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Assessing shift work and its health impacts

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Assessing shift work and its health impacts

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Editorial: Assessing shift work and its health impact

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Editorial on the Research Topic
Assessing shift work and its health impact

There are many work schedules that are called "shift work" (1). Shift work as explained by NIOSH, involves working outside the normal daylight hours. These workers might work in the evening, in the middle of the night, overtime or may have extralong workdays. They also might work regular days at one time or another. The work schedules might "rotate" around the clock, which involves changing work times from day to evening, or day to night. This might happen at different times of the week or at different times of the month. Police officers and firefighters, for example, often work rotating shifts. Other workers might have a "permanent" shift and only work at night or in the evenings. Waiters and waitresses, for example, might work only the evening shift. Night watchmen, on the other hand, might work only the overnight or "graveyard" shift. The IARC monogram on Night shift work (2) defined this as work during the usual sleeping hours of the general population, and included transmeridian air travel. Disruption of normal physiological circadian rhythms is the most marked effect of night shift work. In many industries, night shift work is essential for ensuring that production and activities can continue 24 h per day, 7 days per week.

Shift work is a common work pattern worldwide today but no consensus on its health impact has been made by researchers thus far. The objective of this small collection of original papers is to create a thematic approach to the subject and is aimed at summarizing the evidence from a series of original studies to highlight the impact of shift work on various aspects of the health of workers. A total of 18 manuscripts were received, of which 10 were accepted and eight rejected. Many papers have been published on the various aspects of the health impact of shift work over the years. A Medline search alone, using the key words "shift work," "health impact" yielded 4,614 publications on the topic. Some emerging concerns have been outlined in the IARC report on the subject (2).

Shift work (3) is common in modern societies, and shift workers are predisposed to the development of numerous chronic diseases. Disruptions to the circadian systems of shift workers have been described in numerous publications and are considered important contributors to the biological dysfunction these people frequently experience. In one study (3), the authors suggest that understanding how to alter shift work and time cue schedules to enhance circadian system function is likely improve the health of shift workers.

An umbrella review (4) summarized the evidence and evaluated the validity of the associations of shift work with different health outcomes. In a search of the MEDLINE, Web of Science, and Embase databases from their inception to April 25, 2020, the authors (4) found that shift work was associated with several health outcomes with different levels of evidence. Associations for myocardial infarction and diabetes mellitus incidence were supported by highly suggestive evidence. The IARC Monographs Working Group (2) classified night shift work as "probably carcinogenic to humans" (Group 2A), on the basis of limited evidence of cancer in humans (for cancers of the breast, prostate, colon, and rectum), sufficient evidence of cancer in experimental animals, and strong mechanistic evidence in experimental animals.

An area of concern in shift work is the effect on the circadian system and the corresponding hormonal changes in the workers affected. This may have an impact on the management of occupational fatigue. In one of the papers in this series, Huang et al. explored the association between the trends of cortisol rhythm and the regularity of shift work among midwives in China. Urinary cortisol levels of participants were assayed. The results suggested that cortisol was more inhibited in midwives with irregular shift patterns and the authors opined that hospital managers may need to consider these effects while performing work scheduling for midwives. This is to minimize their occupational fatigue and in the process, this may enhance the safety of mothers and infants in their care.

While insomnia and sleepiness symptoms are common in shift workers (5), 20–30% of affected works experience more severe symptoms and meet the criteria for shift work disorder (SWD). SWD can lead to impairments in cognitive function, physical and mental health, and reduced productivity and increased risk of workplace injury. Booker et al. (5) attempted to evaluate the impact of a shift work individual management coaching program, focusing on sleep education, promoting good sleep hygiene, and providing individualized behavioral strategies to cope with shift schedules.

The effects of the use of emerging technologies on shift work was evaluated in a scoping literature review in one the studies (Bullock et al.). The findings highlight a paucity of published research on the use of mobile phone applications for sleep self-management amongst early start shift workers. Bullock et al. opined that further research is needed, on applications appropriate to this subgroup of shift workers whose unique working conditions require specific interventions and support. The appropriate timing and use of light in both the early morning and evening hours is one example of support that is specifically relevant to this group. Bullock et al. opined that while a large number of mobile phone applications that target sleep self-management already exist in the digital marketplace, few, if any, are designed specifically for use by shift workers. Is there a need, therefore, for a more evidence-based and context-specific approach to the development of mobile phone sleep applications for this group?

The mental health impact of shift work on hospital workers was explored in a cross-sectional study covering 20 hospitals in China, using a questionnaire survey (Li et al.). Li et al. opined that depression and anxiety in shift nurses may be addressed by reducing their workload, sources of stress during night shifts, and facilitating rest and relaxation.

The effects of shift work on cognition and napping was explored. Fan et al. opined that night shifts appear to have adverse cognitive outcomes that might be attenuated by daytime napping. The neurovisceral integration model suggests that resting vagally mediated heart rate variability (vmHRV) is linked with cognitive function. Fan et al. investigated the relationship between resting vmHRV and cognitive function after different nap durations in medical interns after shift work. The authors suggested that demonstrable links were found between daytime napping and improved cognitive control in relation to autonomic activity after shift work in medical interns. Li et al. suggest that autonomic activity when awake plays a crucial role in in information processing and these also affected performance testing. Autonomic activity evaluations provided more insight into understanding the differences in neurocognitive mechanisms underlying information processing after different nap durations.

In this short series, it would be impossible to cover the entire scope of the literature nor to explore the entire breadth of the dimensions on the subject. It is hoped that these highlights would stimulate more research into this engaging topic and more light will be shed on the effects of shift work on the heatlh of the worker.

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
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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

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 ($n = 290$).

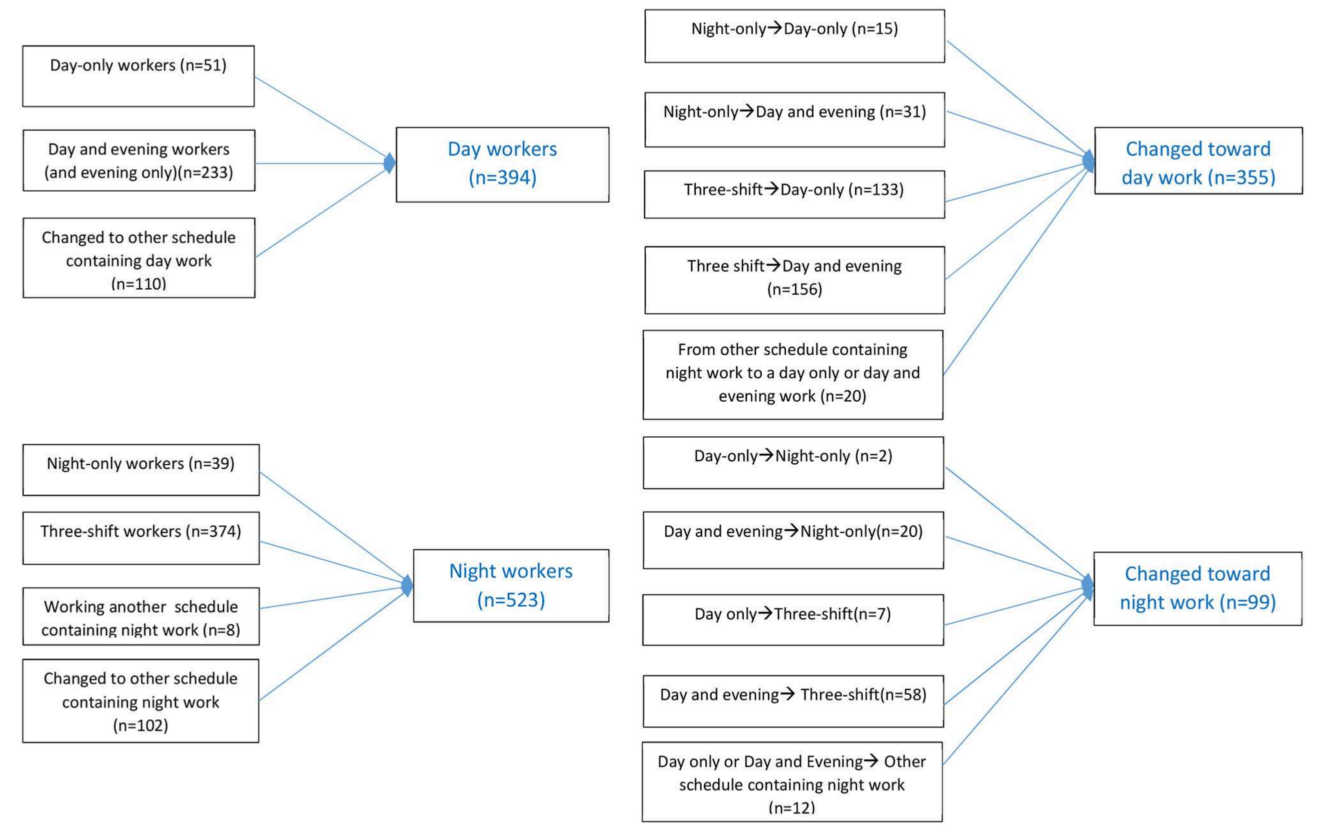

FIGURE 1 | An overview of the four work schedule groups.

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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The Association Between Shift Work and Immunological Biomarkers in Nurses

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Objectives: Shift work is associated with several negative health effects. The underlying pathophysiological mechanisms are unclear, but low-grade inflammation has been suggested to play a role. This project aimed to determine whether levels of immunological biomarkers differ depending on work schedule, self-reported sleep duration, self-reported sleep quality, and presence of shift work disorder (study 1). Furthermore, we aimed to determine whether these biomarkers differ after a night of sleep vs. at the end of a night or a day shift (study 2).

Methods: In study 1, 390 nurses provided blood samples after a night of sleep with the dried blood spot method. In study 2, a subset of 55 nurses also provided blood samples after a day shift and after a night shift. The following biomarkers were measured: interleukin-1alpha, interleukin-1beta, interleukin-4, interleukin-6, interleukin-8, interleukin-10, interleukin-13, monocyte chemoattractant protein-1, interferon-gamma, and tumor necrosis factor-alpha. Multiple linear regressions with adjustment for age, sex and body mass index (study 1) and ANOVAs with repeated measures (study 2) were conducted.

Results: In study 1, neither work schedule, number of night shifts, number of quick returns (<11 h between consecutive shifts), sleep duration, poor sleep quality, nor shift work disorder were systematically associated with most of these biomarkers. Compared with day only work, day-evening work was associated with higher levels of IL-1alpha and IL-13, quick returns were associated with higher levels of IL-1beta and MCP-1, short sleep duration (<6 h) was associated with lower levels of IL-1beta and higher levels of TNF-alpha, and long sleep duration (8+ h) was associated with higher levels of IL-13. In study 2, IL-1beta levels were higher (large effect size) both after a day shift (14% increase) and a night shift (75% increase) compared with levels after a night of sleep. Similarly, TNF-alpha levels were higher (moderate-large effect size) after a day shift (50% increase) compared to after a night of sleep. In contrast, MCP-1 levels were lower (large effect size) both after a day shift (22% decrease) and a night shift (12% decrease) compared with after a night of sleep.

Conclusions: We found some indications that shift work influenced immunological biomarkers. The results should be interpreted with caution due to limitations, e.g., related to the sampling procedure and to low levels of biomarkers in the blood samples.

Keywords: shift work disorder, immunity, inflammatory biomarkers, cytokines, interleukin, tumor necrosis factor-alpha, monocyte chemoattractant protein-1, blood spot method

INTRODUCTION

Shift work is associated with a number of negative health effects, e.g., cardiovascular disorders and cancer (1, 2). Still, the underlying pathophysiological mechanisms are unclear. However, several studies suggest that low-grade inflammation may play a role. Both short sleep and sleep disturbances are associated with increased levels of pro-inflammatory biomarkers such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor (TNF) (3, 4). Despite short sleep and sleep disturbances being common amongst shift workers (1), there is dearth of studies investigating the association between shift work and immunological biomarkers.

Studies investigating the link between shift work and immunity are few and show conflicting results. In a cross-sectional study among airline employees, Puttonen et al. (5) found that rotating shift work was associated with increased systemic inflammation. In a longitudinal study among 68 nurses with shift work and 28 nurses with daytime work, IL-1beta and TNF-alpha were significantly lower among shift workers at baseline, but not at 12 months follow-up. Furthermore, no effect of shift work on immunological biomarkers was present at 12 months follow-up when baseline values and job seniority were adjusted for (6). Another study among nurses showed that natural killer (NK) cell activity was reduced following night work compared to day work (7). Furthermore, a study comparing day workers with rotating shift workers showed higher levels of leucocytes in the latter group (8). The authors suggested that this reflected systemic inflammation, but since leukocyte levels vary extensively across time of day (9), it may also be attributed to group differences in circadian phase at the time of sampling. When comparing 225 shift workers with 137 day workers, no differences in IL-6, TNF-alpha, or lymphocyte count were found (10). Also, in a recent study comparing 254 night shift workers with 57 non-shift workers, no association in relation to work status was detected on a range of cytokines. However, night work was associated with increased number of monocytes and lymphocytes (11). In a clinical review, Faraut et al. (12) addressed the issue of shift work and immunity, and suggested several lines of further studies (e.g., use of non-invasive biological markers, conduct more longitudinal studies) to delineate the pathways by which circadian misalignment and short sleep may influence immunological mechanisms.

Much of the literature concerning sleep and shift work has focused on pro-inflammatory cytokines such as IL-1, IL-6, and TNF-alpha. However, the immune system serves many other functions, and there is a need to measure additional immunological biomarkers to better understand whether the interplay and complexity of immune functions are involved in how shift work may affect health outcomes. For example, there is limited knowledge about how shift work affects anti-inflammatory cytokines, such as IL-4 and IL-10, or other cytokines, such as IL-13 and interferon (IFN), which may have sleep regulatory properties (4). One complicating issue when studying healthy humans is that the blood concentrations of most cytokines are very low, and often not detectable (4).

In the present project, we collected blood from shift working nurses using the dried blood spot technique (13). This is a minimally invasive method in which blood may be collected at home or at the workplace, and by the participants themselves. This blood collection technique analyzed with quantitative antibody array technology allows for quantification of several cytokines from the same sample. By using this technique, we were able to quantify the following immunological biomarkers: IL-1alfa, IL-1beta, IL-4, IL-6, IL-8, IL-10, IL-13, monocyte chemoattractant protein (MCP)-1, IFN-gamma, and TNF-alpha.

This project consists of two studies, with two different aims. Aim of study 1: To determine whether levels of immunological biomarkers differ between nurses ($n = 390$) (a) on different shift schedules, (b) working different number of night shifts, (c) working different number of quick returns (defined as <11 h between consecutive shifts), (d) with short or long vs. normal self-reported sleep duration and (e) with good vs. poor self-reported sleep quality. Furthermore, (f) to determine whether levels of immunological biomarkers differ between nurses with and without shift work disorder. Aim of study 2: In nurses rotating between night and day work ($n = 55$), determine whether levels of immunological biomarkers differ after a night of sleep compared with levels after a night shift (both blood samples taken at about the same time) and after a day shift (blood sample taken at about 3 p.m.). Using these within-subject data, an additional aim was to study the diurnal influence on these immunological biomarkers.

MATERIALS AND METHODS

Participants

Nurses were asked if they wanted to participate in this immunological project when completing a questionnaire in the ongoing cohort study "SUrvey of Shift work, Sleep, and Health (SUSSH)" (14). In the first immunological project (study 1), 485 nurses received the necessary equipment and instructions for sampling blood using the blood spot technique by postal mail. Only nurses who were working either day shifts only, a two-rotational schedule (day and evening shifts) or a three-rotational schedule (day, evening, and night shifts) were invited to participate. They were asked to take fasting blood samples when waking up the morning after a night of sleep, but before the start of the day shift. The participants were instructed to refrain from taking and sending samples if they had been ill or experienced fever during the last 3 days. Furthermore, nurses were asked not to take samples if they were pregnant. A total of 375 nurses returned blood samples together with a short questionnaire in which they answered questions about sleep duration and sleep quality (very good, pretty good, indifferent, pretty bad, and very bad) the night before blood sampling. Thus, response rate was 77.3%. Due to poor quality of some blood samples (insufficient magnitude; 224 samples) and missing questionnaires (4 samples), 228 nurses were sent new blood sample equipment and questionnaire. Still, not all nurses provided satisfactory blood samples, and the final number of samples with sufficient quality for analyses was 334. All nurses who participated in study 1 received a compensation of about EUR 40.

In study 2, 99 nurses working three-rotational shifts were sent blood sampling equipment. Besides the fasting blood samples taken in the morning after a night of sleep, these nurses also provided non-fasting blood samples right after the following day shift (at about 3 p.m.) and immediately after a night shift (taken at about the same time as the blood sample after a night of sleep). These nurses were also instructed not to take any samples if being ill or having fever during the last 3 days, as well as not taking samples if they were pregnant. Sixty-four nurses returned the blood samples together with a similar questionnaire as in study 1, in which the nurses answered questions about sleep duration and sleep quality the night before the first blood sample. Response rate was 64.6% in this study. Due to poor quality of some of the blood samples (27 samples) or lack of completed questionnaire (1 sample), 28 nurses were sent new blood sample equipment and questionnaire. Still, some of the samples had poor quality, resulting in data from a total of 56 participants having three samples each to be analyzed. One participant was excluded from the within-subject analyses due to sleeping during the night shift. Sample 1 from the 56 participants in study 2 was included with the samples in study 1, as all these samples were taken in the morning after a night of sleep. Each nurse in study 2 received a compensation of about EUR 100.

The most common work hours for the Norwegian nursing population are 07:00–15:00 (day shifts), 14:30–22:00 (evening shifts), and 22:00–07:30 (night shifts). Nurses working in outpatient clinics or administratively may work 08:00–16:00. Shift workers have a 35.5 h workweek, while day workers have a 37.5 h workweek.

Blood Sampling Procedure

The dried blood spot method was used for sampling blood. This procedure is minimally invasive and considered to be easy to administer. The nurses pricked their finger with a lancet, and after removing the first blood drop, they applied a small amount of blood on four marked circles on Whatman 903 Protein Saver Snap Apart Cards. To be qualified as a good quality blood sample, the blood should fill the whole circle and should be drenched through to the back of the card. After blood collection, the filter cards were dried in room temperature for 12–24 h, and then returned to the researchers in sealed plastic bags with silica gels to prevent humidity. The filter cards were stored at −70°C until analysis.

Blood Sample Preparation and Microarray Analyses

To elute cytokines from the dry blood samples, one circle (12.5 mm) was punched out of the blood card, minced and put into a 1.5 ml Eppendorf tube containing 150 μl 1× PBS. The Eppendorf tube was placed on gentle shaking for 4 h in room temperature. The filter paper was removed, and the sample was centrifuged 13,000 RPM for 3 min. Then 80 μl eluate was pipetted onto the antibody array slide Quantibody® Human inflammation Array 1 (RayBiotech, Inc., Norcross, GA, USA) and analyzed according to the manufacturer's instructions. After analysis the antibody array slides were stored at 4°C and sent to RayBiotech Life, Inc, USA, for scanning (Innopsys Innoscan 710), data extraction and calculation of the concentration of each cytokine in pg/ml.

Quantibody® uses the principle of microarray (forward phase) and enables the detection of several different proteins. In the current project, the following immunological biomarkers were measured: IL-1alpha, IL-1beta, IL-4, IL-6, IL-8, IL-10, IL-13, MCP-1, IFN-gamma, and TNF-alpha. **Table 1** shows the limit of detection (LOD) (provided by RayBiotech Life) of the analyses for each immunological parameter. Most proteins, with the exception of MCP-1, had a high percentage of values below LOD. However, as the data are epidemiological, we kept all data, as suggested by Whitcomb and Schisterman (15). In cases were protein levels were not detected (=0), we substituted 0 with a random number between 0 and the lowest value detected for each specific protein. The statistical results remained the same irrespective of imputation or no imputation.

Questionnaire

We collected data on self-reported sleep duration and sleep quality the night before blood sampling from a short questionnaire sent out together with the blood sampling equipment. Furthermore, we had data from the invitation questionnaire of the SUSSH cohort. From that questionnaire we collected information about the nurses' age, sex, marital status, work time equivalent, weight, height, work schedule, number of night shifts worked the last year, and number of quick returns worked the last year. In addition, presence of shift work disorder (SWD) was measured with three questions based on the criteria from the third edition of the International Classification of Sleep Disorders [ICSD-3; (16)]. The questions were: (a) Do you have a work schedule that sometimes overlap with the time you usually sleep?, (b) If yes, does this cause insomnia and/or excessive sleepiness due to reduced amount of sleep?, (c) If yes, has this lasted for at least 3 months? Participants were classified as having SWD if they responded "yes" to all three questions. Body mass

TABLE 1 | Statistics of the limit of detection (LOD) for each immunological biomarker.

Biomarker	LOD (pg/ml)	% below LOD
IL-1alpha	9.1	73.9
IL-1beta	3.2	38.7
IL-4	3.3	78.4
IL-6	4.7	92.0
IL-8	9.7	84.1
IL-10	0.3	85.6
IL-13	1.1	85.1
MCP-1	3.6	0.2
IFN-gamma	0.8	64.6
TNF-alpha	2.3	77.4

IL, interleukin; MCP, monocyte chemoattractant protein; IFN, interferon; TNF, tumor necrosis factor. Based on samples from 390 nurses.

index was calculated as weight (kg) divided by the square of height (meters).

