifts. They also found that the risk of obesity was higher among those who had night work as their primary schedule compared to those with rotating shift work as their primary schedule. We did not find a dose–response relationship with respect to average number of yearly night shifts and BMI change, but overall our data also suggested that those with the largest night shift exposure were most at risk.

In terms of limitations, it should be noted that we did not control for the "healthy worker effect" or the "survivor effect". Our study had a low response rate at baseline, which is an increasing problem in epidemiological research. A review by Baruch et al (33) suggests that most study populations have response rates around 53% ± 20% (1 SD from the mean response rate in that review) (34). Our initial response rate was within this range, and the follow-up waves in our study had high and stable response rates around 70–80%. Unfortunately, we have no information about the non-responders at wave 1, preventing us from conducting attrition analyses. Also, as with all studies based on self-report there will be uncertainties in terms of how well the data reflect objective realities. There is for example a tendency for respondents to overestimate height and underestimate weight compared to objectively collected data (34). An important, albeit subjectively assessed, parameter in this study was the number of night shifts worked the last year. Most Norwegian nurses work regular schedules and are thus likely to provide good estimates of this variable. In line with this, Brisson et al (35) found that self-reported data collected close to specific events are highly accurate ensuring high validity. Another limitation was that we did not exclude nurses who were pregnant and gave birth in-between the two BMI measurements. This may have confounded the relationship between night work and BMI gain. However, we did exclude nurses who were pregnant at the time of BMI measurements.

Strengths of the present study entail its homogenous population and clearly defined exposure variables. Data were collected annually and thus increasing the validity and minimizing recall bias (35). With our prospective study design, we have addressed several issues that systematic reviews have emphasized as important (8, 9).

Concluding remarks

We found that night only workers had significantly larger BMI gain than day-only workers in the four-year follow-up period, also after adjusting for relevant confounders. Our findings add to the growing evidence attesting to the negative effects of night work on body weight development. We did not find a dose–response relationship with respect to average number of yearly night shifts. It is concluded that night work might be one parameter to consider as an occupational and societal hazard in terms of weight gain. Relevant countermeasures such as dietary advice and exercise opportunities should accordingly be emphasized for night workers.

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Shift Work and Lifestyle Factors: A 6-Year Follow-Up Study Among Nurses

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Objectives: To evaluate different work schedules, short rest time between shifts (quick returns), and night shift exposure for their possible adverse effects on different lifestyle factors in a 6-year follow-up study.

Methods: Data stemmed from "The Survey of Shiftwork, Sleep and Health," a cohort study of Norwegian nurses started in 2008/9. The data analyzed in this sub-cohort of SUSSH were from 2008/9 to 2015 and consisted of 1,371 nurses. The lifestyle factors were: Exercise (≥1 h/week, <1 h/week), caffeine consumption (units/day), smoking (prevalence and cigarettes/day), and alcohol consumption (AUDIT-C score). We divided the nurses into four groups: (1) day workers, (2) night workers, (3) nurses who changed toward, and (4) nurses who changed away from a schedule containing night shifts. Furthermore, average number of yearly night shifts (NN), and average number of quick returns (QR) were calculated. Paired *t*-tests, McNemar tests, and logistic regression analyses were used in the analyses.

Results: We found a significant increase in caffeine consumption across all work schedule groups and a decline in smoking prevalence for day workers and night workers at follow-up. Analyses did not show any significant differences between groups when analyzing (1) different work schedules, (2) different exposures to QR, (3) different exposures to NN on the respective lifestyle factor trajectories.

Conclusion: We found no significant differences between the different work schedule groups or concerning different exposures to QR or NN when evaluating these lifestyle factor trajectories. This challenges the notion that shift work has an adverse impact on lifestyle factors.

Keywords: shift work, night work, quick returns, health habits, lifestyle habits

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INTRODUCTION

According to the last European Working Conditions Survey, 21% of the workforce is engaged in some type of shift work (1). Increased attention and research have been directed toward the possible adverse health effects of shift work during the last decades. In general, it has been shown that shift workers have elevated risks for a multitude of chronic diseases (2–4). Shift work has for instance been shown to be associated with increased risk of cardiovascular diseases (CVD), metabolic disturbances, and possibly some cancers (3, 5–9).

Models of the observed associations between shift work and chronic disease have primarily focused on two key pathways; behavioral and physiological changes and their reciprocal relationship (2, 4, 10). Shift work contributes to circadian disruption affecting hormonal systems regulating metabolism and stress responses, like glucose, and cortisol regulation (11–13). Night work disrupts the normal sleep-wake cycle giving rise to circadian misalignment interfering with both sleep duration and quality. Disturbed sleep is known as a risk factor for many diseases. For example, the CVD risk profile of shift workers mimics the risk profile for those with short sleep duration (4). Concerning psychosocial stress and social jet lag, shift work could potentially affect work-life balance with increased social and familial constraints. This could lead to difficulties initiating or maintaining lifestyle factors with positive health benefits. It has been hypothesized, although the results are inconsistent, that shift workers with schedules that include night work differ from day workers regarding lifestyle factors with adverse health consequences, for example in relation to smoking, alcohol, and exercise (14–18).

Night work duration and intensity are aspects of shift work believed to contribute to circadian stress and impaired work-life balance, possibly affecting lifestyle factors negatively. Short rest time between shifts (≤11 h), described as quick returns (QR), could also potentially influence lifestyle factors adversely through its association with stress, fatigue, and insomnia (19, 20). In addition, different work schedules might differ with respect to work-life balance impairment and thus possibly affect lifestyle factors.

The vast majority of previous studies on shift work in general and studies addressing shift work and lifestyle factors in particular have resorted to cross-sectional designs and limitations in the assessment of shift work exposure (e.g., shift work duration, night shift intensity, and type of shift work). The methodological limitations of shift work research have been addressed in several papers (5, 21–25). The need for large prospective studies with clearly defined shift work exposure parameters and, optimally, information about different aspects of shift work that might contribute to the increased risk of chronic disease have been emphasized.

This large prospective study of Norwegian nurses aimed to investigate different aspects of shift work and their impact on lifestyle factors. It was differentiated between different shift schedules (day work, night work, and changing of schedule toward- or away from night work). Different work schedules were evaluated for changes within—and between groups. Average yearly quick return exposure and average yearly night work exposure were also evaluated for a dose-response impact on the respective lifestyle factors. Specifically, we evaluated changes in exercise habits, caffeine consumption, smoking habits, and alcohol consumption. We hypothesized that work schedules containing night work, a high exposure to QR or a high exposure to night work would affect the examined lifestyle factors more adversely than schedules without these characteristics during the 6-year follow-up.

MATERIALS AND METHODS

Design

The data in the present study stemmed from "The SUrvey of Shiftwork, Sleep and Health" (SUSSH), initiated in December 2008 (26). The population consisted of registered members of the Norwegian Nurses Organization (NNO) who held at least a 50% full time equivalent working position. At baseline 50.3% of the nurses reported holding a >90% full time equivalent position. NNO includes most of the working nurses in Norway. Written consent were obtained from all participants. At baseline assessment in 2008/2009, 5,400 nurses received a questionnaire, and 2,059 responded, yielding a response rate of 38.1%. After the first initial round was conducted, an additional group of newly educated nurses was invited to the cohort in order to increase the study population. Consequently, 2,741 new nurses received the baseline questionnaire, whereof 906 responded (response rate 33.1%). Thus, the total number of respondents in the first wave consisted of 2,965 nurses. These made up the cohort who were asked again at follow-up unless they for some reason had quit the study ($n = 162$). At follow-up after 6 years 1,892 nurses responded, yielding a response rate of 67.5% (1,892/2,803). In the present study, we excluded nurses who were pregnant at baseline or at follow-up and included only those nurses who reported their work schedule in both questionnaires. This final sub-cohort consisted of 1,371 nurses.

Data

The following data were extracted for the present study:

From baseline: Sex, age, whether the participants had children living at home, and years since graduation. The following were extracted at both time points: Work schedule, self-reported number of quick returns worked the previous year, self-reported number of night shifts worked the previous year, exercise habits, caffeine consumption, smoking habits, alcohol habits, and pregnancy status. Total follow-up time was 6 years.

Work Schedule

Participants were asked about their work schedule: Day only, evening only, two-shift rotation (day and evening), three-shift rotation (day, evening and night), night only, or another schedule including night work.

Those who had the same schedule at both baseline and follow-up were first regarded as separate groups: Day only ($n = 51$), day and evening ($n = 233$), night only ($n = 39$), and three-shift work ($n = 374$). Due to the small group sizes, the day only workers, day and evening workers, and those nurses who changed schedule but maintained a schedule without night work ($n = 110$) in the follow-up period were collapsed into a single group of day workers ($n = 394$). Similarly, night only workers ($n = 39$), three shift workers ($n = 374$), and those who worked another schedule containing night work ($n = 8$) and those who changed but maintained a scheduled containing night work ($n = 102$) were collapsed into a group of night workers ($n = 523$). We classified those who changed from a schedule containing night work into a schedule with day and/or evening work into one subgroup (n = 355). Furthermore, we classified those who changed toward a schedule containing night work from a schedule containing only day and/or evening shifts into another subgroup ($n = 99$). Thus, for our main analysis we had a total of four groups (n = 1,371): day workers, night workers, and those who changed toward- or away from a schedule containing night work. **Figure 1** shows an overview of the four work schedule groups.