Statistics

The statistical analyses were conducted with IBM SPSS Statistics 25 for Windows. Due to positive skewness, all statistical analyses were conducted with log-transformed cytokine values. In study 1, multiple linear regressions were conducted with the different immunological biomarkers as dependent variables, and with adjustment for age, sex, and body mass index [since these variables are shown to influence cytokine levels (17)]. Predictors were work schedule [day only (reference), two-shift rotation, three-shift rotation], number of night shifts during the last year [0 (reference), 1–30, >30], number of quick returns during the last year [0 (reference), 1–30, >30], sleep duration [<6 h, 6–7.9 h (reference), 8+ h], sleep quality [very good/pretty good (reference), indifferent/pretty bad/very bad], and shift work disorder [no (reference), yes]. In study 2, one-way ANOVAs for repeated measures (Wilks' Lambda) with *post-hoc* LSD tests and effect sizes (multivariate partial eta squared in which 0.01, 0.06, and 0.14 suggest small, moderate, and large effect sizes, respectively) were used to compare intra-individual values of the different immunological biomarkers after a night of sleep, after a day shift, and after a night shift. Significance level was set to 0.05.

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West, no 088.08). Informed consent in written form was obtained from all participants.

RESULTS

Most of the immunological biomarkers, with the exception of IL-1beta and MCP-1, were present in very low amounts, and with a high percentage of values below LOD (**Table 1**). Histograms showing the values for the different cytokines are available as a **Supplementary File**.

TABLE 2 | Questionnaire data among shift working nurses ($n = 390$) participating in study 1.

	Mean (SD)
Age (missing = 0)	40.5 (8.5)
Body mass index (BMI) (missing = 2)	25.1 (4.5)
	% (*n*)
Sex (missing = 1)	
Female	93.6 (364)
Male	6.4 (25)
Marital status (missing = 1)	
Married/cohabiting	76.6 (298)
Single	23.4 (91)
Work time equivalent (missing = 1)	
<50%	0.0 (0)
50–75%	15.4 (60)
76–90%	18.8 (73)
>90%	65.8 (256)
Work schedule (missing = 1)	
Day only	27.8 (108)
Day-evening	33.9 (132)
Day-evening-night	38.3 (149)
Number of night shifts last year (missing = 1)	
0	51.7 (201)
1–30	26.2 (102)
>30	22.1 (86)
Number of quick returns last year (missing = 5)	
0	22.9 (88)
1–30	38.7 (149)
>30	38.4 (148)
Sleep duration[a] (missing = 3)	
<6 h	25.6 (99)
6–7.9 h	62.3 (241)
8+ h	12.1 (47)
Sleep quality[a] (missing = 3)	
Very good/pretty good	69.8 (270)
Indifferent/pretty bad/very bad	30.2 (117)
Shift work disorder (missing = 6)	
Yes	33.1 (127)
No	66.9 (257)

[a]*The night before blood sampling.*

The participants in study 1 ($n = 390$) were on average 40.5 years (SD = 8.5), and 93.6% were females. Other demographic information as well as data regarding body mass index, work schedule characteristics, number of night shifts worked the last year, number of quick returns worked the last year, self-reported sleep duration and sleep quality, and shift work disorder are provided in **Table 2**.

Table 3 presents the levels of the immunological biomarkers in relation to different groups of the shift working nurses (study 1). In relation to work schedule, day-evening work was associated with significantly higher levels of IL-1alpha and IL-13 than day only work (**Table 4**). In relation to number of nights worked last

TABLE 3 | Levels of immunological biomarkers in pg/ml after a night of sleep among different groups of shift working nurses ($n = 390$).

	IL-1alpha Median, IQR	IL-1beta Median, IQR	IL-4 Median, IQR	IL-6 Median, IQR	IL-8 Median, IQR	IL-10 Median, IQR	IL-13 Median, IQR	MCP-1 Median, IQR	IFN-gamma Median, IQR	TNF-alpha Median, IQR
Cytokine levels	3.95, 9.45	4.65, 8.70	0.80, 3.03	0.40, 2.54	0.75, 6.97	0.07, 0.06	0.08, 0.56	174.55, 122.08	0.10, 1.55	0.50, 2.04
Work schedule										
Day only	2.50, 9.02	4.15, 7.10	0.50, 2.65	0.30, 2.32	0.30, 5.83	0.07, 0.06	0.08, 0.37	171.00, 132.13	0.10, 1.26	0.30, 1.74
Day-evening	5.10, 9.15	4.55, 8.17	1.10, 3.30	0.70, 2.53	2.15, 7.71	0.08, 0.17	0.10, 0.75	164.70, 129.78	0.25, 1.65	0.65, 2.04
Day-evening-night	3.70, 10.29	4.80, 10.55	0.70, 3.18	0.20, 2.69	0.10, 7.20	0.07, 0.07	0.08, 0.46	184.70, 108.35	0.10, 1.45	0.60, 2.45
NN last year										
0	4.20, 9.64	4.00, 7.60	1.00, 3.04	0.50, 2.64	1.10, 6.85	0.07, 0.06	0.08, 0.66	166.00, 129.55	0.20, 1.65	0.40, 2.03
1–30	3.35, 7.43	4.55, 10.03	0.45, 2.23	0.20, 2.29	0.15, 7.98	0.07, 0.07	0.08, 0.57	176.55, 127.83	0.10, 1.06	0.40, 1.60
>30	3.85, 12.16	5.70, 10.77	0.95, 3.44	0.40, 2.62	0.30, 7.33	0.07, 0.06	0.09, 0.46	185.50, 97.28	0.10, 1.67	0.80, 2.87
QR last year										
0	2.60, 9.23	3.35, 7.05	0.45, 2.85	0.20, 2.62	0.09, 5.71	0.07, 0.06	0.08, 0.44	164.85, 134.70	0.10, 1.41	0.30, 2.10
1–30	4.40, 9.92	5.30, 12.15	1.00, 2.78	0.40, 2.48	0.20, 7.55	0.07, 0.06	0.09, 0.56	170.60, 114.40	0.10, 1.55	0.40, 2.55
>30	3.95, 9.83	3.85, 8.98	0.85, 3.44	0.40, 2.69	1.35, 7.89	0.07, 0.07	0.09, 0.73	179.20, 128.75	0.10, 1.45	0.70, 1.95
Sleep duration										
6.0–<8 h	3.90, 9.52	4.90, 9.60	0.70, 2.69	0.30, 2.49	0.40, 6.85	0.07, 0.06	0.08, 0.46	176.00, 115.55	0.10, 1.45	0.40, 1.99
<6 h	4.40, 9.55	4.00, 10.62	1.00, 3.36	0.60, 3.14	0.40, 7.55	0.07, 0.07	0.08, 0.66	170.60, 132.30	0.30, 1.65	1.10, 3.02
8+ h	3.50, 9.42	4.00, 6.50	1.10, 3.52	0.30, 2.34	1.80, 8.13	0.07, 0.06	0.20, 0.72	154.20, 141.10	0.10, 1.86	0.09, 1.36
Sleep quality										
Good	3.65, 9.38	4.40, 7.82	0.75, 2.93	0.30, 2.46	0.55, 7.08	0.07, 0.06	0.08, 0.56	174.85, 120.90	0.10, 1.55	0.40, 2.04
Indifferent/bad	4.40, 9.75	5.50, 11.95	0.90, 3.19	0.60, 2.84	1.80, 6.99	0.07, 0.06	0.10, 0.56	176.90, 119.10	0.20, 1.50	0.70, 2.49
SWD										
No	4.30, 9.47	4.80, 8.60	0.80, 2.83	0.40, 2.74	0.70, 7.60	0.07, 0.06	0.08, 0.66	174.50, 124.35	0.10, 1.55	0.50, 1.94
Yes	3.70, 10.23	4.40, 10.40	0.90, 3.74	0.40, 2.14	0.90, 6.44	0.07, 0.07	0.08, 0.46	175.50, 118.00	0.10, 1.56	0.40, 2.15

IL, interleukin; MCP, monocyte chemoattractant protein; IFN, interferon; TNF, tumor necrosis factor; NN, night shifts; QR, quick returns; IQR, interquartile range; SWD, shift work disorder.

year, working more than 30 night shifts last year was associated with a near-significant higher MCP-1 level than not working night shifts (**Table 4**). In relation to number of quick returns worked last year, nurses working between 1 and 30 quick returns last year had higher IL-1beta levels, and nurses working more than 30 quick returns had higher MCP-1 levels in comparison to not working quick returns (**Table 4**). In relation to sleep duration the night before blood sampling, short sleep duration (<6 h) was associated with lower IL-1beta levels and higher TNF-alpha levels, in comparison to a sleep duration of 6–7.9 h (**Table 4**). Furthermore, long sleep duration (8+ h) was associated with higher IL-13 levels. In relation to sleep quality the night before blood sampling and in relation to shift work disorder, no association to levels of cytokines was found (**Table 4**).

In study 2 (subset with $n = 55$), the participants were 39.0 years (SD = 8.1) and 94.4% were females. **Table 5** presents the levels of the immunological biomarkers after a night of sleep, after a day shift, and after a night shift within the same nurses. There were significant ANOVAs for IL-1beta, MCP-1 and TNF-alpha. Partial eta squared indicated large effect sizes for IL-1beta and MCP-1, and moderate to large effect size for TNF-alpha (**Table 5**). *Post-hoc* tests showed that IL-1beta levels were higher after a day shift and after a night shift in comparison to levels after a night of sleep. In contrast, MCP-1 levels were lower after a day shift and after a night shift compared with after a night of sleep. For TNF-alpha, *post-hoc* tests showed that the level was higher after a day shift compared to after a night of sleep (**Table 5**).

DISCUSSION

We anticipated (aim of study 1) that there would be differences in several immunological biomarkers depending on work schedule, number of night shifts and quick returns, and depending on sleep duration, sleep quality, and shift work disorder. This notion was partially supported, as levels of IL-1alpha (work schedule), IL-1beta (quick returns and sleep duration), IL-13 (work schedule and sleep duration), MCP-1 (number of night shifts and number of quick returns), and TNF-alpha (sleep duration) differed between the respective groups. However, considering the approach to analyze many biomarkers, the results may indicate that neither shift work, sleep duration nor sleep quality strongly affect immunological biomarkers.

The aim of study 2 was to explore whether the measured immunological biomarkers would differ after a night of sleep compared with after a day shift and after a night shift – in a within-subject design. IL-1beta, TNF-alpha, and MCP-1 significantly differed depending on sample occasion. *Post-hoc* tests showed higher IL-1beta and TNF-alpha levels after the shifts (for TNF-alpha only after a day shift) compared with after a night of sleep, whereas MCP-1 levels were lower after the work shifts compared to after a night of sleep. Thus, there was no clear

TABLE 4 | Results from multiple linear regression analyses with different work characteristics, sleep duration, sleep quality, and shift work disorder as predictors, with adjustment for age, sex, and body mass index.

	IL-1alpha	IL-1beta	IL-4	IL-6	IL-8	IL-10	IL-13	MCP-1	IFN-gamma	TNF-alpha
	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value	β, *p*-value
Work schedule										
Day only (ref)										
Day–evening	**0.14, 0.020**	0.04, 0.479	0.11, 0.071	0.08, 0.196	0.10, 0.095	0.09, 0.154	**0.13, 0.036**	0.02, 0.746	0.07, 0.271	0.09, 0.168
Day–evening–night	0.07, 0.272	−0.01, 0.823	0.05, 0.438	−0.00, 0.946	−0.02, 0.813	0.01, 0.821	0.03, 0.625	0.08, 0.184	−0.01, 0.879	0.06, 0.345
NN last year										
0 (ref)										
1–30	−0.05, 0.347	0.01, 0.895	−0.04, 0.467	−0.02, 0.707	−0.05, 0.319	−0.06, 0.272	−0.07, 0.176	0.07, 0.168	−0.09, 0.104	−0.05, 0.362
>30	0.02, 0.726	−0.02, 0.687	0.01, 0.829	−0.04, 0.473	−0.04, 0.456	−0.04, 0.462	−0.03, 0.635	0.10, 0.051	−0.03, 0.635	0.05, 0.388
QR last year										
0 (ref)										
1–30	0.11, 0.110	**0.14, 0.034**	0.05, 0.451	0.02, 0.751	0.04, 0.543	0.03, 0.670	0.00, 0.982	0.09, 0.177	−0.00, 0.962	0.00, 0.983
>30	0.09, 0.191	0.02, 0.725	0.07, 0.264	0.04, 0.559	0.10, 0.143	0.04, 0.519	0.07, 0.282	**0.13, 0.043**	0.02, 0.787	0.02, 0.743
Sleep duration										
6.0–<8 h (ref)										
<6 h	0.01, 0.890	**−0.11, 0.041**	0.04, 0.430	0.03, 0.573	0.01, 0.856	0.02, 0.693	0.00, 0.987	−0.03, 0.615	0.04, 0.493	**0.11, 0.040**
8+ h	0.00, 0.940	−0.02, 0.679	0.08, 0.144	0.02, 0.702	0.07, 0.178	0.04, 0.407	**0.11, 0.030**	−0.05, 0.367	0.03, 0.638	−0.06, 0.232
Sleep quality										
Good (ref)										
Indifferent/bad	0.07, 0.172	0.00, 0.938	0.03, 0.507	0.02, 0.770	0.03, 0.532	0.02, 0.654	0.04, 0.429	−0.03, 0.584	0.01, 0.840	0.07, 0.165
SWD										
No (ref)										
Yes	0.01, 0.929	−0.04, 0.492	0.01, 0.858	−0.02, 0.652	−0.02, 0.663	−0.06, 0.287	−0.03, 0.531	−0.02, 0.655	−0.05, 0.298	−0.01, 0.790

IL, interleukin; MCP, monocyte chemoattractant protein; IFN, interferon; TNF, tumor necrosis factor; NN, night shifts; QR, quick returns; Ref, reference group; SWD, shift work disorder; β, standardized beta. Significant findings in bold. All regressions were conducted with log-transformed cytokine values due to positive skewness.

influence on the majority of these immunological biomarkers depending on whether the blood sample was taken after sleep or after work periods. It is important to note that the blood samples taken after the day shift and after the night shift were non-fasting, as compared to the fasting blood sample taken after a night of sleep. How this may have affected the results is unclear. Also, diurnal influences may have impacted the results. However, there is poor understanding of the diurnal variation of most cytokines (2, 18, 19). Most evidence concerns IL-6 where a recent meta-analysis showed levels to be lower in the morning (20). Unfortunately, in the present study most IL-6 data were under the LOD and we could not make any clear conclusions as to whether shift workers suffered from a systemic inflammation with regard to IL-6 or whether there was an alteration seen after a night shift.

With respect to the previous literature on how shift work and sleep relate to cytokines, our findings are partially in contrast with several previous studies (5, 7, 8, 12, 21) but in agreement with others (6, 10, 11). In a systematic review and meta-analysis on the link between sleep disturbance, sleep duration and inflammation, Irwin et al. (3) found 72 studies assessing IL-6, TNF-alpha, and C-reactive protein (CRP). It was reported that TNF-alpha was not associated with neither sleep disturbances nor sleep duration, whereas IL-6 was associated with sleep disturbance (higher values) but not short sleep duration, partially lending support to the present findings. Irwin et al. (3) also reported that sleep disturbance and short sleep duration were associated with higher levels of CRP, however, that inflammatory biomarker was not measured in the present study. Furthermore, neither experimental sleep deprivation nor sleep restriction have been found to be associated with IL-6, TNF-alpha, or CRP (3). The authors concluded that sleep disturbance, but not short sleep duration, was associated with higher levels of markers of systemic inflammation (3). In another systematic review, it was concluded that acute or chronic sleep loss do not influence levels of IL-4 and IL-10 (4). In the present study, short sleep duration (<6 h) was associated with lower IL-1beta levels and higher TNF-alpha levels, whereas long sleep duration (8+ h) was associated with higher IL-13 levels. However, we found no association between the immunological biomarkers and sleep quality or shift work disorder. Our findings therefore extend current knowledge of the rather weak associations between shift work, sleep, and immune functioning.

One of the findings in study 2 was reduced levels of MCP-1 after a day shift and in the morning after a night shift compared with morning levels after a night of sleep. MCP-1 is a chemo-attractant and one of the key cytokines that regulate migration and infiltration of monocytes and macrophages into different tissues around the body. It is believed to play a role in the development of atherosclerosis and probably also in autoimmune disease (22, 23). Our finding with regard to

TABLE 5 | Levels of immunological biomarkers in pg/ml after a night of sleep (morning fasting), after a day shift (afternoon not fasting), and after a night shift (morning not fasting) among shift working nurses ($n = 55$) in a within-subject design.

	After sleep (morning sample)		After day shift (afternoon sample)		After night shift (morning sample)			
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Wilks' Lamda[a] F(2,53)**	**Partial Eta squared**
IL-1alpha	4.6	6.4	4.9	5.4	6.4	10.2	0.99, $p = 0.68$	0.015
IL-1beta	7.2	12.2	8.2**	10.0	12.6**	18.2	**0.83, $p = 0.007$**	**0.172**
IL-4	1.5	2.4	1.0	1.6	1.5	2.8	0.99, $p = 0.69$	0.014
IL-6	1.1	1.8	1.1	1.8	1.1	1.7	0.97, $p = 0.40$	0.034
IL-8	4.4	7.4	4.8	7.6	4.5	8.1	0.95, $p = 0.26$	0.049
IL-10	0.3	0.3	0.2	0.2	0.2	0.3	0.99, $p = 0.69$	0.014
IL-13	0.3	0.5	0.5	0.9	0.5	1.1	0.98, $p = 0.59$	0.020
MCP-1	190.9	103.3	149.8**	88.2	167.5*	92.5	**0.86, $p = 0.02$**	**0.144**
IFN-gamma	.6	1.0	1.0	1.5	.9	2.1	0.96, $p = 0.32$	0.042
TNF-alpha	1.0	1.5	1.5*	1.8	1.2	1.7	**0.88, $p = 0.04$**	**0.118**

IL, interleukin; MCP, monocyte chemoattractant protein; IFN, interferon; TNF, tumor necrosis factor; SD, standard deviation. [a]Analyses were conducted with log-transformed cytokine values due to positive skewness.
**$p < 0.05$ vs. "After sleep" on post-hoc Least Significant Difference (LSD).*
***$p < 0.01$ vs. "After sleep" on post-hoc LSD.*

MCP-1 using a within-subject study design is novel. Further studies are needed to clarify the importance of MCP-1 in shift work.

Strengths and Limitations

This present project has several limitations and strengths. The blood spot method allowed the nurses to take samples in their home environment, thus facilitating blood sampling after waking up in the morning after sleep. Also, the antibody array method allowed us to analyze ten different biomarkers from the same sample, which is considered to be a major strength. Furthermore, another asset was that we were able to compare levels of immunological biomarkers at the same time points (after sleep vs. after night work), as well as compare levels at different time points (sample taken in the afternoon vs. morning samples after sleep/after night shift). While participants may have been measured at different circadian phases—due to differences between individuals in terms of diurnal type or alterations within individuals across the work schedule—the present approach should be seen as pragmatic, in order to limit influence from the circadian system when frequent samples covering the entire 24 h window could not be done. The relatively large group of nurses with acceptable response rates is also an asset. Furthermore, we believe our assessment of the exposure to a number of shift work characteristics is a strength. For example, the number of night shifts and quick returns are known to contribute to circadian disruption and are also seen as risk factors for adverse health. Another strength was that we adjusted for age, sex, and body mass index in the group comparisons, as these variables are shown to influence cytokine levels (17). A major limitation with this self-performed blood sampling procedure was that many of the initial samples were of poor quality, usually due to blood not covering the whole circle of the filter cards. Considering that these participants were nurses who are trained to handle blood, it is to be expected that such a sampling procedure may be even more difficult in other populations. Another concern relates to the low levels of immunological biomarkers in the blood samples. For all biomarkers except for MCP-1 and IL-1beta, most of the samples had levels that were below the detection limit. This is however common when measuring cytokines in circulation but is clearly a limitation with the chosen method since other methods are more sensitive with regards to detecting systemic cytokines, such as IL-6. The definition of limit of detection (LOD) is the concentration or the quantity that can be detected with reasonable certainty for a given analytical procedure (15). To avoid biasing estimates it is recommended to use all data including those below LOD in epidemiological studies like the present investigation (15). Also, it is important to note that the concentration of most cytokines in healthy individuals is very low and not always detectable even with more sensitive methods (4). The results are likely to be most robust for the IL-1beta and MCP-1 findings, since more than 61 and 99% of the values were above LOD, respectively. For the other cytokines, many samples were below the lower detection level, and the results regarding these should therefore be interpreted with caution. Another limitation with the approach to include many cytokines is the risk of conducting type-I errors. We did not apply any corrections to reduce the risk for false positive findings as such an approach would have reduced the statistical power, hence increasing the risk of making type-II errors. We believe that these estimates could give directionality for future studies, e.g., as priors in a Bayesian statistic. Still, the fact that the cytokine levels were generally low, suggests that shift work does not strongly affect immunity. Still, it should be noted that some of the group comparisons may have been influenced (e.g., comparing day only to shift worker) by "the healthy shift worker effect" (24). Also, the day only group included nurses with previous shift work experience. How and if this may have affected the results however, is unclear.

Based on previous literature and the present findings, one cannot make strong conclusions regarding how shift work affects immunity. An important step in solving this issue will be to merge data from several studies (e.g., by meta-analytical approaches), increasing the power to make more accurate estimates of possible effects.

In conclusion, the present findings showed some indications of shift workers to have higher levels of inflammatory biomarkers. However, neither work schedule, number of night shifts, number of quick returns, short sleep duration, poor sleep quality, nor having shift work disorder seemed to have a major impact on the levels of a multitude of immunological biomarkers. Yet, levels of IL-1beta and TNF-alpha were higher after a day shift, levels of IL-1beta were higher after a night shift, and levels of MCP-1 were lower both after a day shift and after a night shift, in comparison with morning levels after a night of sleep, respectively, which suggests that work may acutely impact immune function.