Typical work hours for nurses in rotational work schedules in Norway are 07:00–15:00 (day shift), 14:30–22:00 (evening shift), and 22:00–07:00 (night shift). There may be local variations, especially among day only workers in outpatient clinics, where for example 08:00–16:00 shifts are quite frequent. Shift workers in full position in Norway most often have a 35.5 h work-week, whereas day only workers in full position have a 37.5 h-work week.

Average Number of Yearly Quick Returns (QR)

At both baseline and follow-up the nurses were asked about their number of QR the last year. We used these numbers to calculate an average from the two timepoints. This average was used in the statistical analyses as a proxy for average number of yearly QR in the follow-up period. The continuous variable was categorized into three subgroups where the lowest group was chosen as contrast. We minimized the exposure in the reference group while at the same time keeping a sufficient group size: <5 QR ($n = 172$), 5–35 QR ($n = 535$), >35 QR ($n = 583$). In order to investigate the effect of the magnitude of change in QR exposure between baseline and follow-up we made a change score using those shift workers with the lowest change scores as contrast: ±10 difference in number of QR between baseline and follow-up (n = 435), >10 decrease in number of QR ($n = 454$), and >10 increase in number of QR ($n = 401$).

Average Number of Yearly Night Shifts (NN)

At both baseline and follow-up, the nurses were asked about their number of night shifts the last year (NN). As for QR we used this to calculate an average from the two timepoints. This average was used in the statistical analyses as a proxy for the average number of yearly night shifts in the follow-up period. We categorized this continuous variable into three subgroups where the lowest group was chosen as contrast. Again, we tried to minimize exposure in the contrast group while also keeping a sufficient group size: <1 NN ($n = 289$), 1–20 NN ($n = 568$), and >20 NN ($n = 493$). As for QR, we also investigated change from baseline to follow-up for NN: ±10 difference in number of NN between baseline and follow-up ($n = 668$), >10 decrease in NN ($n = 392$), and >10 increase in NN ($n = 290$).

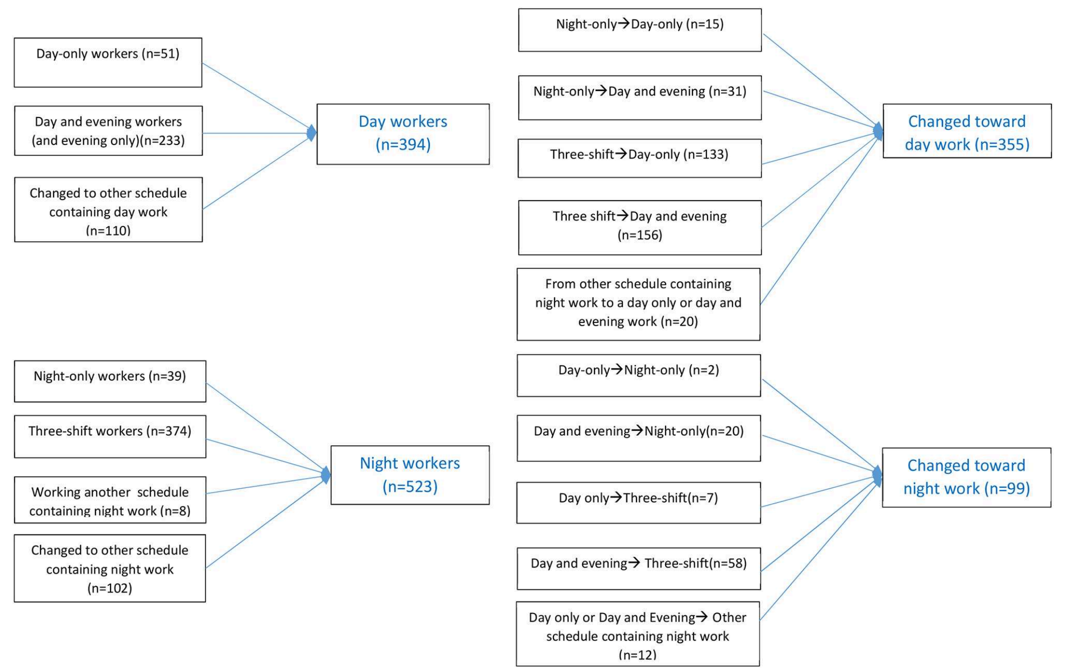

FIGURE 1 | An overview of the four work schedule groups.

Exercise

At both baseline and follow-up the nurses were asked about exercise as measured by an item about hours of sweaty exercise per week (0, <1 h, 1–2 h, ≥3 h). This item was dichotomized (<1 h and ≥1 h per week). Additionally, those who exercised the least (0 h) were compared to those who exercised the most (≥3 h) using a separate dichotomized variable. The question concerning exercise used in the present study has been compared to $V02_{max}$ and activity sensor and was found to be a reasonably valid measure of vigorous activity (27). Regarding the cut-off, one study reported that at least 1 h walking per week predicted lower cardiovascular risk. And, in addition, that vigorous activity predicted lowest risk (comparing highest to lowest categories) (28).