DATA AVAILABILITY STATEMENT

Data cannot be released into a publicly accessible repository in accordance with national guidelines and local legislation due to concerns regarding participant anonymity as raised by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West).

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Regional Committee for Medical and Health Research Ethics of Western Norway (REK-West, no 088.08). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

BB: collecting the data, design of the study, data analysis, interpretation of the results, and drafting the paper. SP, SW, BM, and ET: collecting the data, design of the study, interpretation of the results, and critical review of the paper. JA, ØV, KB, and HB: design of the study, interpretation of the results, and critical review of the paper.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00415/full#supplementary-material

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Night Shift Among Women: Is It Associated With Difficulty Conceiving a First Birth?

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Background: Asynchrony in circadian processes alters many physiological systems, including female reproduction. Thus, there are possible reproductive consequences of night shift work for women including menstrual irregularity, endometriosis, and prolonged time to conception. This study examined whether women who worked night shift were more likely than those who did not to require fertility treatment to conceive a first birth, whether they had specific infertility diagnoses, and if such relationships were age-specific.

Methods: In a retrospective data linkage study of 128,852 primiparous women, fertility treatment data were linked to the state perinatal registry for South Australia (1986–2002). Potential exposure to night shift work was assessed using a job-exposure matrix. First, the association between night shift work and fertility treatment was assessed among (1) all women, then (2) women in paid employment, using logistic regression. Interactions between age and shift work status were also examined. Secondly, among women who conceived with fertility treatment, we assessed associations between night shift work and type of infertility diagnosis. Potential confounders were considered in all analyses.

Results: Among women $\leq$35 years, night shift workers were more likely to require fertility treatment (all: OR = 1.40, 95% CI 1.19–1.64; in paid employment: OR = 1.27, 95% CI 1.08–1.50). There were no associations among women >35 years. Ethnicity, socioeconomic status and smoking did not affect these results. Among women who underwent fertility treatment, night shift workers were more likely than day workers to have menstrual irregularity (OR = 1.42, 95% CI 1.05–1.91) or endometriosis (OR = 1.34, 95% CI 1.00–1.80).

Conclusions: Night shift work may contribute to increased need for fertility treatment in younger women. This increased risk may reflect young women's vulnerability in terms of poor tolerance of night shift work, and/or lack of control and choice about shift schedule.

Keywords: assisted reproduction (ART), endometriosis, infertility, menstrual abnormality, shift work (MeSH), night shift work

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INTRODUCTION

The nature of paid work and the workforce in Western societies is changing, with manual laboring jobs declining and demand for workers in the service and care industries increasing (1). One implication of this is increased non-standard and flexible working time arrangements (2). Such changes in work arrangements disproportionately affect women, who predominate in the growth industries (3).

Night shift work, in particular, may interfere with the lives and reproductive health of women. Quantity and quality of sleep can be affected and the circadian rhythm, the 24-h biological cycle that regulates sleep and wakefulness, can be disrupted (4). Asynchrony in circadian processes alters many physiological systems, including female reproduction (5, 6). Fixed night shift and rotating schedules that include night shift are thought to have the greatest impact (4).

Possible reproductive consequences of night shift work for women include menstrual irregularity (7), endometriosis (8, 9), and prolonged time to conception (10). To our knowledge, no study has investigated the potential relationship between night shift work and the requirement for reproductive assistance (fertility treatment) to conceive. Australia provides an ideal context in which to study this relationship since fertility treatment services are more accessible in Australia than in most other countries. In particular, fertility treatments and associated pharmaceutical costs have been subsidized since as early as 1990 (11), and there are no restrictions to access based on age, number of treatment cycles or existing family size (12, 13).

The aim of this study was to investigate whether primiparous women employed in occupations potentially involving night shift work were more likely than women in occupations not involving night shift work to require fertility treatment, and if so, to characterize the type of infertility diagnoses. We considered the role of age to explicitly address the circumstances that: night shift work is more commonly undertaken by younger women, including within occupations such as nursing where more senior positions typically entail (administrative) day work; access to fertility treatment increases with age, as women are increasingly in a position to bear associated costs (financial, time, relationship strain); the age-related decline in women's fertility changes the demographic and health profiles of women seeking treatment.

MATERIALS AND METHODS

Data Sources and Study Population

As described previously (14), the cohort for this study was retrospectively assembled by linking population-wide data from the South Australian perinatal registry (for the period January 1986 to December 2002) to data relating to patients undergoing assessment and treatment for infertility. Data sets and key variables are depicted in **Figure 1**.

Night Shift Work

The perinatal registry includes a woman's usual occupation prior to and/or during pregnancy (15), coded according to the Australian Standard Classification of Occupations First Edition (16). To assess exposure to night shift work, a shift work job-exposure matrix (JEM) was applied. Job-exposure matrices provide a cross-classification of job codes/titles and the probability of occupational exposure (17). A detailed description of the specific shift work JEM, including its validation, has been published elsewhere (18). The JEM assigns each occupation a probability of exposure to light at night, phase shift, sleep disturbances, and other factors (19). For the present study, exposure to light at night was selected as an indicator of night and rotating shift work that includes nights. Exposure to light at night is a key contributor to circadian disruption and altered melatonin secretion, both of which have been associated with several adverse health outcomes (20). Occupations with exposure to light at night were those in which at least 30% of workers reported exposure, an optimal threshold as determined in previous studies (21). Those labeled "night shift workers" were a member of those occupations. Those without this were assumed to be day workers.

Definition of Variables

Details of infertility diagnosis and fertility treatment were obtained from infertility clinic records (**Figure 1**). Women were considered to have required fertility treatment if they conceived by any form of clinic-based fertility treatment including ovulation induction, intrauterine insemination, *in vitro* fertilization (IVF), and intracytoplasmic sperm injection (ICSI). Births conceived to couples with male-factor infertility as the primary infertility diagnosis ($n = 1,437$) were excluded from all analyses to ensure that these women were not incorrectly classified (with their independent requirement for fertility treatment frequently unclear).

Among women who required fertility treatment to conceive, infertility diagnosis was categorized as: ovulatory dysfunction (including polycystic ovary syndrome), tubal blockage/problem, endometriosis (usually after visual inspection of the pelvic cavity), menstrual irregularity, and unexplained female-factor infertility (22). Menstrual irregularity was derived from self-reported usual cycle length at the beginning of treatment cycle (<24 days or >32 days, or "irregular" in place of length). Apart from unexplained female-factor infertility, women could be assigned more than one diagnosis category.

Demographic, lifestyle, and health characteristics for all primiparous women were obtained from the perinatal registry. Women's age at delivery (5-years age groups) enabled comparison with other women who did not access treatment (for whom age at conception is not a data item). Other covariates considered were ethnicity (Caucasian vs. non-Caucasian) and socio-economic status based on the level of disadvantage of a woman's area of residence (derived from the Socio-Economic Indices for Areas developed by the Australian government) (23). A small number of women for whom postcode, and therefore, socioeconomic quartile was missing ($n = 362$, 0.3%) were excluded from analyses involving this variable. Pre-pregnancy medical conditions considered were diabetes, hypertension and asthma. Smoking status was routinely recorded on the perinatal record from 1998. Body mass index (BMI) was not recorded in the perinatal dataset but was available for around three quarters of fertility treatment patients.

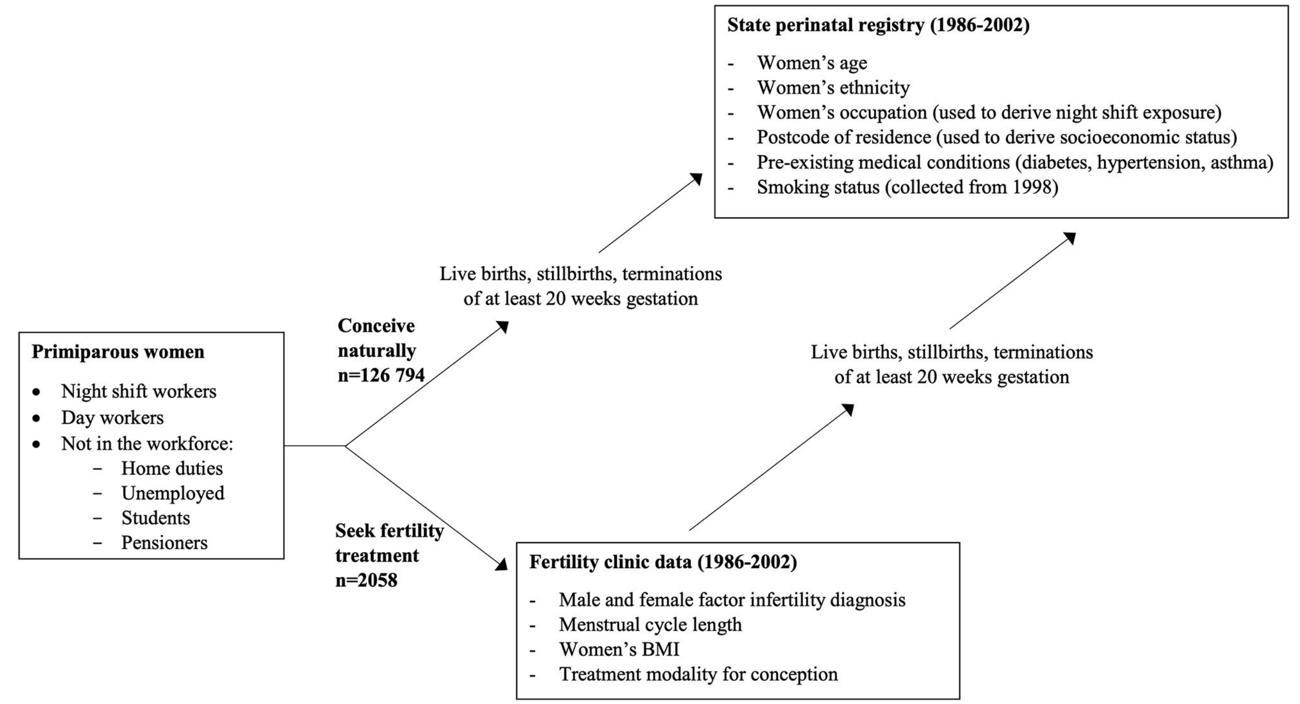

FIGURE 1 | Sources of study data and key variables.

Statistical Analysis

The study population was restricted to primiparous women in order to increase the likelihood that participants were employed in their designated usual occupation around the time of conception and to reduce potential bias associated with the 'infertile worker' effect (24, 25). The infertile worker effect is observed in occupational studies when women who begin family formation earlier and/or conceive quickly leave the workforce, artificially creating the appearance that women who remain, and are therefore available for study, are more likely to be childless. This is an important consideration as half of Australian women (53%) reduce participation in the workforce after giving birth. While most return to work within 2 years, this is usually (84%) part-time, which would affect night shift work exposure (26).

The proportions of women in occupational subgroups, classified by potential night shift exposure, were examined. The proportions conceiving with fertility treatment were calculated for these subgroups and also for those not in the paid workforce (home duties, students, unemployed, pensioners). Categorical variables were summarized using frequencies and percentages, and continuous variables using means and standard deviations. Demographic, lifestyle, and health characteristics were compared between those who did and did not work night shift, and between those who did and did not use fertility treatment, using t-tests for continuous variables, Fisher's exact tests for binary variables, and chi-squared tests for categorical variables.

Relationships between shift work and fertility treatment were assessed using multivariate logistic regression. Characteristics which were related to shift work or fertility treatment in bivariate analyses were included in multivariate analyses. Effect modification by age was assessed with an interaction term. Age at delivery was dichotomized as $\leq$35 or $>$35 years for the purposes of the interaction analysis, consistent with the inflection point for the age at which decline in female fertility is observed (27, 28). Two reference groups were used. First, night shift working women were compared with all other women not exposed to shift work, including those not in the paid workforce. Second, the comparison group was restricted to day workers, that is, women in paid employment who were not classified as potentially exposed to night shift.

A high proportion of female shift workers in Australia are employed as nurses (29), which may introduce bias due to nurses' familiarity with health and the health care system possibly influencing their engagement with treatment for infertility. Therefore, a sensitivity analysis was performed in which women employed as nurses were excluded. Smoking was a potential confounding variable, but as smoking was recorded for only part of the study period, this could only be investigated in a sensitivity analysis using a restricted dataset containing this variable, i.e., from 1998 onwards.

For women whose first birth was conceived with fertility treatment, infertility diagnoses were tabulated according to night shift exposure. Associations were investigated in detail using logistic regression and consideration of potential confounding factors as above. Sensitivity analyses for smoking were undertaken as previously and additional sensitivity analyses for BMI were performed.

All hypothesis tests were two-sided and $p < 0.05$ were considered statistically significant. Data analysis was performed using Stata v.14. (StataCorp, College Station, Texas, USA).

Ethical Approval

The study was approved by the ethics committees of the South Australian Department of Health, the University of Adelaide, and Flinders University. Individual patient consent was not required by the ethics committees.

RESULTS

Of the 128,852 primiparous women who gave birth during the study period, 11,000 (8.5%) were employed in occupations that were likely to have involved night shift (**Table 1**). The majority of potential night shift workers (72.7%) were registered or enrolled nurses (i.e., degree or diploma qualification). The largest occupational groups among presumed day workers were clerks and sales assistants, followed by teachers. One in five women were unemployed or engaged in home duties.

Overall, 1.6% of first births were conceived with fertility treatment (**Table 1**). For night shift workers the proportion was 2.2%. Use of fertility treatment for conception was least common among those not in paid employment: these women accounted for only 14.5% of births conceived with fertility treatment, compared with 25.9% of naturally conceived births.

As expected, maternal age, ethnicity, socioeconomic status and smoking were associated with conception using fertility treatment. Night shift workers tended to be older, Caucasian, and to live in the most economically advantaged areas compared to day workers (**Table 2**). Although smoking was less common among night shift workers overall, smoking prevalence for occupations involving night shift work was highly variable: for example, 4.9% for registered nurses, 12.2% for enrolled nurses, and 26.7% for guards and security officers. Socioeconomic status also varied across night shift working occupations; the proportion of women in the lowest socioeconomic quartile was 13.7% for registered nurses, 17.4% for enrolled nurses and 24.0% for guards and security officers. There was little difference in the overall prevalence of pre-pregnancy medical conditions among

TABLE 1 | Births to primiparous women 1986–2002 by employment status, occupation and mode of conception.

Employment status	All		Proportion of occupation subcategory	Conceived with fertility treatment[c]	
	N	%	%	*N*	%
All women	128,852	100.0	-	2,058	1.6
Night shift occupations	11,000	8.5	100.0	243	2.2
Registered nurses	6,405	5.0	58.2	157	2.5
Other personal service workers (e.g., croupier)	1,818	1.4	16.5	32	1.8
Enrolled nurses	1,596	1.2	14.5	31	1.9
Police	383	0.3	3.5	11	2.9
Radiographers	209	0.2	1.9	5	2.4
Food processing machine operators	148	0.1	1.3	1	0.7
Actors and related professionals	103	0.1	0.9	0	0.0
Other shift working occupations[a]	84	0.1	0.8	2	2.4
Guards & security officers	75	0.1	0.7	2	2.7
Photographic products machine operators	65	0.1	0.6	2	3.1
Securities & finance dealers	62	0.05	0.6	0	0.0
Metal fitters & machinists	52	0.04	0.5	0	0.0
Day work occupations	84,991	66.0	100.0	1,514	1.8
Other clerks	13,071	10.1	15.4	248	1.9
Sales assistants	10,318	8.0	12.1	109	1.1
Teachers[b]	4,573	3.5	5.4	126	2.8
All other day working occupations	57,029	42.8	67.1	1,031	1.8
Not in paid employment	30,147	25.5	100.0	301	0.9
Home duties	14,419	11.2	47.8	240	1.7
Unemployed	11,835	9.2	39.3	32	0.3
Students	3,416	2.7	11.3	14	0.4
Pensioners	477	0.4	1.5	3	0.6
Unknown occupation	2,714	2.1	100.0	12	0.4

[a] *Data combined for shift working occupations where n < 30 (air transport operating support workers, prison officers, production recording clerks, other stationary plant operators, fabric production machine operators).*
[b] *Includes pre-primary, primary, secondary and extra-systematic teachers, but not tertiary teachers.*
[c] *Couples who accessed fertility treatment for any diagnosis other than male factor infertility only.*

TABLE 2 | Demographic, health and lifestyle characteristics of primiparous women giving birth 1986–2002.

Characteristic	Night shift workers (N = 11,000)		Day workers (N = 84,991)		Night shift vs. day workers	Not in paid employment (N = 32,861)		Mode of conception: Fertility treatment conceptions (N = 2,058)		Mode of conception: Natural conceptions (N = 126,794)		Treatment vs. Natural
	N	%	N	%	P-value	N	%	N	%	N	%	P-value
AGE (YEARS)												
<30	7,139	64.9	60,185	70.8	<0.001	28,717	87.4	579	28.1	95,462	75.3	<0.001
30–34	2,951	26.8	19,057	22.4		3,059	9.3	909	44.2	24,158	19.1	
35–39	797	7.3	5,027	5.9		913	2.8	474	23.0	6,263	4.9	
≥ 40	113	1.0	720	0.8		169	0.5	96	4.7	906	0.7	
ETHNICITY												
Caucasian	10,716	97.4	81,581	96.0	<0.001	28,369	86.3	1,978	96.1	118,688	93.6	<0.001
Non-Caucasian	284	2.6	3,410	4.0		4,492	13.7	80	3.9	8,106	6.4	
SOCIOECONOMIC STATUS												
Q1 (lowest quartile)	1,708	15.5	17,114	20.1	<0.001	11,069	33.7	350	17.0	29,541	23.3	<0.001
Q2	2,386	21.7	21,010	24.7		9,112	27.7	428	20.8	32,080	25.3	
Q3	3,012	27.4	21,165	24.9		7,941	24.2	493	24.0	31,625	24.9	
Q4 (highest quartile)	3,851	35.0	25,497	30.0		4,625	14.1	784	38.1	33,189	26.2	
Missing	43	0.4	205	0.2		114	0.3	3	0.2	359	0.3	
SMOKING[a]												
Non-smoker	3,561	79.8	28,906	76.0	<0.001	8,431	56.3	1,512	82.3	39,386	70.8	<0.001
Smoker	877	19.6	8,855	23.3		6,158	41.1	324	17.6	15,556	28.0	
Unknown	26	0.6	283	0.7		378	2.5	1	0.1	686	1.2	
PRE-EXISTING MEDICAL CONDITIONS												
Hypertension	140	1.3	925	1.1	0.08	327	1.0	28	1.4	1,364	1.1	0.2
Diabetes	27	0.3	210	0.2	0.97	103	0.3	6	0.3	334	0.3	0.8
Asthma	541	4.9	3,881	4.6	0.1	2,134	6.5	82	4.0	6,474	5.1	0.02

[a] *Routine reporting of maternal smoking on the perinatal record form did not begin until 1998. Therefore, smoking data are unavailable for 71,377 pregnancies occurring before this date.*

women in paid employment when stratified by exposure to night shift work.

There was a significant interaction between age ($\leq$ 35, $>$35 years) and night shift work (Adjusted β = 0.379, SE = 0.158, p = 0.02) in relation to requirement for fertility treatment. As shown in **Table 3**, among younger women, night shift workers were more likely to require treatment compared to all other women (Adjusted OR = 1.40, 95% CI 1.19–1.64). When the comparison group comprised day workers, results were somewhat attenuated but both the interaction term and the association between night shift work and fertility treatment remained statistically significant. No association was observed among older women. Associations did not change appreciably upon adjustment for ethnicity and socioeconomic status.

In sensitivity analyses women employed as nurses were excluded. This reduced the sample size available but results indicated a similar pattern of associations, with women's age remaining an important modifier of the effect. For example, when night shift workers were compared with all other women, the adjusted result for those $\leq$35 years was OR = 1.34, 95% CI 1.00–1.80; when the comparison group was day workers, the adjusted result was OR = 1.22, 95% CI 0.90–1.64.

In the 4-year period in which information on smoking was available, smokers were 60% less likely to have conceived using fertility treatment (consistent with findings for socioeconomic status). Inclusion of smoking in the fully adjusted model did not alter the overall association between night shift work and use of fertility treatment for conception, regardless of the comparison group. For example, when night shift workers were compared with all other women, the adjusted result for those $\leq$35 years was OR = 1.44, 95% CI 1.08–1.93; when the comparison group was day workers, the adjusted result was OR = 1.32, 95% CI 0.98–1.77.

Table 4 shows the prevalence of infertility diagnoses separately for night shift workers, all other women and day workers. Endometriosis and menstrual irregularity were more common among night shift workers compared to the other two groups (**Table 4**). Conversely, unexplained infertility was less likely among night shift workers, although these results did not reach statistical significance. There was little difference in the prevalence of ovulatory dysfunction or tubal blockage/problem among the groups.

In sensitivity analyses, smoking was assessed as a potential confounder of the associations between night shift work and infertility diagnoses. Interrogation of the restricted dataset

TABLE 3 | Use of fertility treatment to conceive a first birth among women who work night shift compared to all other women and day workers.