Caffeine

At both baseline and follow-up the nurses were asked to estimate average number of caffeine containing units consumed per day and to report this as a continuous variable. Caffeine consumption was evaluated as a dichotomous parameter (drinking three or more caffeine containing units vs. <3 units per day). An umbrella review of meta-analyses suggested that the optimal risk reduction for various health outcomes was found for intake of 3–4 cups of coffee per day (29). Another large epidemiological study found that lower mortality was observed for all groups of those consuming coffee compared to non-drinkers (30). A significant trend was found for both male and female coffee drinkers: those consuming 2–3 cups of coffee per day or more had reduced mortality than those with lower consumption (30).

Smoking

Smoking prevalence was assessed at both baseline and follow-up. The nurses were asked "do you smoke daily now (yes/no)?" Furthermore, those who smoked were in addition asked "If you smoke daily, how many cigarettes do you smoke per day?"

Alcohol

At both baseline and follow-up, alcohol consumption and habits were evaluated using the short form of the Alcohol Use Disorders Identification Test Consumption (AUDIT-C). AUDIT-C is a self-report instrument with three items. The instrument appears to be a practical, valid primary screening test for heavy drinking, and/or active alcohol abuse or dependence (31). A score of 3 or higher on the AUDIT-C might indicate potential alcohol misuse. In a primary care setting a threshold score of 3 in females, and 4 in males maximized sensitivity and specificity (32). In our analysis, we used the AUDIT-C score both as a continuous as well as a dichotomous parameter (AUDIT-C cut off: ≥3 for females and ≥4 for males). For AUDIT-C we only had complete and accurate baseline and follow-up measurements of the sub-cohort of newly educated nurses.

Statistical Analysis

SPSS, version 25 was used for the analyses. Continuous variables were expressed as means (±SD) or median (IQR) and categorical variables as proportions (%). For demographic data among different work schedules, ANOVA and Kruskal-Wallis Test were used to compare means/medians, and chi-square tests were used to compare proportions. The lifestyle factors were analyzed for both within and between group changes in the follow-up period when investigating day workers, night workers, those who changed away from a schedule containing night work, and those who changed toward a schedule containing night work. For evaluating within-group changes in different work schedules we compared continuous variables using paired *t*-tests, and proportions by McNemar's tests.

The relationship between the individual dependent variables (exercise, caffeine, smoking, alcohol) and the collapsed work schedule groups were studied using logistic regression. In addition, the original groups, the day only workers, day and evening workers, night only workers, and three-shift workers were evaluated in the logistic regression models. In addition to adjusting for age and sex, we adjusted for years since graduation because of possible work-related effects (e.g., experience) beyond our follow-up period, children living at home (yes/no) due to the potential for non-work related disruption of work-life balance and sleep, and baseline values of the respective dependent variable. Work schedule was dummy coded using day workers as a contrast, and the other work schedules were compared separately to the day workers. For average number of yearly QR and NN we used the groups with the lowest exposure as contrasts when evaluating the individual dependent variables in the same manner as for the four defined work schedules. The same was done for the change score variables for QR and NN. Significance level was set to $p < 0.05$.

Ethics

The project was approved by the Regional Committee for Medical and Health Research of Western Norway (REK-WEST) (NO. 088.88).

RESULTS

Demographics

In this study of 1,371 nurses, the mean age was 32.6 years [standard deviation (SD) = 8.5 years] at baseline. The study population consisted predominately of females (89.6%). At baseline, mean years since graduation were 3.8 years (SD = 4.1). 68.5% ($n = 935$) reported being in a relationship and 45.6% ($n = 602$) reported having children living at home. At baseline, three-shift rotation was most common (52.6%, $n = 721$), followed by two-shift rotation (30.6%, $n = 420$), night only (8.4%, $n = 115$), day only (5.3%, $n = 72$), and other schedules including night work (3.1%, $n = 42$), respectively. Only one person reported working evening only. At baseline, 69.6% of the nurses reported working in a somatic hospital department, 13.1% in a psychiatric service, 8.0% in nursing homes, 6.6% in home care services, and 2.7% in other positions. Mean number of average yearly quick returns was 31.3 (range 0–171, SD = 23.6). Mean number of average yearly night shifts was 21.2 (range 0–215, SD = 25.8). An overview of the distribution on these variables for day workers, night workers, and those who changed work schedule toward- or away from a work schedule containing night work is provided in **Table 1**.

TABLE 1 | Demographics of Norwegian nurses with different work schedules in the 6-year follow-up period ($n = 1,371$).