		Use of fertility treatment			Night shift workers vs all other women		Night shift workers vs day workers	
		Night shift workers	All other women	Day workers	Unadjusted OR [95%CI]	Adjusted[a] OR [95%CI]	Unadjusted OR [95%CI]	Adjusted[a] OR [95%CI]
Women aged ≤ 35 years	*n*	177	1,311	1,065	1.49 [1.28–1.75]	1.40 [1.19–1.64]	1.31 [1.12–1.54]	1.27 [1.08–1.50]
	Total	10,909	111,018	79,242				
	%	1.6	1.2	1.3				
Women aged > 35 years	*n*	66	504	449	0.98 [0.75-1.28]	0.96 [0.74-1.25]	0.92 [0.71–1.21]	0.92 [0.71 – 1.21]
	Total	910	6,834	5,749				
	%	7.3	7.4	7.8				

CI, confidence interval; OR, odds ratio.
[a]Analyses adjusted for ethnicity and socio-economic indexes for areas.

TABLE 4 | Associations between female infertility categories and night shift work among women who required fertility treatment to conceive a first birth.

Infertility category	Prevalence of infertility diagnoses n (%): Night shift workers (*n* = 243)	All other women (*n* = 1,815)	Non-shift employed workers (*n* = 1,514)	Night shift workers vs all other women: Unadjusted OR [95%CI]	Adjusted[a] OR [95%CI]	Night shift workers vs day workers: Unadjusted OR [95%CI]	Adjusted[a] OR [95%CI]
Ovulatory dysfunction	48 (19.8)	379 (20.9)	318 (21.0)	0.93 [0.67–1.30]	0.93 [0.66–1.31]	0.93 [0.66–1.30]	0.90 [0.64–1.27]
Endometriosis	76 (31.3)	451 (24.8)	390 (25.8)	1.37 [1.03–1.84]	1.39 [1.04–1.87]	1.31 [0.98–1.76]	1.34 [1.00–1.80]
Tubal blockage/problem	77 (31.7)	648 (35.7)	520 (34.3)	0.84 [0.63–1.11]	0.82 [0.62–1.10]	0.89 [0.66–1.19]	0.88 [0.65–1.18]
Menstrual irregularity	76 (31.3)	451 (24.8)	366 (24.2)	1.38 [1.03–1.84]	1.38 [1.03–1.85]	1.42 [1.06–1.91]	1.42 [1.05–1.91]
Unexplained infertility	31 (12.8)	307 (16.9)	269 (17.8)	0.72 [0.48–1.07]	0.73 [0.49–1.08]	0.68 [0.45–1.01]	0.69 [0.46–1.03]

CI, confidence interval; OR, odds ratio.
[a]Analyses adjusted for ethnicity and socio-economic indexes for areas.

showed that smoking would not influence associations between night shift work and either endometriosis or menstrual irregularity, since it was not associated with these diagnoses (hence effect estimates did not change when smoking was including in a multivariate analysis). Body mass index was available for 1,774 women who underwent fertility treatment. The distributions of BMI were similar for all groups with BMI mean[sd] kg/m^2 for night shift workers 24.9 [5.2] vs. 24.4 [4.9] for day workers ($p = 0.24$) and 24.6 [5.0] for all other women ($p = 0.46$).

DISCUSSION

We found the association between potential night shift work and use of fertility treatment to conceive a first birth was significantly modified by women's age. Potential night shift work increased the likelihood of fertility treatment in young women up to and including 35 years by an estimated 27–40%, depending on the reference group, but no association was observed among women over 35 years, when compared to day workers. Night shift workers who received fertility treatment were 30–40% more likely to have an infertility diagnosis of endometriosis or menstrual irregularity, and 30% less likely to experience unexplained infertility, compared to other women requiring treatment to achieve a first birth.

To our knowledge, this is the first study to investigate night shift work and use of fertility treatment. Our results are consistent with a population based Danish study which investigated age-standardized differences in female fertility treatment rates across industries, finding that hospital workers—among whom night shift is common—were significantly more likely to undergo fertility treatment than other economically active women (30). Inherent bias may exist among healthcare workers seeking fertility treatment compared to other occupations because of health care workers' increased awareness of the availability, and perhaps perception of need for fertility treatment. While there is some suggestion in the literature that this is the case, the strongest factor predicting fertility awareness is education level (31, 32). Further, sensitivity analysis in the present study showed that the findings also applied to women who worked night shift but were not nurses.

Other studies have investigated infertility (defined in terms of time to conception) among shift workers. In a 2014 meta-analysis of five cohorts, female shift workers had a significantly higher rate of infertility compared to non-shift workers (OR = 1.80, 95% CI 1.01–3.20) (10). Conversely, a later study of 1,739 women in the Nurses' Health Study 3 Cohort found no associations between different shift work patterns and time to conception (33). Similarly, a recent preconception cohort study of 6,873 women found no association between shift work patterns and fecundability (34).

Our results regarding the infertility diagnoses and reproductive conditions among night shift workers are consistent with previous literature on shift work, menstrual irregularity and prolonged time to conception (7, 10), and a smaller literature on shift work and endometriosis (8, 9). In addition, an association between shift work and menstrual irregularity has been demonstrated in studies of different design and among different samples. This includes questionnaire-based studies, where data on menstrual function was collected independently of the clinical infertility treatment setting (7), and studies where nurses did not form the majority of the sample (35).

The more frequent diagnoses of menstrual irregularity and endometriosis among night shift workers requiring fertility treatment are consistent with biological mechanisms associated with night and rotating shift work. Different hormone systems follow different secretory patterns and adapt at different rates to circadian disruption, so night and rotating shift work is likely to produce at least some asynchrony in these systems (36, 37). Circadian activity is coordinated by the suprachiasmatic nucleus in the hypothalamus, which relays information from environmental stimuli to other parts of the brain and peripheral organs (36, 38). Animal studies suggest that optimal functioning of the suprachiasmatic nucleus is required to produce the luteinizing hormone (LH) surge and ensuing ovulation and that melatonin interacts with gonadotropins, including augmentation of the LH surge (36, 39). In this circumstance, perturbation of the LH surge may disrupt the cyclicity of ovulation in women who otherwise do not have anovulatory infertility or poor ovarian reserve. In a prospective study of couples attending a fertility center, women who worked evening/night/rotating shifts had significantly lower oocyte yield following controlled ovarian stimulation compared to day workers, but no difference in measures of ovarian reserve, such as antral follicle count and follicle stimulating hormone (40).

Circadian misalignment and impaired sleep are also associated with neuroendocrine stress (increased cortisol and catecholamine activity), oxidative stress, altered immune function and low-grade system inflammation (41). Impaired immune function and inflammatory responses in night shift workers may contribute to increased susceptibility to endometriosis, as impaired immune surveillance and reactive oxygen species have been implicated in the inflammatory and pathophysiological processes of the disease (42–44).

Individuals have been shown to vary in their ability to tolerate night shift work. Those with poor tolerance experience symptoms such as gastrointestinal disturbance, sleep disturbance, fatigue, and changes in mood (irritability, low affect) and behavior (45, 46). Thus, self-selection into or out of shift schedules is probable (47). It is possible night shift workers who required fertility treatment for a first birth had relatively poor tolerance for shift work, but limited choice about the matter, for example, as occurs in more junior nursing roles. In a systematic review of individual differences in tolerance to shift work (48), evidence regarding age and tolerance of shift work was mixed, but few studies were conducted among female workers and even fewer considered women aged under 30 years.

The elevated use of fertility treatment among night shift workers was magnified when the comparison group comprised all primiparous women, including those not in paid employment. The group of women who reported being engaged in home duties, in particular, was larger than expected for primiparous women. The great majority of these women had their first birth at less than age 30 years and were relatively disadvantaged, suggesting that any paid work they had prior to pregnancy may have been low skilled, lacked paid maternity leave, and was not seen as a career. Hence a degree of non-reporting of former occupation is likely among such women (15). It is difficult to gauge whether misclassification bias could arise from this source, but some reassurance is provided by the fact that assisted conception occurred in 1.7% of women reporting home duties, similar to the proportion for women in paid employment who did not work night shift (1.8%).

Strengths of this study are the large, population-based cohort of over 128,000 primiparous women, and the detailed health information available for women undergoing fertility treatment. Restriction of the analysis to primiparous women substantially addresses any bias due to the infertile worker effect, whereby childless women are more likely to remain in the workforce (24). The JEM used was developed in a representative population of women of the same nationality and contemporary to the study population. In a validation study, the JEM performed almost as well as job specific questionnaires in terms of reproducing an established association (18). JEMs are a well-accepted and commonly-used method to extrapolate exposure from occupational data where direct measurements cannot be made (49, 50). A further strength of a JEM is that it is applied consistently to all study participants, attenuating observation bias or at least rendering it non-differential.

The use of JEMs to classify exposure has limitations. JEMs classify exposure at the occupation-level rather than the individual-level. No information was available on the actual night shift exposure of individual women. There is therefore likely to be exposure misclassification. However, as misclassification occurs independently of outcome status (i.e., non-differentially), this would tend to move estimates toward the null.

It is also important to note that women who access fertility treatment may not be representative of all infertile or subfertile women, particularly in terms of socioeconomic status. Residual confounding may also be present, as due to the nature of the registry data, we are unable to consider other potential confounders such as diet, education level and working hours. A further limitation of this study is that we do not have information on fertility treatment for treated women who did not conceive or whose gestation did not reach 20 weeks (51), and we do not know if our findings are affected by survivorship bias. We also do not have information on menstrual irregularity or endometriosis among women who conceived naturally. Lastly, given the timeframe of the data, there may have been changes to working conditions and the accessibility of fertility treatment over time that may alter the associations observed in this study. Alternatively, the advantage of an older data set is that the average age of first birth was younger (and more women attempted parenthood at a younger age) and there was more reluctance to undergo treatment.

In conclusion, this study adds to literature implicating night shift work in reproductive health problems (4, 7, 10). Adverse effects appeared in women <35 years only, who may represent a vulnerable subgroup with poor tolerance of the sequelae of night shift work, and this deserves further research. Providing these women with a degree of control and choice about shift schedule may be the best way to enable them to maintain income and career and health, while accommodating shift work (52). Other strategies to mitigate circadian disruption exist, for example tailored sleep plans (53); these should be promoted and further practical avenues explored.

DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: The authors do not have permission to share the data as they were provided specifically for the scope of research as approved by the ethics committees. Requests to access these datasets should be directed to https://www.santdatalink.org.au/.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by South Australian Department of Health Human Research Ethics Committee, University of Adelaide Human Research Ethics Committee and Flinders University Human Research Ethics Committee. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

RF participated in study design, planned and conducted the statistical analysis, interpreted the results, and drafted the manuscript. VM, JM, MW, and MD participated in study design, interpretation of results, critically reviewed, and contributed to the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Association of Night Shift Work With Chronic Spontaneous Urticaria and Effect Modification by Circadian Dysfunction Among Workers

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Purpose: Night shift work is common in the current working environment and is a risk factor for many diseases. The study aimed to explore the relationship between night shift work with chronic spontaneous urticaria (CSU), and the modification effect of circadian dysfunction on it.

Methods: A cross-sectional survey was conducted among Chinese workers. Exposure was measured by night work history and duration. Circadian dysfunction was characterized by excessive daytime sleepiness (EDS). The diagnosis of CSU was made by dermatologists who were investigating on the spot. The effect size was expressed as odds ratios (ORs).

Results: A total of 8,057 participants were recruited, and 7,411 (92%) with complete information were included in the final analyses. The prevalence rates of CSU for workers without night shift and those with night shift history were 0.73 and 1.28%, respectively. Compared with workers who never worked night shifts, the risk of CSU increased with the length of night shift work: OR = 1.55 (95% confidence interval [CI]: 0.78–3.06) for duration <5 years and OR = 1.91 (95% CI: 1.12–3.26) for duration ≥5 years. EDS s EDS has been shown to modify this combination. Among workers without EDS, there was no association between night shift and CSU (OR = 0.94; 95% CI: 0.49–1.79). Whereas, in participants with EDS, the correlation was significant (OR = 3.58; 95% CI: 1.14–11.20). However, the effect modification by sleep disturbance was not observed.

Conclusions: Night shift work is a risk factor for CSU, and there is a dose-response relationship between night shift work hours and the risk of CSU. This connection may be modified by circadian dysfunction.

Keywords: circadian dysfunction, chronic spontaneous urticaria, effect modification, night shift work, excessive daytime sleepiness

INTRODUCTION

Chronic spontaneous urticaria (CSU) is a common allergic skin disorder characterized by wheals or angioedema along with intense itch (1). Although it is usually self-limited and benign, it can cause severe discomfort, lasting from months to years, and rarely represents a serious systemic disease or life-threatening allergic reaction (2). It affects 0.5–1% (1) of the general population, and 0.1–0.3% (3) of children. The burden of urticaria ranked the 5th among all skin conditions according to the 2016 Global Burden of Disease Study. It was estimated that urticaria contributed to 55.49 per 100,000 years loss of healthy life globally (4). The pathophysiology of CSU has not been fully elucidated, but it is clear that the degranulation of mast cells and activation of basophil play the core role in the etiology of urticaria. Previous studies suggest that CSU occurs mostly at night or in the evening with no identifiable triggers, and the severity of cutaneous signs and symptoms is also exacerbated between midnight and morning and shows a significant 24-h rhythm (5–7).

Night shift work is defined as work performed outside of typical daytime work hours. Night shift work is common in the industry to ensure the need for 24-h operation. In industrialized countries, about 20% of the workforce is engaged in shift work (8). Night shift work is a well-established social and biological stress. Previous epidemiological studies suggest that night shift work is a risk factor for obesity (9), diabetes (10, 11), cardiovascular disease (12), breast cancer (13), and mental disorders (14, 15). Night shift work can lead to daily sleep-wake and fasting cycles, and the imbalance of the endogenous circadian timing system, which wildly affects the physiology and behavior, and harmfully influences healthy immune and allergy system.

However, no epidemiologic study has examined the association of night shift work and CSU. In the current study, we conducted a cross-sectional investigation in two groups of workers who frequently worked night shifts. The aim was to investigate the association of night shift work with CSU and to examine the effect modification by circadian dysfunction.

MATERIALS AND METHODS

Study Population

Cross-sectional data from two independent studies were analyzed. The study population comprised of automobile manufacture workers in Shiyan, Hubei who were participants in the Dongfeng-Tongji Cohort Study (16), and non-ferrous metal smelting workers in Hengyang, Hunan who were participants in the Hunan Chronic Disease Cohort Study (17). The Dongfeng-Tongji Cohort was established in 2008 and initially recruited retired workers. The cohort began to recruit in-service workers since 2016. In the current analysis, we used the baseline data collected from the in-service workers. The Hunan Chronic Disease Cohort Health Study was established in 2015 and recruited residents and workers in Hunan rural regions. In the current analysis, we only included participants who were workers to ensure comparability and homogeneity.

Exposure Assessment

History and duration (years) of rotating night shift work were inquired in the face-to-face interview. Night shift work was defined as "at least three nights per month in addition to working days or evenings." If a history of the night shift was reported, the cumulative night shift work was then inquired by the investigator. The duration of night shift work was categorized into three groups: never, <5 years, and ≥ 5 years.

Outcome Assessment

Diagnosis of skin diseases and inquiry of disease history were performed by certificated dermatologists during the field survey. Clinical manifestation, disease history, and family history of participants were asked, and physical examinations were conducted to diagnose all skin diseases. CSU was diagnosed according to persistent or recurrent typical clinical manifestations of urticaria, with unknown triggers, for more than 6 weeks during the past year.

Assessment of Covariates

Height and weight were measured by research nurses according to standardized methods. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). Marital status, socioeconomic status (annual family income and educational level), smoking habits, and passive smoke exposure, and alcohol drinking were inquired by investigators. Anxiety and depression were assessed by the 2-item Generalized Anxiety Disorder (GAD-2) (18) and 2-item Patient Health Questionnaire (PHQ-2) (19), respectively. GAD-2 $\geq$3 and PHQ-2 $\geq$3 were the cut-offs for anxiety and depression, respectively. Sleep quality and daytime sleepiness were assessed by the Pittsburgh Sleep Quality Index (PSQI) (20) and Epworth Sleepiness Scale (ESS) (21), respectively. PSQI $>$5 and ESS $>$10 were the cut-offs for sleep disturbance and excessive daytime sleepiness (EDS), respectively. History of urticaria was not adjusted since it may cause collider bias in the hypothesized pathway: history of night shift (X) $\rightarrow$ history of CSU (C_1) $\leftarrow$ genetic susceptibility (C_2) $\rightarrow$ current CSU (Y).

Statistical Analysis

Continuous data were presented as means and standard deviations, and between-group difference was tested using analysis of variance (ANOVA). Categorical data were presented as number (%), and the between-group difference was tested using the chi-square test. A two-level logistic regression model (participant as level-1 unit and study site as a level-2 unit) was used to estimate the association of night shift work with CSU, adjusting for level-1 covariates (age, gender, ethnicity, annual family income, cigarette smoking, alcohol drinking, anxiety, depression) and the random effect (intercept) of study sites. The effect size was presented as odds ratio (OR) and 95% confidence interval (CI). The center effect was examined using the intra-cluster correlation coefficient (ICC). Cubic spline regression was used to examine the potential non-linear association of the duration of night shift work (years) with the prevalence of CSU.

Previous studies have identified associations between circadian and health outcomes (22), and effect modification of associations between night shift work and diseases by circadian

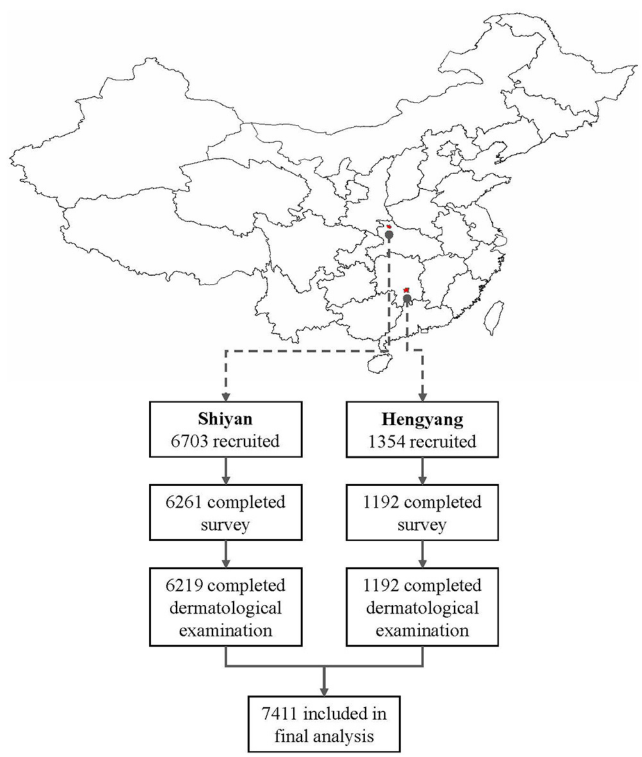

FIGURE 1 | Study sites and flowchart of inclusion of study participants.

and chronotype (11, 23, 24). Therefore, we assessed possible effect modifications of the association between night shift work and CSU by EDS, an indicator of circadian dysfunction. To test for effect modification, we included a multiplicative interaction term in regression models. Stratification analysis by EDS was then conducted if a significant interaction term was identified. In addition, subgroup analysis was conducted by sleep disturbance as determined by PSQI. $P < 0.05$ was considered statistically significant for all tests. Statistical analysis was performed in SAS 9.4 (SAS Institute Inc., Cary, USA).

RESULTS

A total of 8,057 participants were recruited, and 7,411 (92%) with complete information were included in the final analyses (**Figure 1**). The mean age was 42.5 ± 8.4 years and 74.9% were male. Comparing the characteristics across the history and duration of night shift work, night shifts were associated with slightly older age, male gender, the Han ethnicity, lower socioeconomic stratum (income and education), smoking behavior, more impaired sleep quality, and more symptoms of depression (**Table 1**).

Prevalence of CSU

The overall prevalence of CSU was 1.07% (79/7,411). The prevalence rates in the two study sites were 1.05% (Shiyan) and 1.17% (Hengyang), respectively, and the center effect of clinical diagnosis was not identified according to the two-level null model (ICC = 0%). In workers who reported no history of night shifts, the prevalence of CSU was 0.73%, while in those who reported a history of night shifts, the prevalence rate was 1.28% ($P = 0.025$). Among subjects who ever worked night shifts, the prevalence rates of CSU were 1.14 and 1.33% in subjects who reported duration <5 years and ≥5 years, respectively (**Supplementary Table 1**).

Association of Night Shift Work With CSU

Night shift work was significantly associated with a higher risk of CSU in a dose-response manner when adjustments were made for age and gender (**Figure 2A**). Compared with workers who never worked night shifts, the risk increased with the duration of night shift work: OR = 1.55 (95% CI: 0.78–3.06) for duration <5 years and OR = 1.91 (95% CI: 1.12–3.26) for duration ≥5 years. However, when more covariates were included in the models, the result was not statistically significant, although the effect size still indicated a higher risk of CSU (OR = 1.41; 95% CI: 0.82–2.44; $P = 0.216$).

The possible non-linear association of the duration of night shift work as a continuous variable with CSU was examined with the cubic spline. In general, the duration of the night shift was positively associated with CSU, but variations could be observed (**Figure 3A**).

Effect Modification

A multiplicative interaction term between EDS and night shift work was then included in regression models. After adjustments, a significant interaction term was identified ($\beta = 1.33$, $P = 0.032$), indicating a modification effect. Stratification analysis by EDS was then conducted (**Supplementary Table 1**). In participants without EDS, the effect size of night shift work was close to null (OR = 0.94; 95% CI: 0.49–1.79; $P = 0.841$) (**Figure 2B**). In contrast, in workers with EDS, night shift work was significantly associated with CSU (OR = 3.58; 95% CI: 1.14–11.20; $P = 0.029$) after full adjustments with a greater effect size (**Figure 2C**).

Similarly, when treating the duration of night shift as a continuous variable, the association of night shift with CSU was an irregular curve in subjects without EDS; while in those with EDS, night shift was almost linearly associated with CSU (**Figure 3B**). We also examined the effect of modification by sleep disturbance. However, the associations of night shift work with CSU were consistent in two subgroups (**Supplementary Figure 1**).

DISCUSSION

This cross-sectional study investigated the association of night shift work with CSU among Chinese workers. Unique effect modification by daytime alertness was identified, leading to differential associations of night shift work with CSU. That is, in workers with specific circadian dysfunction manifested as daytime sleepiness, the night shift was a risk factor for CSU with strong effect size, while in those with normal daytime alertness, the effect of night shift diminished substantially.

TABLE 1 | Characteristics of participant by the history and duration of night shift work.

Characteristics	History and duration of night shift work			
	Never (n = 2,876)	<5 years (n = 1,232)	≥5 years (n = 3,303)	Ever (n = 4,535)
Study site				
Shiyan	2,762 (96.0)	1,081 (87.7)	2,376 (71.9)	3,457 (76.2)
Hengyang	114 (4.0)	151 (12.3)	927 (28.1)	1,078 (23.8)
Age (years)	41.5 ± 9.1	39.5 ± 9.5	44.4 ± 6.6	43.1 ± 7.8
Male	1,976 (68.7)	984 (79.9)	2,593 (78.5)	3,577 (78.9)
Han ethnicity	2,823 (98.2)	1,217 (98.8)	3,264 (98.8)	4,481 (98.8)
Marital status				
Unmarried	345 (12.0)	222 (18.0)	133 (4.0)	355 (7.8)
Married or live together	2,440 (84.9)	960 (77.9)	3,012 (91.2)	3,972 (87.6)
Widowed	15 (0.5)	7 (0.6)	21 (0.6)	28 (0.6)
Divorced	76 (2.6)	43 (3.5)	137 (4.2)	180 (4.0)
Annual family income (CNY)				
<30,000	122 (4.3)	94 (7.6)	477 (14.4)	571 (12.6)
30,000–49,999	532 (18.5)	359 (29.1)	1,222 (37.0)	1,581 (34.8)
50,000–99,999	1,324 (46.0)	570 (46.3)	1,343 (40.7)	1,913 (42.2)
≥100,000	898 (31.2)	209 (17.0)	261 (7.9)	470 (10.4)
Educational level				
Middle school and below	101 (3.5)	79 (6.4)	468 (14.2)	547 (12.1)
High school	778 (27.1)	497 (40.3)	1,900 (57.5)	2,397 (52.8)
College and above	1,997 (69.4)	656 (53.3)	935 (28.3)	1,591 (35.1)
Smoking				
Never	2,000 (69.6)	722 (58.6)	1,656 (50.1)	2,378 (52.4)
Past	145 (5.0)	97 (7.9)	337 (10.2)	434 (9.6)
Current	731 (25.4)	413 (33.5)	1,310 (39.7)	1,723 (38.0)
Passive smoke exposure	1,641 (57.1)	785 (63.7)	2,028 (61.4)	2,813 (62.0)
Alcohol drinking				
Never	1,828 (63.5)	724 (58.8)	1,986 (60.1)	2,710 (59.8)
Past	62 (2.2)	53 (4.3)	138 (4.2)	191 (4.2)
Current	986 (34.3)	455 (36.9)	1,179 (35.7)	1,634 (36.0)
BMI (kg/m^2)	24.0 ± 2.7	24.1 ± 2.9	24.2 ± 2.8	24.1 ± 2.8
Sleep disturbance (PSQI >5)	898 (31.2)	443 (36.0)	1,365 (41.3)	1,808 (39.9)
Daytime sleepiness (ESS >10)	918 (31.9)	426 (34.6)	1,013 (30.7)	1,439 (31.7)
Anxiety (GAD-2 ≥3)	166 (5.8)	77 (6.3)	214 (6.5)	291 (6.4)
Depression (PHQ-2 ≥3)	171 (6.0)	89 (7.2)	285 (8.6)	374 (8.3)

CNY, Chinese yuan; BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; GAD-2, 2-item Generalized Anxiety Disorder; PHQ-2:2-item, Patient Health Questionnaire.

We identified a correlation between night shift work and CSU, and the risk of CSU increased with the duration of night shift work compared to workers who have never worked overnight. Since the early 1960's, many reports have confirmed the importance of circadian rhythm in allergic diseases (25, 26). Allergy-related peripheral clocks (e.g., mast cell clocks) have been considered as significant drivers for rhythmic allergic reactions. Recent studies have shown that abnormal light/dark environments that mimic jet lag can exacerbate viral-induced asthma-like inflammation. When studying the relationship between night work and food allergies, nurses who participated in night shifts had a higher incidence of food allergies than nurses worked as a regular shift schedule (27). Collectively, these studies suggest that mismatched environmental zeitgeber arrivals may exacerbate allergic reactions.

Urticaria is caused by the release of histamine and other inflammatory mediators from mast cells and basophils mediated by immunoglobulin E- and non-immunoglobulin E. (2). CSU is an endogenous disease that is closely related to autoimmunity, especially the immunoglobulin G (IgG) antibody to the alpha subunit of the IgE receptor, which is seen in 35–40% of patients. Basophils and cutaneous mast cells can be activated, leading to a late-phase-like perivascular infiltration about small venules and hive formation (28). Several *in vivo* studies demonstrated that circadian rhythms drive daily rhythms in IgE/mast cell-mediated allergic reactions. It was reported that wild-type mice had a

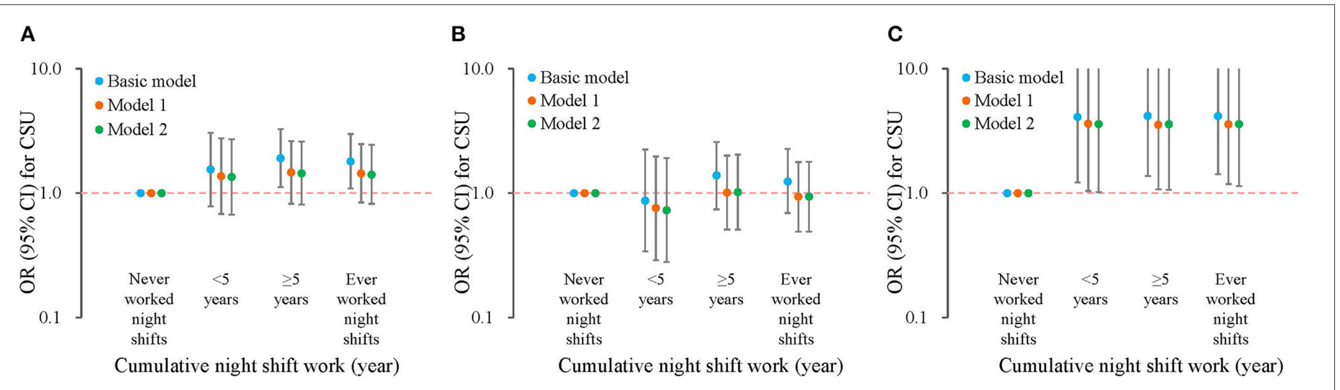

FIGURE 2 | Association of night shift work and chronic spontaneous urticaria, stratified by excessive daytime sleepiness. The basic model was adjusted for age and gender; model 1 was additionally adjusted for ethnicity, marital status, income, educational level; model 2 was additionally adjusted for smoking, passive smoke exposure, alcohol drinking, anxiety, and depression. Logarithmic axis was used for odds ratios. **(A)** All participants; **(B)** participants without EDS; **(C)** participants with EDS. CSU, chronic spontaneous urticaria. EDS, excessive daytime sleepiness; OR, odds ratio; CI, confidence interval.

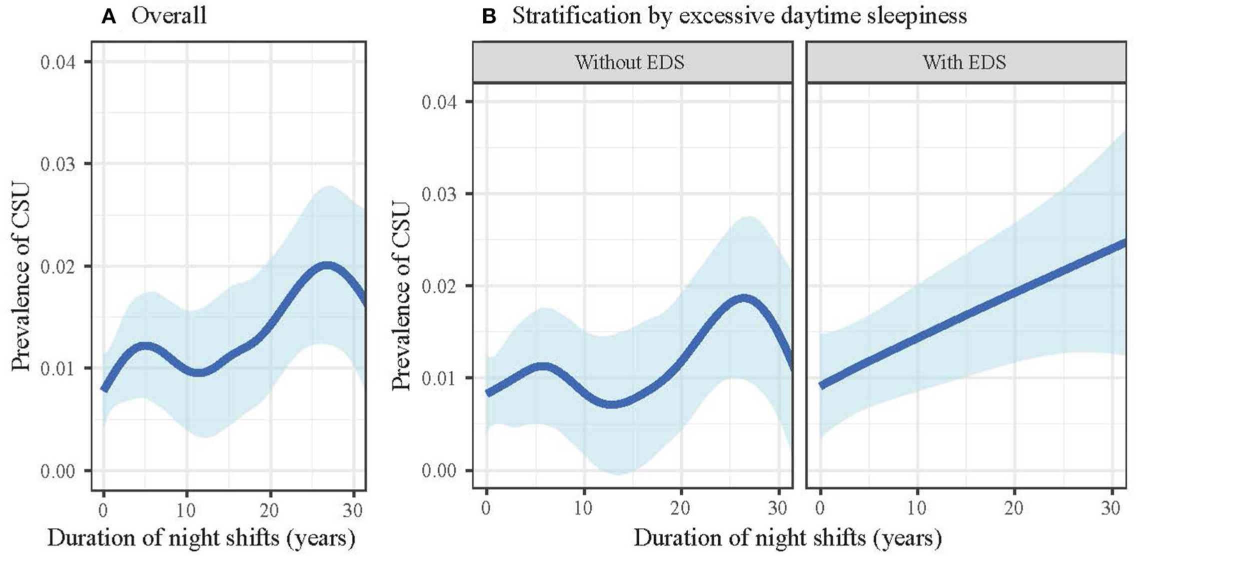

FIGURE 3 | Duration of night shift work and the prevalence of chronic spontaneous urticaria, stratified by excessive daytime sleepiness. The blue curve signifies the estimated prevalence of urticaria, and the light blue band signifies the 95% confidence interval. **(A)** All participants; **(B)** stratification analysis by EDS. CSU, chronic spontaneous urticaria; EDS, excessive daytime sleepiness.

24-h time-dependent change in passive skin allergic reaction and passive systemic allergic reaction of IgE/mast cell-dependent allergic reactions (29). Similarly, this time-dependent change also did not occur in mice undergoing mechanical disruption of the central suprachiasmatic nucleus clock or in mice undergoing adrenalectomy (30, 31). These findings suggest that the circadian clock plays a crucial role in the production of daily rhythms of IgE/mast cell-mediated allergic reactions (32).

Based on the stratification analysis, we found that EDS showed a modification effect on this association. While no study or report that directly support our epidemiological finding, a genome-wide association study identified a total of 42 loci and genes to be associated with EDS (33). Among the genes involving EDS reported by Wang et al., four genes [DOCK1 (34), ERBB4 (35), SLC39A8 (36), and CACNA1C (37)] were reported to be associated with allergic reactions in previous studies. Among them, DOCK1 (34), ERBB4 (35), and SLC39A8 (36) were reported to be related to asthma, and CACNA1C (37) was proved to impact the prognosis of CSU. Despite the lack of direct evidence, we speculate that night shift may result in certain epigenetic changes on the genes that link EDS and allergy. This hypothesis needs further investigation.

Limitations and Strengths

The study was the first to investigate the association of night work with CSU. The study has several strengths. First, we introduced several covariates that might confound the association of night shift with CSU, including income, education, smoking, alcohol, depression, and EDS. Second, the sample size of the study was relatively large, and night shift work was common among workers; this enables us to investigate the association with sufficient power of a statistical test. Third, this was a population-based study, and the Berkson bias was minimized compared to hospital-based studies.

The primary limitation of the study is that no conclusion on the causal relationship can be drawn owing to the cross-sectional design. Second, the study population was workers; this may limit the external validity of the findings and the generalizability to populations. Last but not least, workers might be exposed to complex occupational factors that were not observed in our study. For example, the level of physical activity of workers is higher than that of the general population (38), and they may be exposed to occupational risks including heavy metals, environmental pollutants, and noise at work (39). Nevertheless, the dose and type of occupational exposures are not likely to be altered by the timing of work.

In summary, we identified a link between night shift work and CSU. Circadian dysfunction might modify the association of night work with CSU. Future research may require more delicate assessment on the exposure to night shift work as well as longitudinal observations on its effect on the incident CSU. This study has clinical implication for dermatologists and primary care physicians with respect to the treatment and management of CSU. The study also provides new evidences for mechanism studies.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by this study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving study participants were approved by the Institutional Research Ethics Boards of Xiangya School of Public Health, Central South University (approve# XYGW-2016-10), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology (approve# 2016-IEC-S128), and Hubei University of Medicine (approve# 2016-74-41). Written informed consent was obtained from all participants before the investigation. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

ZH, MH, XC, and MS designed the study. MS and DJ analyzed the data. YX and YH drafted the manuscript. YH, DJ, JS, ZH, HL, JT, MH, and XC interpreted the data and critically revised the manuscript. JS and MH obtained the funding. All authors participated in the field survey, data collection, and gave final approval to the version submitted for publication.

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SUPPLEMENTARY MATERIAL

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Psychosocial Work Stress and Health Risks – A Cross-Sectional Study of Shift Workers From the Hotel and Catering Industry and the Food Industry

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Purpose: Psychosocial work stress, and shift and night work are considered risk indicators for impaired health. Using the effort-reward (ER) model, it was possible to examine which relationships exist for shift workers between clusters (CL) of different levels of psychosocial work stress and overcommitment (OC) and cardiovascular or psychological health indicators, and which predictive value is evident in individual health indicators to explain the clusters.

Methods: The data were collected as part of an occupational health prevention program. The analysis sample consisted of 199 shift workers from alternating shift systems with and without night work (43%) (average age: 40 ± 12 years, men: 47%). Psychosocial work stress was recorded using the ER imbalance (ERI) questionnaire. To determine the clusters, ERI and OC were entered into a cluster analysis. Blood pressure, body mass index, waist-hip ratio, PROCAM score (risk of a heart attack within the next 10 years), sporting activity, and smoking were included as cardiovascular indicators, psychological wellbeing (GHQ-12) and inability to recovery (IR) (FABA) as psychological health indicators. Shift system, sex, and age were entered into the statistical analyses as control variables. Multinomial logistic regression models were used to identify health-related predictors to explain the ER-OC clusters.

Results: Three different ER-OC clusters emerged: low-stress: 36%, normal: 44%, risk: 20%. While normal psychosocial work stress is present in the low-stress and the normal CL, in the risk CL 28% of the shift workers show a health-endangering ERI and 48% show an excessive OC. No significant cluster-specific differences were determined for the cardiovascular health indicators. Rather, the known sex and age effects were confirmed and the shift system had no significant effect. Significantly more shift workers in the risk CL had impaired psychological health (18 vs. 1/6%) and an IR (52 vs. 0/12%) than in the low-stress and normal CL. IR turned out to be the strongest predictor of the explanation for the ER-OC clusters (49%).

Conclusion: IR could be assigned an independent diagnostic value for the assessment of psychosocial work stresses and discussed as a new component of occupational health screening concepts for shift workers. Independently of this, the health indicators signal an urgent need for occupational health prevention and care.

Keywords: shift work, psychosocial work stress, effort-reward imbalance, overcommitment, cardiovascular and psychological health

INTRODUCTION

The effects of psychosocial work-related stress on the health of shift workers have so far been underestimated in preventive occupational health and occupational health care in Germany. Psychosocial work stress is rarely part of occupational health care programs of shift workers, although psychosocial work-related stress has been recognized as a risk factor for impaired health (1–10). In addition, shift and night work themselves can have a negative impact on health (11–20).

In stress theory observations, high work demands (effort) with low material or immaterial rewards are considered to as psychosocial work-related stress or Siegrist et al. (21) hereinafter referred to as *professional gratification crisis* or effort-reward imbalance (ERI). Experiencing such a crisis triggers intense stress reactions in those affected, which have a negative impact on health indicators and unhealthy behavior in the medium and long term, increase the risk of stress-related diseases and are intensified by excessive occupational overcommitment (OC). Individual differences in the interaction between ERI and OC have so far been largely ignored. It is assumed that shift workers who are characterized by high ERI and high OC at the same time (interaction hypothesis) have the highest risk of impaired health and impaired wellbeing (21, 22). The fact that such a stress constellation in shift workers consequently also leads to insufficient recovery has so far been neglected, as has the verification of the interaction hypothesis itself, and data on shift workers are not available.

For shift and night work, different correlations are known regarding cardiovascular (12, 14, 16–20) and psychological health indicators (11, 15), health behavior (14, 23–25) and recreational behavior (20, 26, 27). The health behavior of shift workers compared to day workers is characterized by unfavorable eating habits (14, 28, 29), more smokers (14, 29) and fewer sporting activities (23, 24, 29, 30). In addition, it is known that shift and night workers have restrictions in family and social life (13, 31, 32) and opportunities for recreation (14, 18).

Nevertheless, the percentage of shift work has increased in Germany and many other industrialized countries over the past 20 years (33, 34). In Germany, the percentage of shift workers was around 16% in 2018 (34). According to the Federal Institute for Occupational Safety and Health (35), around 20% of employees in Germany work outside the period from 07:00 to 19:00 h including 8% with staggered working hours (e.g., fixed early or late shifts), 7% in alternating shifts with night or recurring night work and 5% in alternating shifts without night work. Weekend work has also become part of everyday life for more and more employees (33).

Internationally, the definitions of shift work and night work differ widely and are often indeterminate (36). In addition, the existence of the innumerable shift systems with their different positions and lengths of working hours does not allow a uniform assessment. There is a consensus that shift work is a particular form of workload. According to the International Labor Organization, shift work is a "method of work organization that enables workers to work one after the other at the workplace, so that work processes can continue beyond individual shifts and include day and night hours" (37). Night work is defined in Germany by Section 2 and 6 of the Working Hours Act (ArbZG) and generally covers the period from 23:00 to 06:00 h with deviations. It applies to "any work that takes more than 2 h of the night" (38).

During shift work, the organism cannot adapt to the constant change in working hours, so that the shift in the circadian rhythm (sleep-wake cycle) results in restrictions on the duration and quality of sleep and has consequences for health status. Even on early and late shifts, shift workers have to work and sleep at unnatural times of the day. Since recovery deficits increase the risk of health impairments (14, 18), shift work requires balanced recovery after work.

Shift and Night Work and Health Effects

The effects of shift and night work can be reflected in an increased activation of the sympathetic nervous system (14), which results in an increase in blood pressure (16), but also show themselves in other cardiovascular changes (e.g., inflammatory processes, blood clotting disorders) and thus influence the risk of cardiovascular diseases (12, 14). However, meta-analyses have not provided any convincing evidence for a connection between shift work and cardiovascular diseases (18, 39–41). This applies equally to cardiovascular and metabolic risk factors (17, 42). In the review by Proper et al. (42), inconsistent results on the

Abbreviations: BGN, German Government Safety Organization Foods and Restaurants; CL, cluster; ArbZG, Working Hours Act; FI, food industry; HCI, hotel and catering industry; ER, effort-reward; ERI, effort-reward imbalance; OC, overcommitment; IR, inability to recovery; BP, blood pressure; BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; DBP, diastolic blood pressure; SBP, systolic blood pressure; PROCAM, Prospective Cardiovascular Münster; SPSS, Statistical Package for the Social Science; ESH, European Society of Hypertension; ESC, European Society of Cardiology; ERI-Q, Effort-Reward Imbalance Questionnaire; GHQ-12, General Health Questionnaire-12; FABA, Questionnaire for Faulty Attitudes and Behavioral Analysis Relevant to Coping with Work Demands; DEGS1, German Health Interview and Examination Survey for Adults.

connection between shift work and hypertension were reported. While the systematic review by Esquirol et al. (16) and the study by Stieler et al. (20) provide information on the association between shift work and hypertension, the longitudinal study by Gholami Fesharaki et al. (43) shows no correlation in this regard. Liu et al. (19) postulated in their meta-analysis that shift work is positively associated with the risk of becoming overweight and obese. Saulle et al. (44), on the other hand, did not determine such a relationship in their meta-analysis. Torquati et al. (45) postulate in their review that a non-linear association exists between shift work and cardiovascular disease that seems to show only after 5 years of shift work. After the first five years of shift work, the risk of cardiovascular events increased by 7.1% for each subsequent 5-year exposure.

There also seems to be no clear evidence of the effects of shift work on psychological health: the review by Fossum et al. (46) and the cross-sectional studies by Mauss et al. (47) and Radstaak et al. (48) confirmed no connections between shift work and indicators of wellbeing, while the longitudinal study (10-year period) by Driesen et al. (15) indicated a slight effect of shift work on the development of a depressive mood. Vallières et al. (49) assumed on the other hand, that shift workers are more prone to depression than day workers. In contrast, the survey by Bara and Arber (11) found a clear association to psychological impairments for shift workers in England. And according to the meta-analysis by Lee et al. (50), night shift work is clearly associated with an increased risk of depression.

Psychosocial Work Stress and Health Effect

Several studies have been able to show that psychosocial (ERI-related) stress can be a risk factor for cardiovascular disease (2, 6, 7, 9) and psychological impairments (3, 5, 51, 52). Chronic stress at work is increasingly assumed to be the main cause of psychological disorders (53). The risks for this are, however, unevenly distributed in society, since socially disadvantaged population and occupational groups are more often affected by them (54).