	Day workers (n = 394)			Night workers (n = 523)			Stopped working nights (n = 355)			Started working nights (n = 99)			*P*-value
Sex (% female)[a]	$N = 392$	90%		$N = 521$	88%		$N = 355$	91%		$N = 98$	91%		0.56[b]
Age[a] mean (SD)	$N = 392$		34.7 (9.3)	$N = 522$		31.5 (7.6)	$N = 355$		32.5 (8.4)	$N = 99$		30.4 (8.0)	**<0.001[c]**
Children living at home (% yes)[a]	$N = 379$	51%		$N = 506$	43%		$N = 341$	47%		$N = 93$	36%		**0.02[b]**
Years since graduation[a] median (IQR)	$N = 393$		2.0 (0.0-8.0)	$N = 521$		3.0 (0.0-7.0)	$N = 354$		3.0 (0.0-7.0)	$N = 99$		1.0 (0.0-3.0)	**<0.001[d]**

[a]*Data recorded at baseline.*
[b]*Evaluated using Pearson Chi-Square.*
[c]*Evaluated using one-way ANOVA.*
[d]*Evaluated using Kruskal-Wallis Test.*
N, number of individuals included in the analysis; SD, Standard Deviation; IQR, 25–75 percentiles.
Bold values represent $p < 0.05$.

Exercise

We did not find any significant differences when analyzing the four defined work schedule groups and exercise (<1 h and ≥1 h per week) for within-group changes in the follow-up period (**Table 2**). Regarding the three predictors (work schedule, QR and NN), we did not find any significant differences among the subgroups concerning exercise habits (**Table 3**). Neither did we find any differences when comparing those workers who exercised the least to those who exercised the most (data not shown). Furthermore, no differences were found between the change score variables for QR and NN and exercise (data not shown).

Caffeine

For all four work schedule groups there was an increase in caffeine consumption. The increase in caffeine consumption from baseline to follow-up was significant both when caffeine consumption was measured as a continuous parameter (units/day) and as a dichotomous parameter (≥3 units/day) (**Table 2**). We did not find any significant differences in caffeine consumption in our crude or adjusted logistic regression models between different work schedules, QR or NN groups (**Table 3**). Furthermore, no differences were found between the change score variables for QR and NN in terms of caffeine (data not shown).

Smoking

Smoking prevalence decreased significantly in the follow-up period for both day and night workers (**Table 2**). For the two work schedule groups that stopped or started working nights there was a non-significant decrease in smoking prevalence. For all groups, except those who changed to a work schedule including night work, there was a significant decrease in number of cigarettes smoked per day among the smokers in the follow-up period (**Table 2**). We did not find any between-group differences in our logistic regression models with respect to smoking prevalence for different work schedules, OR or NN (**Table 3**). Furthermore, no differences were found between the change score variables for QR and NN and smoking (data not shown).

Alcohol

Day workers were the only group with a significant increase in their AUDIT-C score (**Table 2**) in the follow-up period. We did not find any significant between-group changes with respect to alcohol consumption for different work schedules, QR and NN (**Table 3**). Furthermore, no differences were found between the change score variables for QR and NN and AUDIT-C (data not shown).

Additional Analyses

We also analyzed the original work schedule groups (day only (contrast); day and evening; night only; three-shift rotation) in separate logistic regression models for each of the lifestyle factors. No significant differences were detected (data not shown).

DISCUSSION

To the best of our knowledge this is one of few papers that addresses the relationship between shift work and lifestyle factors using a prospective design. This paper investigated different work schedules, different exposures to QR and different exposures to NN during a 6-year follow-up. We found a significant increase in caffeine consumption in all four defined work schedules. However, we did not find any differences in lifestyle factor trajectories across the different work schedules or across differences in exposure to QR or NN.

A significant increase in caffeine consumption across all work schedules was found in the present study. Several studies have found positive effects of caffeine concerning increased performance and alertness and that caffeine could be an effective intervention to mitigate sleepiness and prevent injuries and errors (33–35). The increase found in our study might be due to nurses using caffeine to enhance alertness and mitigate sleepiness or as a result of a general increased consumption with age (36). However, we did not find any longitudinal relationship between caffeine consumption and different work schedules, QR or NN. However, the findings are consistent with Drake et al. who did not find any significant difference

TABLE 2 | Baseline and 6 year follow-up values of lifestyle factors among Norwegian nurses with different work schedules ($n = 1,371$).

	Day workers ($n = 394$)				Night workers ($n = 523$)				Stopped working nights ($n = 355$)				Started working nights ($n = 99$)			
	N	Baseline (SD)	Follow-up (SD)	*P*-value	*N*	Baseline (SD)	Follow-up (SD)	*P*-value	*N*	Baseline (SD)	Follow-up (SD)	*P*-value	*N*	Baseline (SD)	Follow-up (SD)	*P*-value
Exercise habits (≥1 h/week)[a]	364	65%	63%	0.40	493	67%	64%	0.42	331	65%	62%	0.28	95	74%	71%	0.70
Caffeine consumption (units/day)[b]	391	3.2 (2.5)	3.8 (2.4)	**<0.001**	520	3.1 (2.5)	3.7 (2.8)	**<0.001**	352	2.8 (2.2)	3.5 (2.2)	**<0.001**	99	2.6 (2.2)	3.4 (2.2)	**<0.001**
≥3 units/day[a]	391	54%	69%	**<0.001**	520	55%	69%	**<0.001**	352	51%	69%	**<0.001**	99	48%	64%	**<0.001**
Smoking prevalence (%yes)[a]	378	17%	11%	**0.003**	508	11%	7%	**0.003**	239	7%	5%	0.31	97	11%	5%	0.07
Number of cigarettes/day[b,c]	63	9.1 (5.1)	3.9 (5.5)	**<0.001**	57	8.7 (5.3)	4.3 (6.4)	**<0.001**	23	9.0 (4.1)	3.1 (4.9)	**<0.001**	11	10.9 (5.9)	3.6 (5.5)	0.09
Average AUDIT-C score[b]	121	2.8 (1.9)	3.2 (1.8)	**0.04**	135	3.3 (0.19)	3.2(1.8)	0.96	93	3.4 (1.7)	3.1 (1.7)	0.20	43	3.2 (1.8)	3.4 (1.9)	0.33
Above screening threshold[a]	121	58%	62%	0.51	135	64%	64%	1.00	93	73%	65%	0.19	43	61%	65%	0.79

[a] *McNemar's test for paired proportions. Proportions as percentages (%).*
[b] *Paired t-test for continuous variables. Means (SD, Standard deviation).*
[c] *Among smokers.*
N, number of individuals included in the analysis.
Bold values represent $p < 0.05$.

between day workers, permanent night workers, or rotating shift workers concerning caffeine intake in a cross-sectional study (37). In contrast, Ramin et al. found a significantly higher caffeine intake when comparing those who had always worked nights with those who had never worked night shifts (38). Both early morning shifts and night shifts may be challenging for nurses since both shift-types may interfere with the nurses' individual circadian rhythms and thus result in high levels of sleepiness. The same argument could be valid for QR and NN. High exposure of QR or NN could potentially leave the shift worker in constant circadian misalignment, challenged by conflicting work and domestic demands. Still, caffeine consumption was not higher in these subgroups of nurses.

Concerning exercise, we did not find any clear differences between the four defined work schedules, different exposure to QR or different exposure to NN in the follow-up period. Our measurement of heavy exercise might be too crude to detect any minor difference between groups. However, several former studies have looked at shift work and exercise, and overall no clear differences have been found (16, 39, 40). Loef et al. reported that shift workers spend more time walking but found no difference among shift workers and non-shift workers with regards to other non-occupational physical activities (39). Other studies have also found shift workers not to differ from day workers in terms of leisure time physical activity, but shift workers seem to have a lower activity level at work (16, 40). While not finding any differences in physical activity between day and shift workers, Kiwimaki et al. still found higher rates of obesity among shift workers than day workers (16). This is consistent with previous studies from this same cohort among Norwegian nurses (41, 42). Since the present and previous studies do not report any significant differences in physical activity levels between day and shift workers, one may speculate that the observed differences in weight and weight gain might be due to differences in the distribution and the temporal changes in eating habits or changes in metabolism due to circadian disruption and insufficient sleep (11, 43).

The overall decline in smoking prevalence was probably not unique to our cohort and probably reflects preventive measures and increased health awareness in the general population. According to Statistics Norway, the smoking prevalence of females in Norway decreased from 22 to 10% between 2007 and 2017 (44). Ramin et al. found a higher smoking prevalence among ever night workers compared to never night workers (38). However, the study did not have a prospective design and could thus not evaluate trends in smoking prevalence between the different groups. A few studies have taken a different approach and looked at smoking cessation and the proportion of workers starting smoking. Van Amelsvoort et al. found higher odds of being a smoker among shift workers compared to day workers at baseline. Furthermore, the follow-up also revealed that shift workers were more prone to start smoking compared with day workers (45). This finding is consistent with a Danish study which found fixed night workers to have a higher odds of smoking relapse and lower odds of smoking cessation compared to fixed day workers (46). However, we found no significant

TABLE 3 | Logistic regression models evaluating lifestyle factors among Norwegian nurses ($n = 1{,}371$) with respect to work schedules, average number of yearly quick returns and average number of yearly night shifts at 6-year follow-up.