Comparable to shift work, no consistent correlations were found between psychosocial work stress or overcommitment and increased blood pressure (hypertension). In the review by Gilbert-Ouimet et al. (4), there was a significant effect of psychosocial work stress on blood pressure in four out of seven studies, but the average increase in blood pressure was only 1 to 4 mmHg. In another five out of six studies, there was a connection between ERI and hypertension, and in two out of four studies overcommitment had a hypertensive effect. In the earlier Canadian longitudinal study by Gilbert-Ouimet et al. (1) no significant correlation between ERI and blood pressure could be found. Overcommitment, on the other hand, was associated with a significant increase in blood pressure in men and woman.

The results of the large European multi-cohort study of the IPD-Work Consortium (individual-participant data meta analysis in working populations consortium) (9) and the review by Gilbert-Ouimet et al. (4) suggest that, especially in men, there is a significant correlation between psychosocial work stress and an increased risk of cardiovascular diseases, which seems to be independent of the classic risk factors like hypertension or obesity. In the case of psychosocial work stress, an up to 1.6-fold higher risk of developing coronary heart disease or stroke was found as opposed to no work stress (10). However, this work stress risk was lower than this risk associated with the classic risk factors (i.e., smoking, high blood pressure, high serum cholesterol, obesity).

According to the meta-analysis by Rugulies et al. (8) (n = 84,963 employees and 2,897 new cases of depressive disorders) a consistent relationship between ERI and impaired psychological health can be assumed for both sexes. Compared to non-professionally stressed employees, an increase in the relative risk of 20 to 80 percent has been observed for ERI sufferers (25). According to Rugulies et al. (3), employees with increased psychosocial work stress are more than twice as likely to develop depressive symptoms in the next 5 years. Niedhammer et al. (5) postulate that 16% of psychological disorders can be traced back to an effort-reward imbalance.

It can be assumed that psychosocial work stress with excessive commitment of those affected also has an unfavorable effect on the psychological recovery processes in the non-working period. Psychological detachment from work during rest period is seen as a central component of individual relaxation (20, 26, 27). It is regarded as a link between working conditions and strain-related outcomes (including symptoms of fatigue and exhaustion) and is discussed as an early indicator of work-related impairments (27, 55). Richter et al. (56, 57) describe the inability to detach from work as an inability to recover. According to Wendsche and Lohmann-Haislah (58), there are differently strong correlations between psychological detachment and health indicators. There are only low correlations with cardiovascular stress indicators (20, 55).

In longitudinal studies, Sonnentag et al. (59) predict exhaustion for employees who have poor psychological detachment. And according to Siltaloppi et al. (60), employees with good recoverability suffered the least from burnout and sleep problems after 1 year. In the Finnish longitudinal study with managers (n = 298, three measurement times) by Feldt et al. (61), five long-term ERI-OC patterns were identified. Employees in the so-called high-risk pattern (high ERI and high OC; 20% of participants) showed poorer recovery compared to those in the low-stress pattern (normal ERI and normal OC; 24% of participants).

Hotel and Catering Industry and Food Industry

The hotel and catering industry (HCI) and the food industry (FI) are sectors in which more than two thirds of employees do shift work - often including night work, weekend or holiday work (62, 63). Both sectors are heterogeneous branches of the economy and comprise a large number of different professions. In addition, low wages, a lack of appreciation and limited career prospects are prevalent in both sectors (64). Also, the HCI sector is characterized by long, irregular working hours which are difficult to plan, lots of overtime and, above all, high time pressure and staff shortages (63), which requires a high degree of flexibility from employees. These working conditions are perceived as exhausting and disadvantageous by more than 70% of employees (64) and often lead to problems with work-life balance (63, 65). While mainly young women (<35 years) work in the HCI sector (66, 67), 70% of the employees in the FI are older than 35 years (68). In one of the few studies on psychosocial work stress in HCI (69), 50% of the 941 hotel room cleaners reported an ERI and 60% reported poor health. In Germany too, stress at work and psychosocial risk factors have been identified in HCI (66).

Aim of Study

In view of the work stress of working life, the question also arises in the HCI and FI as to whether certain psychosocial stress constellations increase the risk of health impairment in their shift workers. Such a study does not yet exist in German-speaking countries.

The aim of this study was therefore to use the stress-theoretical effort-reward (ER) model to clarify which relationships exist for shift workers in the HCI and FI between clusters (CL) of different levels of psychosocial work stress and overcommitment (OC) and cardiovascular or psychological health indicators, and which predictive value is evident in individual health indicators to explain the clusters. It was hypothesized that shift workers with a "risk pattern" (high ERI and OC scores) are expected to have a higher risk of decreased cardiovascular and psychological health.

METHODS

The present study is a cross-sectional study. The data from this examination were collected from 2016 to 2019 as part of an occupational health screening programme. Participation in the study was voluntary (participation rate: 75% of employees approached).

The screening programme was offered to the hotels and businesses. In the run-up to the investigation, notices and flyers were used to draw attention to the study. Immediately before the start of the study, the participants received an information letter regarding data protection, the study process and data evaluation, as well as the conditions for participation in the study. The anonymity of the data was guaranteed by transaction numbers (TANs) and a six-digit personal code.

Three hundred fifty-five employees took part in the study, 333 of which met the data quality requirements. One hundred ninety-nine shift workers, who form the database for this study, were among them. Non-shift day workers were explicitly excluded from the study because the psychosocial work stress of shift workers with and without night shifts was to be investigated in the form of easily interpretable clusters. In this approach, day workers cannot act as a control group; there is no pure cluster with only day workers. They are distributed in the clusters; such heterogeneous clusters do not contribute to explaining the relationship between different psychosocial workloads and health among shift workers.

Survey Instruments

An occupational health survey and a cardiovascular screening programme were used as survey instruments. The survey and examinations were carried out on site in the hotels or businesses of the participants.

Occupational Health Survey

The survey consisted of a shift work questionnaire (70) modified according to Barton et al. (71) and other standardized survey instruments as well as additional questions. Besides to socio-demographic information (e.g., sex, age, school leaving certificate, marital status, etc.), job and shift work-specific details (including job description, weekly working hours, shift system, years of work in shift work). The questionnaire also contained questions on health behavior, psychosocial work stress and overcommitment (21), as well as psychological health defined by psychological wellbeing (72) and the (in)ability to recover (56, 57). The questions about shift work formed the basis for assignment to a shift system.

Health behavior was surveyed through questions about sporting activity and smoking status. In the case of sporting activity, questions were asked about the frequency (not at all, occasionally, regularly) and the amount of time per week. For smoking, it was recorded whether someone was a smoker (YES/NO) and the average number of cigarettes smoked daily.

Psychosocial work stress was collected using the short version of the Effort-Reward Imbalance Questionnaire (ERI-Q: 21). This questionnaire allows standardized measurement of professional gratification crises and the intrinsic component of overcommitment. This version included the main scales effort (3 items, range: 3–15 points) and reward (7 items, range: 7–35 points), as well as the effort-reward ratio (ER ratio). The reward scale is made up of the three subscales job promotion, esteem and job security. Each item was measured on a five-point scale from 1 (effort: disagree, reward: agree) to 5 (effort: agree, and very distressed, reward: disagree, and very distressed). High total values for effort or reward indicate a high perception of effort or reward. The ER ratio is formed from the total values of the two main subscales using the following rule: ER ratio $= \sum$ effort / ($\sum$ reward * 0.54) (21). An ER ratio of >1 indicates an effort-reward imbalance (ERI) which is said to be associated with a health risk (21). The greater the ERI (gratification crisis), the higher the health risk is.

Overcommitment (six items) was recorded with the same ERI-Q (21) on a four-point Likert scale (1 = strongly disagree to 4 = strongly agree). A total score was formed from the six items on this scale (value range: 6–24 points), according to which high values indicate a high tendency to overcommitment. The upper third of the total score is defined as the risk group (21).

Validity and Reliability of the German ERI questionnaire were rated as satisfactory. For all subscales of the short version of the ERI-Q (21) the values of the internal consistency were above 0.70 (effort: 0.74, reward: 0.79, overcommitment: 0.79). For the ER scales of the present study, Cronbach's alphas >0.70 were also determined (effort: 0.76, reward: 0.77, overcommitment: 0.81), which can be classified as acceptable or good (73).

Psychological Wellbeing was assessed by the General Health Questionnaire-12 (GHQ-12-Q: 72), which gives indications of psychological impairment or depressive symptoms. The procedure is based on a self-assessment of the wellbeing in the previous 4 weeks – in relation to normal wellbeing. The GHQ-12 contains six positively-phrased (pp) and 6 negatively-phased (np) questions. A four-point scale is used to rate the degree to which a symptom has been experienced during the last week (pp: better than usual, same as usual, less than usual, much less than usual; np: not at all, no more than usual, rather more than usual, much more than usual). Three scoring methods can be found in the literature. We used the classic binary "GHQ scoring" (0-0-1-1). The GHQ-12 total value (hereinafter GHQ score) can be between 0 and 12, whereby a higher total value is associated with increased psychological impairment (74). Based on Üstün and Sartorius (75), the cut-off value for impaired psychological health (GHQ score) is ≥5.

The validity and reliability of the GHQ-12 should be comparable to longer GHQ versions and the quality criteria should be of correspondingly high quality (Cronbach's Alphas: 0.82–0.86) (76). For the current data, Cronbach's Alpha was 0.89 and can therefore be assessed as good (73).

The inability to recover (IR) is a subscale of the questionnaire for faulty attitudes and behavioral analysis relevant to coping with work demands (FABA: 56, 57). It indicates extreme work commitment, which is associated with an accepted limited ability to recover in the sense of an inefficient coping style. IR was recorded with six items on the basis of a four-level ranking scale (1 = does not apply at all to 4 = applies very much). Then, the IR score (range: 6–24 points) was formed over the six items, which can be assigned using percentile values to normal (6–18 points), noticeable (19–21 points) and very noticeable (22–24 points) recovery values.

The reliability of the subscale inability to recover is given with a Cronbach's alpha of 0.79 (57). In the present study, a Cronbach's alpha of 0.86 was determined for the IR score, which can also be assigned to the good range (73).

Cardiovascular Screening Programme

Cardiovascular health was studied using the following indicators:

- home blood pressure monitoring.
- body measurements (body-mass-index, waist-hip-ratio).
- PROCAM score [Prospective Cardiovascular Münster score (77)].

Blood pressure (BP) measurement was carried out as a self-measurement on 4 days in accordance with the guidelines of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) (78). BP was measured on the upper arm and while sitting; a BOSO medicus (Bosch + Sohn GmbH, Jungingen, Germany) measuring device was used to measure BP. The participants were instructed to take six BP measurements daily between 06:00 and 10:00 h, at intervals of 2–3 h after 3 min of rest (total of $n = 24$ measurements). BP mean values were calculated from these 24 measured values and used to determine BP status (hypertensives ≥135/85 mmHg, normotensives <135/85 mmHg (78). In addition, it was determined whether antihypertensive drugs were being taken. Shift workers taking antihypertensive medications were classified *per se* as hypertensives and considered separately in BP-related analyses.

Body measurements serve to estimate the fat distribution pattern in the body and represent important determinants for the health risk in the case of being overweight or obese (24, 79, 80). Body weight and height as well as waist and hip circumference were measured for all participants. The body-mass-index (BMI) and waist-hip-ratio (WHR) were calculated from these values using the appropriate formulas:

$$\mathrm{BMI} = \frac{\text{body weight [kg]}}{\text{body lengthe } [\mathrm{m}^2]}.$$

According to the criteria of the German Adiposity Society (81), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obesity (≥30 kg/m^2) can be determined using the BMI.

$$\mathrm{WHR} = \frac{\text{waist circumference } [\mathrm{cm}]}{\text{hip circumference } [\mathrm{cm}]}.$$

WHR values above 1.0 in men and above 0.85 in women indicate abdominal obesity (82), which is associated with an increased risk of a metabolic syndrome (83).

PROCAM score estimates the individual risk of suffering a heart attack (myocardial infarction) in the period of the next 10 years. It is based on the epidemiological PROCAM Study (*Prospective Cardiovascular Münster*) and applies to women and men aged 20–75 years. Here, the rapid test was used to calculate cardiovascular health, which was introduced as a simplification of the precise PROCAM score (84) and did not record blood parameters (cholesterol, triglycerides) (77). The following eight classic risk factors are included in the calculation of the simplified PROCAM score, each of which contributes independently to the individual heart attack risk: age, sex, systolic BP, BMI, anamnestic data on antihypertensive drugs, diabetes mellitus, smoking habits and any family history of heart attacks.

Depending on the severity, different point values are assigned for the risk factors and then added to the PROCAM total score (hereinafter only PROCAM score). The score can be between 0 and 59 for men and between 0 and 56 for women. The lower the PROCAM score, the better the cardiovascular health of a shift worker is. In addition, the risk of heart attack risk can be assessed using an evaluation table by Assmann et al. (84): if the result is in the green range, there is a low risk of heart attack (<10%) over the next 10 years, in the yellow range there is a medium risk (10–20%) and in the red range a high risk (>20%).

Statistical Analyses

The statistical analysis of the data was carried out using *Statistical Package for the Social Science* (SPSS INC, Chicago, IL, USA) for Windows (Version 27).

The focus of this article is on the comparison of clusters with different psychosocial work stress and their relationship to indicators of cardiovascular and psychological health. First, the health indicators for the clusters were descriptively analyzed

TABLE 1 | Characteristic of effort-reward (ER) subscales and overcommitment (OC) in the ER-OC clusters (CL).

Characteristic	Low-stress CL (n = 71)	Normal CL (n = 88)	Risk CL (n = 40)	Test size	p-Value	Effect size
		Means ± standard deviation				$\eta^2_{partial}$
Effort [3–15 pts]	5.9 ± 2.0	9.3 ± 1.7	10.3 ± 2.8	81.81	<0.001***	0.458
Reward [7–35 pts]	30.4 ± 3.7	26.3 ± 4.2	24.2 ± 5.1	29.11	<0.001***	0.231
- Job promotion [3–15 pts]	12.1 ± 2.1	10.3 ± 2.4	9.7 ± 2.9	13.92	<0.001***	0.125
- Esteem [2–10 pts]	8.6 ± 1.7	7.1 ± 1.9	6.3 ± 1.8	23.59	<0.001***	0.196
- Job security [3–15 pts]	9.6 ± 0.9	8.9 ± 1.4	8.2 ± 2.0	14.05	<0.001***	0.126
ER ratio	0.4 ± 0.2	0.7 ± 0.2	0.8 ± 0.3	81.48	<0.001***	0.475
Overcommitment (OC) [63–24 pts]	9.9 ± 2.3	13.7 ± 1.9	18.5 ± 2.0	215.58	<0.001***	0.690
Classification		Frequency (number)				d
- ER ratio >1	% (n)	3.4 (3)	27.5 (11)	32.77	<0.001***	0.888
- OC >18	% (n)	1.1 (1)	47.5 (19)	77.72	<0.001***	1.601

*pts, points. High values of the subscales mean high effort, high reward or high overcommitment. % (n): frequency in percent (number of shift workers). Chi-square test (test size: χ^2-value, effect size: d); covariance analyses (design: constant term + ER-OC cluster, test size: F-value, effect size: $\eta^2_{partial}$: partial eta-square); p-value: significance (two-sided): **p < 0.01. ***p < 0.001. Effect size according to Cohen (86): d: <0.20 = no effect, 0.20–0.49 = small effect, 0.50–0.79 = medium effect, ≥0.80 = large effect; $\eta^2_{partial}$: <0.01 = no effect, 0.01–0.05 = small effect, 0.06–0.14 = medium effect, >0.14 = large effect.*

(mean values, standard deviations, medians, quartiles). In addition to shift work, sex and age were included as control variables in all statistical analyses (exception: PROCAM score).

In order to identify differences (mean value comparisons) between the cardiovascular and psychological indicators within the ER-OC clusters, univariate covariance analyses were carried out with the control variables. The Chi^2 test was used to test the difference between categorical variables.

Multinomial logistic regression analyses were carried out to examine the relationship of the cardiovascular and psychological health indicators (independent variables) as well as the control variables on the ER-OC clusters (criterion variable). For this purpose, the individual health indicators or control variables were correlated with the ER-OC clusters in the first step of the analysis (Spearman rank correlation) and evaluated according to the recommendations of Bühl (85). The influence of the control variables on these relationships was adjusted using partial correlations (85). Correlation coefficients r ≤ ±0.10 are interpreted as being independent of one another.

A probability of error of $\alpha < 0.05$ was specified as a statistical significance criterion and supplemented by effect sizes. The interpretation of the effect sizes was based on the conventions of Cohen (86). In the analysis of variance and in the Chi^2 test, small effect sizes from $\eta^2_{partial}$ ≥0.01 or d ≥0.20 were considered statistically significant effects.

A *post-hoc* power analysis was performed to assess the significance of the study (statistical power) using the *G*Power* program (87). This analysis was calculated for a univariate ANOVA with main effects (three groups). Given the total sample size (n = 199), the alpha error probability (α err prob = 0.05), a medium effect size (f = 0.25), and a number of degrees of freedom (df = 2), this analysis returns an actual power (1 – β err prob) of 0.90, and an error probability of the test (β) of 0.10, respectively. With an effect size of η^2 = 0.06 (corresponding to an f of about 0.25) and a power of 0.90, one would need 68 subjects per cluster (204 in total) to obtain a significant result with a one-factor ANOVA ($\alpha < 0.05$).

Determination of the Clusters With Different Psychosocial Work Stress

Groups of shift workers with different psychosocial work stress experiences were identified using a two-step cluster center analysis of the z-transformed values (85) of the effort-reward ratio (ER ratio) and overcommitment (OC) (ER-OC clusters). There were 199 complete records of shift workers included in the cluster analysis. Based on theoretical considerations, a three-cluster solution with the following well-interpretable clusters (CL) was favored (**Table 1**): low-stress cluster (LC: n = 71, 36%), normal cluster (NC: n = 88, 44%) und risk cluster (RC: n = 40, 20%).

Compared to those in the normal and high-risk cluster, the shift workers in the low-stress cluster showed on average the significantly (p < 0.001) lowest effort (∅ 6 points), the highest reward (∅ 30 points) and the lowest overcommitment (∅ 10 points). Conversely, the risk cluster stands out on average due to the highest effort (∅ 10 points), the lowest reward (∅ 26 points) and the highest overcommitment (∅ 19 points). The average values of the three subscales of the normal cluster are in each case between the low-stress and risk cluster, but differ significantly from both clusters (p = 0.027–<0.001). It is assumed that (normal) psychosocial work stress without health risk exists in the low-stress cluster and in the normal cluster. In contrast, more than a quarter (28%) of shift workers are in the risk cluster with a health-endangering effort-reward imbalance and around half (48%) with an excessive propensity to overcommitment (**Table 1**). Almost every fifth shift worker in the risk cluster (18%) is at risk from both psychosocial work stress and excessive effort.

TABLE 2 | Socio-demographic data in the ER-OC clusters (CL).

Personal und job-related characteristic	Dimension	Low-stress CL (*n* = 71)	Normal CL (*n* = 88)	Risk CL (*n* = 40)	Test size	*p*-Value	Effect size
Age [years]	M ± SD	41.2 ± 12.4	38.7 ± 11.3	39.6 ± 10.9	0.89^{++}	0.411	0.009
- <40	% (n)	53.4 (39)	58.0 (51)	52.5 (21)	1.50	0.827	0.129
- 40–50	% (n)	20.5 (15)	21.6 (19)	27.5 (11)			
- >50	% (n)	26.0 (19)	20.5 (18)	20.0 (8)			
Working time [hours/week]	M ± SD	39.1 ± 3.3	40.6 ±3.8	43.0 ± 7.2	11.3^{++}	0.001***	0.104
Shift work [working years]	M ± SD	10.1 ± 8.2	9.8 ± 7.6	10.3 ± 7.4	0.05^{++}	0.950	0.001
Sex							
- Men	% (n)	49.3 (35)	51.1 (45)	32.5 (13)	4.13^{+}	0.127	0.291
- Women	% (n)	50.7 (36)	48.9 (43)	67.5 (27)			
Shift system							
- Permanent shift system	% (n)	4.2 (3)	8.0 (7)	12.5 (5)	2.59^{+}	0.629	0.230
- Alternating shift without night work	% (n)	50.7 (36)	50.0 (44)	47.5 (19)			
- Alternating shift with night work	% (n)	45.1 (32)	42.0 (37)	40.0 (16)			
School graduation							
- Lower secondary education	% (n)	22.5 (16)	15.9 (14)	10.0 (4)	6.61^{+}	0.359	0.371
- Middle secondary education	% (n)	54.9 (39)	63.6 (56)	65.0 (26)			
- Upper secondary education	% (n)	18.3 (13)	19.3 (17)	25.0 (10)			
- Other school education	% (n)	1.1 (1)	1.1 (1)	— (—)			

*M ± SD, mean ± standard deviation; % (n), frequency in percent (number of shift workers). + = Chi-square test (test size: χ^2-value, effect size: d); ++ = covariance analyses (design: constant term + ER-OC cluster, test size: F-value, effect size: $\eta^2_{partial}$); p-value: significance (two-sided): ***p < 0.001. Effect size according to Cohen (86): d: <0.20 = no effect, 0.20–0.49 = small effect; $\eta^2_{partial}$: <0.01 = no effect, 0.01–0.05 = small effect, 0.06–0.14 = medium effect, >0.14 = large effect. Corrected R-squared: age = 0.020, working time = 0.111, shift work = 0.005.*

Sample

The sample consisted of 199 shift workers from the hotel and catering industry (HCI) as well as the food industry (FI) affiliated by the German Government Safety Organization Foods and Restaurants (BGN). About half of it was made up of female (53%) and male shift workers (47%) with an average age of 41 ± 11 years; all shift workers were employed full-time. More than half of the shift workers were younger than 40 years and 22% were older than 50 years. The distribution of the sexes ($p = 0.172$) and the age of the shift workers ($p = 0.411$) did not differ in the three ER-OC clusters (**Table 2**).

However, the average weekly working time in the ER-OC clusters was significantly different ($p = 0.001$, medium effect): With an average of 39 hours/week, the shortest working time was found in the low-stress cluster and the longest working time with 43 hours/week in the risk cluster. On average, the employees have been working in shifts for 10 years, most of them in an alternating shift system (93%), only a small proportion (7%) in a permanent shift system. For 50% of employees, the alternating shift system consisted of a morning (start: 06:00 to 09:00 h, end: 02:00 to 05:00 h) and afternoon shift ((start: 06:00 to 09:00 h, end: 02:00 to 05:00 h) and afternoon shift (start: 12:00–03:00 h, end: 08:00–11:00 h with a small percentage of night shift), 43% worked in a forward-rotating, three-shift system with early (06:00–02:00 h), late (02:00–10:00 h) and night shift (10:00–6:00 h).

The school education of shift workers did not differ in the three ER-OC clusters ($p = 0.413$) [German secondary schools are divided into three main categories: lower-level secondary school (*Hauptschule*), middle-level secondary school (*Realschule*) and upper-level secondary school (*Gymnasium*)]: 17% of participants indicated lower-level secondary education and 61% middle-level secondary education, and 20% had completed upper-level secondary education.

The field of activity of the participants was manifold. These activities have been assigned into six job categories and are composed of kitchen staff (12%), restaurant and hotel specialists (18%), line/plant operators (22%) as well as employees in warehouse logistics/packaging (18%), food production and food sales (15%) and other service areas (15%) (e.g., maintenance, house services, security, cleaning staff). There were no statistically significant differences between the ER-OC clusters for the individual areas of activity ($p = 0.061$). From this range of activities, around a third could be assigned to the predominantly physical (41%), a quarter to the predominantly psychological (21%) and almost half to the "mixed" (38%) work stress ($p = 0.187$).

RESULTS

To detect differences in cardiovascular and psychological health indicators between ER-OC clusters, univariate analyses of covariance were performed with the control variables (shift system, sex, age; exception: PROCAM score).

Psychosocial Work Stress and Cardiovascular Health

For the cardiovascular indicators (exception: diagnosis of hypertension), no statistically significant differences ($p > 0.05$)

TABLE 3 | Main effects and classification of cardiovascular indicators in the ER-OC clusters (CL).

Cardiovascular indicator	Dimension	Low-stress CL ($n = 71$)	Normal-CL ($n = 88$)	Risk-CL ($n = 40$)	Test size	p-Value	Effect size	R^2-value
Blood pressure (BP)								
- Systolic BP [mmHg]	M ± SD	135.3 ± 12.3	131.4 ± 10.2	132.9 ± 16.8	2.16^{++}	0.118	0.022	0.178
- Diastolic BP [mmHg]	M ± SD	83.6 ± 8.5	81.1 ± 8.1	82.5 ± 11.3	1.31^{++}	0.272	0.013	0.079
- Hypertension	% (n)	64.8 (46)	44.3 (39)	50.0 (20)	6.76^{+}	0.034*	0.375	
- Taking antihypertensives	% (n)	12.7 (9)	15.9 (14)	10.0 (4)	0.89^{+}	0.640	0.134	
BP without antihypertensives								
- Systolic BP [mmHg]	M ± SD	134.3 ± 12.6	131.2 ± 10.4	132.6 ± 12.9	1.15^{++}	0.320	0.014	0.173
- Diastolic BP [mmHg]	M ± SD	82.9 ± 8.7	81.0 ± 8.4	82.1 ± 11.7	0.53^{++}	0.591	0.006	0.058
- Hypertension	% (n)	59.7 (37)	43.2 (32)	47.2 (17)	3.78^{++}	0.151	0.278	
Body measurements								
Body-mass-index [kg/m^2]	M ± SD	26.6 ± 4.0	26.5 ± 4.3	25.8 ± 3.8	0.22^{++}	0.799	0.002	0.035
- Normal weight	% (n)	38.0 (27)	36.4 (32	52.5 (21)	6.95^{+}	0.326	0.381	
- Overweight	% (n)	39.4 (28)	45.5 (40)	32.5 (13)				
- Obesity	% (n)	22.5 (16)	18.2 (16)	15.0 (6)				
Waist circumference [cm]	M ± SD	92.2 ± 13.2	90.5 ± 13.3	87.5 ± 10.5	0.56^{++}	0.575	0.006	0.252
- Normal risk	% (n)	40.8 (29)	48.9 (43)	55.0 (22)	3.10^{+}	0.542	0.252	
- Increased risk	% (n)	19.7 (14)	21.6 (19)	15.0 (6)				
- Significantly increased risk	% (n)	39.4 (28)	29.5 (26)	30.0 (12)				
Waist-hip-ratio	M ± SD	0.90 ± 0.11	0.88 ± 0.10	0.86 ± 0.11	0.34^{++}	0.715	0.003	0.180
- Normal risk [♂ ≤1.0, ♀: ≤0.85]	% (n)	69.0 (49)	79.5 (70)	75.0 (30)	2.32^{+}	0.314	0.217	
- Increased risk [♂: >1.0, ♀: >0.85]	% (n)	31.0 (22)	20.5 (18)	25.0 (10)				
PROCAM score [pts]								
Heart attack risk ($n = 152$)	M ± SD (n)	18.0 ± 9.6 (62)	16.2 ± 10.2 (74)	15.1 ± 7.1 (36)	0.90^{++}	0.409	0.011	0.305
- Low (<10%)	% (n)	92.7 (51)	87.9 (58)	96.8 (30)	7.38^{+}	0.117	0.452	
- Medium (10–20%)	% (n)	1.8 (1)	10.6 (7)	3.2 (1)				
- Large (>20%)	% (n)	5.5 (3)	1.5 (1)	– (–)				
Health behavior								
Sporting activity								
- Sport (no)	% (n)	46.5 (33)	43.2 (38)	35.0 (14)	1.39^{+}	0.499	0.168	
- Sport (yes – regularly)	% (n)	43.7 (31)	40.9 (36)	37.5 (15)				
- Sport (yes – occasionally)	% (n)	9.9 (7)	15.9 (14)	27.5 (11)				
- Sport (yes – time [hours/week])	M ± SD (n)	2.7 ± 2.2 (38)	2.8 ± 2.5 (50)	2.1 ± 1.7 (26)	0.71	0.492	0.013	0.010
Smoking status								
- Non-smoker	% (n)	45.1 (32)	61.4 (54)	55.0 (22)	4.21^{+}	0.122	0.294	
- Smoker	% (n)	54.9 (39)	38.6 (34)	45.0 (18)				
- Smoker – cigarettes [number/day]	M ± SD (n)	12.3 ± 5.2 (39)	13.1 ± 7.0 (34)	13.4 ± 6.3 (18)	0.38^{++}	0.687	0.088	0.015

*pts, points; M ± SD: mean ± standard deviation; % (n): frequency in percent (number of shift workers). $^{+}$ = Chi-square test according to Pearson (test size: χ^2-value, effect size: d); $^{++}$ = covariance analyses (design: constant term + ER-OC cluster + shift system + sex + age, test size: F-value, effect size: $\eta^2_{partial}$); p-value: significance (two-sided): *p < 0.05. Effect size according to Cohen (86): d: <0.20 = no effect, 0.20–0.49 = small effect; $\eta^2_{partial}$: <0.01 = no effect, 0.01–0.05 = small effect, 0.06–0.14 = medium effect. R^2, corrected R-squared.*

were found between the three ER-OC clusters (**Table 3**). The trend, however, shows that the cardiovascular indicators are more unfavorably pronounced in the low-stress cluster than in the risk cluster. There are no or only very slight correlations between the cardiovascular indicators and the ER-OC clusters (R = −0.07 to −0.13).

Essential, significant main effects, however, occur for blood pressure (BP) and body measurements in the classic control variables sex ($p = 0.008$-<0.001; $\eta^2_{\text{partial}} = 0.038$–$0.197$, small to large effects) and age ($p = 0.004$-<0.001; $\eta^2_{\text{partial}} = 0.012$–$0.122$, small to medium effects); the shift system has no effect on any indicators ($p > 0.05$) (**Table 4**).

The effects on health behavior are reversed: no sex or age effects ($p > 0.05$) can be determined, but a small shift system effect for smoking ($p = 0.042$; d = 0.210). There are significantly more smokers in the alternating shift system with night shifts (53%) than in those without night shifts (41%) or the permanent shift system (33%) (**Table 4**).

It could be confirmed that the BP values in men are significantly higher than in women (mean: 138/84 vs. 129/81

TABLE 4 | Main effects of covariates of cardiovascular indicators in the ER-OC clusters (CL) ($n = 199$).

Cardiovascular indicator	Shift system			Sex			Age [years]		
	Test size	*p*-Value	$\eta^2_{partial}$	Test size	*p*-Value	$\eta^2_{partial}$	Test size	*p*-Value	$\eta^2_{partial}$
Blood pressure (BP) taking antihypertensives									
- Systolic BP [mmHg]	0.01	0.959	<0.001	34.82	<0.001***	0.153	12.36	<0.001***	0.060
- Diastolic BP [mmHg]	1.25	0.264	0.006	8.17	0.005**	0.041	13.48	<0.001***	0.041
BP without taking antihypertensives									
- Systolic BP [mmHg]	0.10	0.750	0.001	33.02	<0.001***	0.166	7.94	0.005**	0.046
- Diastolic BP [mmHg]	1.01	0.316	0.006	7.18	0.008**	0.041	8.74	0.004**	0.050
Body measurements									
Body-mass-index [kg/m^2]	2.69	0.103	0.014	7.57	0.006**	0.038	2.35	0.127	0.012
Waist circumference [cm]	0.08	0.783	<0.001	47.21	<0.001***	0.197	26.84	<0.001***	0.122
Waist-hip-ratio	1.21	0.272	0.006	29.42	<0.001***	0.132	24.17	<0.001***	0.111
PROCAM score [pts]$^{++}$	3.85	0.051	0.019	—	—	—	—	—	—
Health behavior									
Sporting activity^{+}	3.19^{+}	0.076	0.016	2.21^{+}	0.138	0.011	0.36^{+}	0.552	0.002
Sport (yes) – time [hours/week]	0.04	0.845	<0.001	1.71	0.194	0.016	0.03	0.861	<0.001
Smoking status^{+}	4.15^{+}	0.042*	0.016	1.84^{+}	0.177	0.009	0.06^{+}	0.805	<0.001
Smoker – cigarettes [number/day]	0.01	0.909	<0.001	1.89	0.172	0.022	1.00	0.321	0.012

pts, points. $^{+}$ = Chi-square test (test size: χ^2-value, effect size: d); covariance analyses (design: constant term + ER-OC cluster + shift system + sex + age, test size: F-value, effect size: $\eta^2_{partial}$); p-value: significance (two-sided): $^{**}p < 0.01$, $^{***}p < 0.001$. Effect size according to Cohen (86): d: <0.20 = no effect; $\eta^2_{partial}$: 0.01–0.05 = small effect, 0.06–0.14 = medium effect. $^{++}$ The PROCAM score included sex and age as risk factors.

mmHg, $\eta^2_{\text{partial}} = 0.118/0.022$, medium/small effect), and that BP increases with age (<40 vs. >50 years, mean: 131/81 vs. 137/84 mmHg, $\eta^2_{\text{partial}} = 0.027/0.038$, small effects); it explains 18% of the variance in systolic and 8% in diastolic BP. The same sex and age effects were recorded for WC, BMI, WHR and PROCAM score, with the explanation of variance varying between 3 (BMI) and 30% (PROCAM score) (**Tables 3**, **4**). Regardless of this, more than half of the shift workers have hypertonic BP (54%) and are overweight or obese (60%). Elevated values for the waist-hip ratio are found in a quarter (25%) of shift workers. 5% of shift workers have a medium risk and 2% a high risk of having a heart attack in the next 10 years. In addition, only 41% of them participate in regular physical activities (sport) and 46% are smokers; they smoke an average of 13 cigarettes a day (**Table 3**).

Psychosocial Work Stress and Psychological Health

For psychological health, there are significant differences between the ER-OC clusters — both for psychological wellbeing ($p < 0.001$; $\eta^2_{\text{partial}} = 0.069$, medium effect) as well as for inability to recover (IR) ($p < 0.0001$; $\eta^2_{\text{partial}} = 0.430$, large effect). Taking the control variables into account, psychological wellbeing explains 9% and the inability to recover 44% of the variance in the ER-OC clusters (**Table 5**).

According to Üstün and Sartorius (75) a GHQ score of five points or more shows indications of psychological impairment. This affected 7% of all shift workers, only 1% in the low-stress cluster, but 18% in the risk cluster ($p = 0.004$; d = 0.485; small effect).

Sex and shift system have a significant influence on psychological wellbeing ($p = 0.030$-<0.001; $\eta^2_{\text{partial}} = 0.024$–0.093, small to medium effects), but not age ($p = 0.179$). Psychological impairment is significantly more common in women than in men (10 vs. 2%: $p = 0.019$, d = 0.337, small effect) and shift workers who do night shifts report significantly more conspicuous GHQ scores (12%) and thus depressive symptoms than those from the other two shift systems (0–3%: $p = 0.033$, = 0.378, small effect).

Even in the case of inability to recover, the most favorable recovery values (∅ 11 points) are shown in the low-stress cluster and the most unfavorable recovery values (∅ 19 points) in the risk cluster, whereby the cluster mean value is at the limit of the conspicuous area. Accordingly, all shift workers in the low-stress cluster reported normal recovery values, but only 48% in the risk cluster ($p < 0.001$, d = 1.33, large effect). The severity of the inability to recover is only influenced by sex ($p = 0.047$, $\eta^2_{\text{partial}} = 0.020$, small effect), not by age and shift system ($p > 0.05$). On average, women indicate significantly higher IR scores than men (∅ 15 vs. 13 points: p = 0.021, $\eta^2_{\text{partial}} = 0.027$, small effect).

Relationship of Health Indicators to ER-OC Clusters

The correlation analyses of the examined health-related indicators confirmed that there is no or only a very low correlation ($R = -0.14$–0.10) between the cardiovascular health indicators (BP, BMI, WHR, PROCAM score, sport activities (hours/week), smoking status) and the ER-OC clusters. For the psychological health variables, the ER-OC clusters also yielded

TABLE 5 | Main effects of psychological indicators and covariates and classification of psychological indicators in the ER-OC clusters (CL).

Psychological indicators	Dimension	Low-stress CL (*n* = 71)	Normal CL (*n* = 88)	Risk CL (*n* = 40)	Test value	*p*-Value	Effect size
Psychological wellbeing	M ± SD	0.4 ± 1.0	0.8 ± 1.7	1.9 ± 3.4	7.16++	0.001***	0.069
[GHQ score: 0–12 pts]	M (Q_{25}, Q_{75})	0.0 (0, 0)	0.0 (0, 1)	0.0 (0, 2)			
Covariate							
- Shift system					19.89+	<0.001***	0.093
- Sex					4.80+	0.030*	0.024
- Age (years)					1.82++	0.179	0.009
Classification GHQ score							
- Normal [0–4 pts]	% (n)	98.6 (70)	94.3 (83)	82.5 (33)	11.04+	0.004**	0.485
- Impaired [5–12 pts]	% (n)	1.4 (1)	5.7 (5)	17.5 (7)			
Inability to recover (IR)	M ± SD	11.3 ± 2.8	14.7 ± 3.1	18.5 ± 3.2	73.30++	<0.001***	0.430
[IR score: 6–24 pts]							
Covariate							
- Shift system					0.55+	0.459	0.003
- Sex					3.98+	0.047*	0.020
- Age (years)					2.28++	0.133	0.012
Classification IR score							
- Normal [6–18 pts]	% (n)	100.0 (71)	87.5 (77)	47.5 (19)	61.10+	<0.001***	1.331
- Noticeable [19–20 pts]	% (n)	– (–)	9.1 (8)	17.5 (7)			
- Very noticeable [≥21 pts]	% (n)	– (–)	3.4 (3)	35.0 (14)			

*pts, points; M ± SD, mean ± standard deviation; M (Q_{25}, Q_{75}), median and quartile; % (n), frequency in percent (number of shift workers). + = Chi-square test (test size: χ^2-value, effect size: d); ++ = covariance analyses (design: constant term + ER-OC cluster + shift system + sex + age, test size: F-value, effect size: $\eta^2_{partial}$); p-value: significance (two-sided): *p < 0.05, **p < 0.01, ***p < 0.001. Effect size according to to Cohen (86): d: 0.50–0.79 = medium effect, ≥0.80 = large effect; $\eta^2_{partial}$: <0.01 = no effect, 0.01–0.05 = small effect, 0.06–0.14 = medium effect. + The PROCAM score included sex and age as risk factors. Corrected R-squared: GHQ score = 0.093, IR score = 0.444.*

only a low correlation to the GHQ score (R = 0.24) and a medium correlation to the IR score (R = 0.66). This is also confirmed by the partial correlation coefficients. Psychological well-being (GHQ score) and inability to recover (IR score) were significantly decreased in the risk cluster. There were no correlations of the control variables shift system (R = −0.03), sex (R = 0.10), and age (R = −0.07) with the ER-OC clusters, i.e., they did not contribute to the explanation of the ER-OC cluster.

Since a total model with cardiovascular indicators and control variables would not yield significant effects, these variables were omitted from the multinomial logistic regression model. Thus, only the variables GHQ score and IR score were entered into the multinomial logistic regression model, with the low-stress cluster being used as a reference category. **Table 6** summarizes the effects of the indicators estimates of each predictor.

The regression model contains a significant explanatory component ($\chi^2(4) = 119.73$, $p < 0.001$). Psychological wellbeing (GHQ score) and inactivity to recovery (IR score) were confirmed as predictors of the level of psychosocial work stress in overcommitted shift workers. Both variables explain 52% of the variance of the ER-OC clusters. Thereby, the GHQ score alone explains 8% and the IR score alone 49% of the variance of the ER-OC clusters. However, both variables appear to have different relevance for the normal and risk clusters.

Whereas, in the normal cluster only the IR score turned out to be a predictor for the ER-OC clusters, in the risk cluster, the GHQ score, in addition to the IR score, also showed to be a significant predictor. Compared to the low-stress cluster, the chance of belonging to the normal cluster increases by almost 50% when the IR score increases by one point. As expected, this effect is more pronounced in the risk cluster: If GHQ and IR score each increase by one point, the relative probability of a shift worker of belonging to the risk group increases by 1.4 and 2.3 times, respectively (**Table 6**). About 70% of all shift workers are assigned to the correct ER-OC cluster using this model.

DISCUSSION

For the shift workers in the hotel and catering industry and food industry, a three-cluster solution was found using the *model of the professional gratification crisis* (21), in which a risk cluster was shown in addition to a low-stress and normal cluster. In shift work, this cluster is characterized by a specific work-related risk constellation (high ERI and high OC at the same time) for an increased risk of psychological health impairments (depressive symptoms), but above all inadequate recovery. In the low-stress cluster there are neither shift workers with an imbalance of effort and reward, nor people with high overcommitment, in the normal cluster there is only a small proportion (ERI: 3%, OC: 1%).

In addition, the shift workers in the low-stress cluster worked an average of 4 h a week less than those in the risk cluster. The mean values of the GHQ and IR scores in the low-stress and normal clusters initially indicate good psychological health; they explain 45% of the variance of the ER-OC clusters. Inability to recover turned out to be the strongest predictor (explained

TABLE 6 | Regression model of psychological indicators to explain ER-OC clusters in shift workers ($n = 199$).

Model	Parameter estimates						
	Regression coefficient B	SE	Wald test	p-value	Exp(B)	95% confidence interval for B	
						Lower bound	Upper bound
Normal cluster							
(constant)	−5.05	0.94	28.75	<0.001***			
GHQ-score	0.11	0.14	0.63	0.427	1.115	0.85	1.46
IR-score	0.39	0.07	29.22	<0.001***	1.484	1.29	1.71
Risk cluster							
(constant)	−13.00	1.72	57.23	<0.001***			
GHQ-score	0.31	0.15	4.36	0.037*	1.367	1.02	1.83
IR-score	0.80	0.11	54.79	<0.001***	2.217	1.80	2.74

*SE, standard error. Dependent variable: ER-OC cluster, independent variables (predictors): GHQ-score, IR-score. Multinomial logistic regression (method: enter), number of degrees of freedom: 1, reference category: low-stress cluster (n = 71). P-value: significance (two-sided): *p < 0.05, ***p < 0.01.*

variance: 43%) and is interpreted as a new finding in the context of the *model of the professional gratification crisis* (21). In contrast, the individual cardiovascular indicators (BP, BMI, WHR, PROCAM score, sport activities (time/week), smoking status) each explain less than one percent of the variance of the ER-OC clusters. This supports the assumption of Cottini (88) that psychosocial work stress affects psychological health rather than physical health. It is known that a lower social status is associated with a higher risk of many physical and psychological illnesses (89). However, it is possible that shift workers with physical health problems stoped working in the hotel and catering industry and food industry and left shift work.

Rather, the known significant main effects for sex and age were confirmed for the cardiovascular indicators, according to which, in particular, more men than women indicated health-endangering cardiovascular risks. The shift system had almost no influence on the cardiovascular indicators. There was only a small shift system effect for smoking.