	Exercise habits (≥1 h/week)		Caffeine consumption (≥3 units/day)		Smoking prevalence		Alcohol consumption (above screening threshold)	
	Crude (*N* = 1283/1205/1263) OR (CI)	Adjusted (*N* = 1224/1152/1205) OR (CI)	Crude (*N* = 1362/1281/1341) OR (CI)	Adjusted (*N* = 1299/1224/1279) OR (CI)	Crude (*N* = 1309/1231/1290) OR (CI)	Adjusted (*N* = 1250/1178/1231) OR (CI)	Crude (*N* = 392/374/388) OR (CI)	Adjusted (*N* = 375/359/371) OR (CI)
WORK SCHEDULE								
Day workers (contrast)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Night workers	1.06 (0.79–1.43)	1.11 (0.82–1.52)	0.96 (0.69–1.33)	1.01 (0.71–1.42)	0.75 (0.44–1.28)	0.86 (0.50–1.51)	0.96 (0.55–1.67)	1.32 (0.73–2.41)
Stopped working nights	0.96 (0.69–1.32)	0.99 (0.71–1.38)	1.10 (0.76–1.57)	1.10 (0.76–1.60)	0.68 (0.36–1.31)	0.76 (0.39–1.50)	0.84 (0.46–1.55)	1.02 (0.54–1.94)
Started working nights	1.30 (0.78–2.17)	1.47 (0.85–2.54)	0.86 (0.51–1.47)	1.07 (0.61–1.87)	0.50 (0.17–1.41)	0.61 (0.21–1.79)	1.16 (0.51–2.45)	1.43 (0.63–3.26)
AVERAGE NUMBER OF YEARLY QUICK RETURNS								
<5 (contrast)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
5–30	1.00 (0.68–1.48)	1.10 (0.74–1.65)	0.95 (0.61–1.46)	0.98 (0.62–1.53)	1.03 (0.46–2.27)	1.26 (0.54–2.95)	0.70 (0.31–1.58)	0.73 (0.32–1.67)
>30	0.95 (0.64–1.39)	1.02 (0.68–1.53)	1.12 (0.72–1.73)	1.15 (0.73–1.81)	1.05 (0.48–2.29)	1.24 (0.54–2.86)	0.95 (0.42–2.15)	1.02 (0.44–2.36)
AVERAGE NUMBER OF YEARLY NIGHT SHIFTS								
<1 (contrast)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
1–20	0.84 (0.61–1.16)	0.90 (0.64–1.26)	1.25 (0.87–1.77)	1.35 (0.93–1.96)	0.88 (0.50–1.55)	0.95 (0.52–1.71)	0.95 (0.52–1.7)	1.19 (0.63–2.25)
>20	1.04 (0.74–1.45)	1.06 (0.74–1.50)	1.20 (0.83–1.73)	1.33 (0.90–1.95)	0.62 (0.34–1.13)	0.73 (0.39–1.37)	0.93 (0.48–1.78)	1.28 (0.63–2.60)

In the crude model only baseline values of the respective dependent variables were adjusted for. Age, sex, years since graduation, children living at home or not, and baseline values of the respective lifestyle factors were covariates in the adjusted model. In addition, the original work schedules were analyzed using day only workers as contrast: no significant differences were found. N, number of individuals included in the analysis (work schedule/average number of yearly quick returns/average number of yearly night shifts); OR = Odds Ratio, CI = 95% Confidence Interval.

differences in smoking between the work schedules or in relation to exposure to QR and NN.

Day workers were the only group with a significant within-group increase in the AUDIT-C score at follow-up. Thus, our hypothesis that shift work would affect this habit adversely was not supported. Using AUDIT-C as a dichotomous parameter (under/above screening threshold), we neither found any significant longitudinal difference across different work schedules nor concerning QR and NN exposure. This is consistent with another study with respect to total alcohol intake (16). Similarly, Morikawa et al. did not find any differences between day workers or shift workers in the volume of alcohol consumption or heavy drinking. However, Morikawa et al. found the highest frequency of heavy drinking in a subgroup of night workers sleeping poorly, leading the authors to suggest that alcohol might be used as a sleep aid (47).

The strengths of this study were its large sample size, the prospective design, and evaluation of different aspects of shift work that might contribute to altered health behaviors. Also, the relatively wide range of lifestyle factors (exercise, caffeine, alcohol, and smoking) constitutes a strength. We believe that potential long-term changes in lifestyle factor trajectories could be of clinical importance, for example, concerning cardiometabolic health. Our follow-up period over 6-years is thus one of the major assets of the present study. It should also be noted that we have addressed some of the limitations in other studies as reviewed by Proper et al. by employing a large prospective design, evaluation of different aspects of shift work, and investigation of the possible mediating role of lifestyle factors (21). The present cohort was relatively young and relatively newly educated. One could argue that lifestyle factor trajectories over time might not have a linear but a curve-linear relationship, consequently, changes in lifestyle factors could attenuate over the relatively long follow-up time. From such a viewpoint it might be a strength that this cohort comprises relatively newly educated nurses.

Our study relies on self-reported data that may have uncertainties and potential for different kind of biases. Concerning recall bias, the data used in the present study were collected with a maximum of 1-year recall. Brisson et al. found that self-reported data collected close to specific events are highly accurate and have high validity (48). Due to small group sizes among day only and night only workers, the original work schedule groups were collapsed into one group for nurses without night work and one group for nurses with night work in the follow-up period. This was done to ensure sufficient group size and statistical power, and at the same time still be able to compare nurses with night work to those without night work. Still, this is a limitation and caution is warranted in interpreting the results. However, we did also analyze the original working schedules (day only, day and evening, night only, three-shift rotation) without finding any significant differences. Obviously, a limitation of this approach was the small group sizes of some of the working schedules. Still, similar findings shown when collapsing work schedule groups strenghten our conclusion. We investigated those who changed toward- or away from night work during the follow-up period. A limitation here is that we did not account for when they changed schedule. Regarding QR and NN as exposure variables, most of the nurses worked regular schedules and should thus be able to make good estimations of the magnitude of these variables on a yearly basis. When comparing different levels of exposure, we wanted the contrast group to have low exposure to night shifts and quick returns. It was however not possible to have contrast groups with no exposure, since very few nurses reported no QR or no NN. However, we will argue that the exposure in the contrast groups (<5 QR/year and <1 NN/year) was still very low and makes as such an adequate contrast. Due to how the schedules are organized and that many nurses work extra shifts almost all nurses were exposed to QR. We therefore had to have a different cut-off in the contrast group for QR compared to for NN. We cannot rule out the possibility of an uneven exposure to these two parameters in the follow-up period. Nurses moving from high to low, or low to high exposure of these two parameters may be an important group due to selection effects. We tried to address this by doing separate analyses comparing those with a stable exposure to those who increased or decreased their exposure to QR and NN, respectively. Still, the results remained the same.

One may question the generalizability of our study, as the cohort was based upon Norwegian nurses, most of them being female. The results are still likely to be valid for all Norwegian nurses, as the study was based upon a sample of the total population in this country. However, the results might be different in other occupational groups. Also, the results may not be valid for other countries, as working conditions and e.g., smoking regulations are different from country to country. In terms of smoking decline, there has since 1998 been a legal protection from exposure to smoking in workplaces in Norway, only allowing smoking in separate smoking rooms (49). Norway, like all Scandinavian countries, is a welfare state and has well-organized and regulated work environments with relatively few working hours in a full-time equivalent work week (35.5–37.5 h), which may limit generalizability. Another limitation concerning the measure of alcohol habits in the present study was that we only had complete and accurate data for a subgroup of the nurses. If this subgroup is not representative of the whole cohort population, this may thus limit generalizability. The AUDIT-C is a validated screening tool with 3 questions about potential alcohol misuse. A limitation is that while the two first questions address frequency and volume, we do not have exact information about daily or weekly alcohol consumption, for example units/week. The data may, thus, fail to detect nuances and changes in lighter or normal alcohol consumption habits which could be of importance. One of the inclusion criteria in the SUSSH cohort was that nurses had to hold at least a 50% full time equivalent working position. Still, there will be variations in their weekly hours. This could be a limitation, especially for working schedules which do not account for this. However, it should also be noted that many nurses with smaller permanent positions work extra shifts which are not accounted for in the data. Concerning NN and QR exposure, these parameters are reported as a continuous parameter and should thus reflect the nurses' actual exposure.

In this cohort, many of the nurses changed their work schedule away from night work ($n = 355$). Another study found that between 8 and 35%, depending on their type of shift work, changed to day work during a 6-year follow-up (50). The selection biases within shift work could be seen as a "healthy worker effect": It is more likely that healthy workers tend to choose and stay in a challenging work schedule (22). This could potentially underestimate the real effect of shift work on lifestyle factors trajectories. Another potential for underestimation of the true effects is misclassification bias. Härmä et al. when comparing self-reported data to objective registry data, found that for those who reported working shift work without night shifts there was a low sensitivity (62%) due to the fact that many nurses worked nights but did not report this (50). The authors concluded that this exposure misclassification was likely to bias results. Misclassification bias could be present in our study and could be a source of underestimation of true effects.

Our study had a low initial response rate, but a high response rate at follow-up. A review by Baruch et al. suggested that most study populations have a response rate about 53 ± 20% (1 SD from the mean response rate) (51). The low response rate in the first wave might have resulted in a skewed sample, but this is of less importance in the present study where we looked at changes over time.

CONCLUSION

We did not find any differences in relation to different work schedules, different exposure to QR, or different exposure to NN concerning exercise, caffeine consumption, smoking prevalence, and alcohol consumption in this 6-year follow-up study. This suggests that shift work may not affect lifestyle factors adversely and challenges the notion that shift work has an adverse impact on lifestyle factors. More prospective studies are needed to verify our findings.

DATA AVAILABILITY STATEMENT

The anonymized data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

AUTHOR CONTRIBUTIONS

HB: design of the study, data analysis, interpretation of the results, drafting the paper. SP, SW, BM, and BB: collecting the data, design of the study, interpretation of the results, critical review of the paper. All authors have approved the final manuscript.

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