For psychological wellbeing and inability to recover there was also a small significant effect for sex: women were more psychologically impaired and reported less favorable ability to recover than men (GHQ score ≥5: 10 vs. 2%; IR score: 18 vs. 14%). In addition, 12% of the shift workers in the alternating shift system with night shift showed impaired psychological health and only 3% of the shift workers without night work (shift system effect). This confirms the already known effect that shift systems with night work in particular seem to increase the risk of depressive symptoms (50).

Conforming to the interaction hypothesis of the ERI model (21, 22) and the research literature (1, 3–5) 18% of the shift workers with increased psychosocial work stress and a strong tendency to overcommit (risk cluster) reported impaired psychological wellbeing, while this only affected 1% in the low-stress cluster and 6% in the normal cluster. Overall, 7% of all shift workers reported depressive symptoms. Comparative data on the prevalence of depressive symptoms in the general adult population from Germany are only indirectly available through the *German Health Interview and Examination Survey for Adults (DEGS1 study)* (90), because the German version of the Patient Health Questionnire (PHQ-9) in the study was used to record depressive symptoms (91, 92). Depressive symptoms (PHQ-9 ≥10 points) existed here (age range: 18–59 years) for 9% of the adults. Thus, the share of psychologically impaired shift workers is initially comparable with that of the general German population (90, 93). In the risk cluster, however, this proportion is twice as high (18%) and somewhat lower in the normal cluster (6%) than in this population.

The fact that the inability to recover (56, 57) or the inability to "psychologically detach from work" (55) functions as the most important predictor to explain the ER-OC clusters is an new aspect in the context of the ERI model (21). In the risk clusters, more than half of the shift workers (52%) noticed that they had poor recovery ability, while in the low-stress cluster the phenomenon of inability to recover did not occur at all and in the normal cluster it was 12%. This underlines that the balance between high psychosocial work stress and recovery is disturbed, especially among the overcommitted shift workers in the risk cluster.

In recent times, research results show how important it is for the regeneration process to be able to "switch off" (20, 26, 27, 55, 94). According to the results from a representative survey among employed persons in Germany ($n = 4{,}511$, age range: 31–60 years) (94), 12% of shift workers can be expected to have insufficient recovery. In our sample, 16% of all shift workers were impaired in their recovery. Schulz et al. (94) postulate depressive symptoms and sleep disorders as consequences of an inability to recover. According to de Bloom et al. (95), the recovery processes after work make a decisive contribution to maintaining psychological wellbeing and health. For the present study, there was only a very low correlation between psychological wellbeing and the ability to recover ($r = 0.18$).

Regardless of cluster membership, it is relevant from a preventive perspective that a relatively high proportion of shift workers have cardiovascular risk factors that can lead to health problems or incapacity for work in the medium and long term; for example, for these indicators, more than half of the sample showed hypertonic blood pressure (54%), more than a third (39%) were overweight and a quarter (22%) obese, as well as an increased waist-hip ratio (25%). Furthermore, more than half (57%) of the shift workers stated that they only carried out sporting activities occasionally or not at all, and just under half of the shift workers were smokers (45%). The risk of a heart attack could, however, be classified as low for the majority of shift workers (94%).

In the *DEGS1 study*, if the classic sex and age effects are taken into account, the prevalence of most cardiovascular risk factors are significantly lower than in the present study. In line with this, the age range from 18 to 69 years was also considered in the *DEGS1 studies*. In this age range, a hypertension prevalence of around 24% (men: 30%, women: 19%) is given for the general German population (96). Two thirds of men (67%) and half of women (53%) in Germany are overweight and a quarter of adults (men: 23%, women: 24%) suffer from obesity (79). The higher a person's body fat percentage is above normal, the more dangerous the health consequences are to be expected (97, 98). Obesity in particular leads to increased stress on the musculoskeletal system and promotes the development of lipid metabolism disorders and hypertension (97).

With regard to smoking status, in the *DEGS1 study* was stated that 36% of adults are smokers, with 39% of men and every third woman (33%) in Germany affected (99). Compared to this *DEGS1 study*, significantly more shift workers smoked in our study, namely over half (51%) of the men and 42% of the women. The highest proportion of smokers was recorded in the low-stress cluster (55%), the lowest proportion of smokers in the normal cluster (39%; risk CL: 45%), whereby the shift system effect must be taken into account. The high proportion of smokers is known for hotel and catering industry (66, 100) and shift workers (14, 17, 23, 29).

According to the *DEGS1 study*, about a third (34%) of adults are also inactive in sports, but men are said to be more active, more often (more than 4 hours/week) than women (25 vs. 17%) (101). Although regular physical activity has a positive effect on health at any age, fewer and fewer adults are physically active with increasing age. This affects 15% of 18–29-year-olds, but around half (49%) of those 65 and over (101). In comparison, 43 and 16% of the shift workers stated that they did not or only occasionally exercised. 41% of shift workers reported doing sports regularly. Classification of the results on the basis of the WHO recommendations on health-promoting physical activity was not possible with the available data, but indicates a current field of action for prevention.

The PROCAM Score is of particular importance for the assessment of myocardial infarction risk. Our study confirmed a higher cardiovascular risk for men than for women and this risk increased with age. From the age of 50, 4% of men had a risk >20 and 2% of women had a medium risk of myocardial infarction (10–20%). This means that the risk of myocardial infarction is somewhat lower than in the PROCAM study by Assmann et al. (102), representing the general population in Germany. Also, in the DETECT study by Silber et al. (103), the mean 10-year coronary morbidity risk was estimated to be 4.9% using the PROCAM score and thus higher than in our study. This effect is in contrast with the results of the meta-analysis by Vyas et al. (18), which found that shift workers had a higher cardiovascular disease risk compared with non-shift day workers. However, our shift worker sample is significantly younger (average age: 40 years) than in the comparative studies considered, and the influence of health behavior and social status must be taken into account.

Also, the results of the cardiovascular indicators can be classified contrary to the assumed interaction effect in the ERI model (21). There were no or only very slight correlations between increased psychosocial work stress and health-endangering characteristics of the cardiovascular indicators ($R = 0.07–0.13$). In the literature reviewed, however, no consistent associations with psychosocial work stress were reported for most cardiovascular indicators either (1, 4). Since more than half (52%) of the shift workers were younger than 40 years of age in our study and cardiovascular restrictions occur more frequently at a later age (104), associations to cardiovascular risk factors may not yet be directly demonstrated. In addition, there is the healthy worker effect (105).

However, neither psychosocial work stress nor shift work necessarily lead to health problems. There are also "healthy" shift workers! More recent studies have addressed the fact that classic cardiovascular risk factors (e.g., lack of exercise, smoking, diet) have a much greater impact on the health of employees than shift and night work (20). According to Struck et al. (106), the health hazards of shift and night work are based more on "third-party variables" (e.g., socio-demographic influencing factors, stressful workplaces) that occur regardless of the working hours. The association between shift and night work and impaired health must be interpreted more cautiously and in a more differentiated manner. Overall, it remains unclear whether shift and night work *per se* lead to health problems, or whether the change in lifestyle and particular personality traits (e.g., excessive willingness to overcommit) are responsible for this, or to what extent the conditions at the workplace (e.g., including social relationships, recognition, employment status) are initially hazardous to health. In addition, the replicability of the clusters in future shift work studies needs to be further examined, as the clusters found resulted from a relatively small sample from two industries.

In summary, for shift work in the hotel and catering sectors and food industries, psychosocial workload seems to be less related to cardiovascular health but more related to psychological health. However, this effect underestimates the considerable health risk for shift workers, which exists due to the health-endangering characteristics of the cardiovascular indicators and signals further need for action in this area. From an occupational health perspective, the prevalence of high blood pressure among shift workers, with an average age of 41, is particularly worrying. There is a clear discrepancy between unknown and treated hypertension since most of the shift workers were not aware of their blood pressure values, nor were they undergoing medical treatment. However, medical therapy to lower blood pressure and thus avoid secondary diseases caused by hypertension is only given to diagnosed patients. To this end, occupational health care are not used sufficiently.

The originality of the study is that the interaction hypothesis of the *ERI model* (21) was tested for the first time in shift workers in hotel and catering and the food industry using a three-cluster solution. Another special feature that must be emphasized is that the blood pressure status from a 4-day self-measurement was generated from 24 measured values according to the guidelines of the European Society of Cardiology and the European Society of Hypertension (78) and the criteria for the diagnosis of "hypertension" were met. Thirdly, with the characteristic of inability to recover in the context of the *ERI model* (21), a new aspect that had not been investigated was introduced into this model.

Limitations of the Study

When interpreting the results, the following limitations of this study must be taken into account:

Sample

Since participation in the study was voluntary and it was therefore an convenience sample, selection effects can also exist. Due to the age of the sample and the known drop-out rate in three-shift systems with night work and in the hotel and catering sector, a healthy worker effect cannot be ruled out, which can lead to an underestimation of the health risks.

Research Design

As the data were collected as part of the cross-sectional design, no statements can be made on the cause-and-effect relationship. But reverse causality should be considered. Shift workers who have health problems may report more stress.

Questionnaires

Some of the variables were recorded by questionnaires or self-assessment. Data collected in this way are subject to known quality restrictions (e.g., distortion due to social desirability, response tendencies, memory deficits, recall bias). This method-critical objection was largely remedied by including objective health indicators (e.g., self-measurement of blood pressure, measurement of body dimensions). This is also one of the strengths of this investigation.

Health Behavior

Alcohol consumption, although a specific health characteristic in hotel and catering industry and may be associated with increased psychosocial stress, was excluded from the analyses because the data often reflect a bias due to social desirability.

ERI-Q

The model structure of the ERI-Q (21) was checked in several validation studies (107–109), whereby a factor-analytically unclear structure and no uniform operationalisation were found for the overcommitment component (OC) in some studies. The OC construct (21) is also described in the literature as a lack of ability to distance oneself from work (61, 109–111), and striving for perfection (112).

CONCLUSION

The results of the three-cluster solution signal the need for occupational health prevention and care. They contribute to the assessment of the burden of illness through psychosocial work stress among shift workers. The significance of psychosocial work stress in combination with severe overcommitment is only confirmed in the present study by the data on psychological health. However, this result underestimates the considerable health risk for shift workers, which exists due to the health-endangering characteristics of the cardiovascular indicators. Men are particularly affected here, while psychological health impairments are more prevalent among women, and especially those who worked in the alternating shift system with night shifts.

Preventive occupational health programmes represent a suitable approach to detecting endangered shift workers or risk groups at an early stage. In addition to health behavior, the job characteristics themselves, the working conditions and the design of the shift or working time models are among the preventive starting points for company medical practices and occupational health screening concepts for shift workers. Even if the cardiovascular indicators could not contribute to the explanation of the ER-OC clusters in the present study, it is necessary to integrate these indicators into a precautionary concept for shift workers, in order to be able to estimate the cardiovascular risk of the employees. These concepts should be supplemented by the topics of psychosocial work stress and the ability to recover. Both constructs have achieved a new status in the modern working world, but many new questions still need to be clarified in future research. Our results support the fact that recovery has an independent diagnostic value for assessing work stress. It is interpreted as an early indicator for the detection of psychosocial work stress in above-average committed shift workers. It is crucial to identify and influence psychosocial work stress and health hazards as well as work and health resources at an early stage.

In order to cope with the high work stress caused by shift and night work, a balance between work and recovery and sufficient regeneration phases are an essential prerequisite for high performance. A high level of effectiveness and productivity at work is only possible if the employees succeed in fully regenerating their performance requirements. Since ability to recover has been shown to be the most important predictor for explaining the psychosocial work stress, it should be definitely included in future shift work studies.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, when a reasoned request is made to the authors. There is an agreed data protection obligation towards the participants.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Technical University

Dresden (EK 250397). The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RS and BH made the funding acquisition. RS designed the study, performed the statistical analyses and interpretation of the data, and wrote the first draft of the manuscript. Both authors made the project administration and collected the data. BH commented critically on the manuscript. Both authors approved the submitted version.

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Effects of Factors Related to Shift Work on Depression and Anxiety in Nurses

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Background: Although shift work is the foundation of the provision of 24-h continuous care in hospitals, it can negatively impact mental health in hospital workers such as nurses. Despite the connection between mental health and overall health, little is known about the effect of shift work-related factors on mental health in this population.

Objectives: We investigated the effect of scheduling practices, physical and psychological characteristics related to shift work, and personal habits during shift work on depression and anxiety among nurses.

Methods: In this multi-center cross-sectional study, 11,061 nurses from 20 hospitals in the Shandong Province of China completed an online survey between December 2020 and February 2022. Multivariate ordered logistic regression analysis was performed to examine shift-related factors associated with depression and anxiety in the study population.

Results: The completion rate of all nurses' questionnaires was 83.00% ($n = 9,181$). Among the 9,181 respondents, 66.20% ($n = 6,078$) were shift nurses. Depression and anxiety were found in 58.82 and 62.08% of shift nurses, respectively, and these rates were influenced by fatigue during shift work, psychological stress before/during/after night shifts, feeling of being refreshed after resting before/after night shifts, using sleep medication before/after night shifts, physical discomfort during night shifts, busyness during night shifts, food intake during shift work, working > 40 h/week during shift work, and sleep quality before/after night shifts.

Conclusions: Depression and anxiety in shift nurses may be addressed by reducing their workload, sources of stress during night shifts, and facilitating rest and relaxation.

Keywords: China, nurses, shift work, anxiety, depression, cross-sectional study

INTRODUCTION

Shift workers alternate and rotate morning, afternoon, and night shifts, and often work outside standard h (i.e., 7:00 to 18:00) (1). Given the demand for medical services, most healthcare sectors rely on shift workers, including core staff such as nurses (2). Shift work may negatively impact mental and physical health (3–5) because it disrupts the sleep-wake cycle (circadian rhythm) (6, 7). Mental health, which is associated with overall health and wellbeing, is affected by demographic, biological, psychosocial, and genetic factors, and by circadian rhythms (8–10). Mental health disorders are a main cause of illness-related absenteeism or presenteeism worldwide (11, 12), and poor mental health has been more strongly linked with absenteeism than physical illness or injury (8, 13, 14). Therefore, understanding how shift work influences mental health is essential for improving the occupational health and working conditions of shift workers.

Although chronic health conditions have been increasingly related to shift work, conclusions linking shift work with mental health have been inconsistent (7). Driesen et al. found that poor mental health was positively correlated with shift work (8). For instance, symptoms of depression were two times more frequent in shift workers compared with those who worked regular daytime h (8). Rosenberg et al. also found that adverse mental health issues were more common in shift workers than in non-shift workers, and that shift work carried a 33% increase in the risk of depressive symptoms (15). Furthermore, these workers had an increased risk of anxiety (although this was not statistically significant) (15). Sweeney et al. found *via* subgroup analysis that in comparison with non-shift workers, female shift workers had a 21% greater chance of reporting signs of major depression (7). This difference was not significant among male shift workers (7). Although previous reports have indicated that shift workers have an increased risk of depression and anxiety (16, 17), Øyane et al. reported that working at night was not linked with heightened depression and anxiety (18). Surprisingly, some studies have found that mental health in shift workers was superior to that in workers who did not do shift work (19, 20). These contradictory results may be explained by differences in occupational, industrial, and shift work characteristics across countries. Healthcare workers have been exposed to highly stressful work environments as a consequence of the COVID-19 pandemic, and this is likely to have affected their mental health (11). Nurses, as the mainstay of the healthcare workforce, are constantly exposed to workplace stressors that can have negative psychological effects such as anger, anxiety, depression, burnout, and irritability (21). Therefore, we examined how shift work, one of workplace stressors, could have impact on mental health in nurses in the present study.

A previous meta-analysis of longitudinal studies included a sensitivity analysis for the effect of gender on mental health in nurses (22). However, the authors did not analyze the characteristics associated with shift work because this information was not available (22). To fully explore the mechanisms by which shift work might influence mental health, it is necessary to consider specific characteristics of the working environment (e.g., fixed/permanent shifts, number of night shifts worked, start times, and the speed and direction of shift rotation) (23). The data could enable us to develop appropriate interventions. Therefore, in addition to collecting general demographic data from nurses, we aimed to explore detailed characteristics of shift work in terms of mental health.

Given that several studies with large samples have recently associated mental health with shift work (7, 24, 25), we attempted to explore how shift work might be related to depression and anxiety among Chinese nurses using data from a large multi-center sample from the Nurses' Health Cohort Study of Shandong. Our primary objective was to evaluate and describe the mental health status of Chinese nurses, including symptoms of depression and anxiety, while focusing on the effects of shift work-related characteristics such as psychological stress during or associated with shift work, work schedules, and personal habits during shift work on mental health outcomes. Finally, we sought to provide a framework for the development and implementation of health promotion programs and policies in the workplace, as well as to provide recommendations regarding the reduction of mental health risks associated with shift work.

METHODS AND MATERIALS

Setting, Design, and Participants

In this multi-center cross-sectional study, we used baseline data collected from the Nurses' Health Cohort Study of Shandong (registration number: ChiCTR2100043202) (26) between December 2020 to February 2022. Health data were collected from nurses in 20 hospitals and eight cities in Shandong Province. The study participants were registered qualified nurses who volunteered to participate. Participants were excluded if they were nurses who had (a) retired or were practice nurses, (b) had <6 months of work experience, or (c) were on work leave during the investigation.

Measures

Demographic Characteristics of Nurses

We examined demographic characteristics of the study population including age, department, education, gender, marital status, monthly income, professional title (the title of a technical or professional post), shift work (yes/no), and years of working as a nurse.

Characteristics of Shift Work

We classified the characteristics of shift work into three main categories: shift scheduling, shift work-related physical and mental characteristics, and personal habits during shift work. Therefore, the variables collected in this study included work schedule (two shifts/three shifts), shift rotation direction (counterclockwise/clockwise), shift work experience, months in which shift work was undertaken per year, the number of night shifts each month, interval between night shifts, night shift staffing, psychological stress before/during/after night shifts (yes/no), feeling of being refreshed after resting before/after night shifts (yes/no), use of medication to aid sleep before/after night shifts (yes/no), physical discomfort during night shifts (yes/no), busyness during night shifts (yes/no), food intake during shift work (normal/more/less), meal timing during shift work (regular/early/delayed), working >40 h/week during shift work (0–4 weeks/month), sleep quality before/after night shifts (normal/poor), and resting during night shifts (yes/no).

Mental and Physical Fatigue in Nurses During Shift Work

The 14-item Fatigue Scale (FS-14) is widely used to measure the degree of fatigue. The FS-14 was developed by Chalder et al. (27), and the Chinese version was created by Wang et al. (28). Its Cronbach's α was 0.773 and the test-retest reliability was 0.745 (28), which indicated that the test was culturally sensitive and valid (29). The scale consists of 14 questions with "yes" (1 point) or "no" (0 point) answers that correspond to the two dimensions of mental and physical fatigue. A higher score on this scale reflects a greater fatigue level. The Cronbach's α of the FS-14 was 0.803 in this study.

Anxiety Severity

The Generalized Anxiety Disorder 7-Item Scale (GAD-7), developed by Spitzer et al., with a test-retest reliability of 0.830 and a Cronbach's α of 0.920 indicating good reliability and validity, has been widely employed to screen for the presence and severity of anxiety (30). The total GAD-7 score ranges from 0–21 points, and each of the seven items is scored from zero (not at all) to three (nearly every day) such that 0–4, 5–9, 10–14, and 15–21 points represent normal, mild, moderate, and severe anxiety, respectively (30). The reliability and validity of the Chinese version of the GAD-7 were verified by He et al., who found that the test-retest reliability was 0.856 and the Cronbach's α was 0.898 (31). The Cronbach's α of the GAD-7 was 0.937 in this study.

Depression Severity

The 9-item Patient Health Questionnaire (PHQ-9) has been widely employed to measure depression symptoms (32). Kroenke et al. tested the reliability and validity of the PHQ-9 in medical institutions, and found the test-retest reliability to be 0.840 and the Cronbach's α of the questionnaire to be 0.890 (33). The total PHQ-9 score ranges from 0–27 points, and each of the 9 items is scored from zero (not at all) to three (nearly every day) such that 0–4, 5–9, 10–14, 15–19, and 20–27 points represent normal, mild, moderate, moderately severe, and severe depression, respectively (33). The reliability and validity of the Chinese version of the PHQ-9 for use with the general population were verified by Wang et al., who found a test-retest reliability of 0.860 and a Cronbach's α of 0.860 (34). The Cronbach's α of the PHQ-9 was 0.923 in this study.

Data Collection

With the support of the Health Commission of Shandong Province, the research team signed a research project cooperation agreement with the participating hospitals and obtained the informed consent of each participant. In this web-based questionnaire survey, the participants first registered their personal information using the official WeChat account of the Nurses' Health Cohort Study of Shandong. They then completed the electronic questionnaire sent by the WeChat official account. The questionnaire took about 10 to 15 min to complete. During data collection, the research team set up an independent cloud server and a MySQL database cluster. The collected electronic questionnaire data were stored in the database in real time using security encryption technology, and the data were protected *via* a disaster recovery backup mechanism. Data managers could access the data platform of Nurses' Health Cohort Study *via* an authentication mechanism to perform data interface calls, data maintenance, and data status monitoring.

Ethical Considerations

Participation in this study was voluntary, and the nurses provided electronic informed consent. The Shandong University Qilu Hospital Medical Ethics Committee approved the study (Registration number KYLL-202011-085).

Data Analysis

We conducted statistical analyses using R software version 4.0.5 (R Development Core Team, Vienna, Austria). This study had two dependent variables including depression and anxiety. The analysis had the following steps: First, the effect of shift work on depression and anxiety was verified in all nurses. Second, we explored the effects of different characteristics of shift work on depression and anxiety in shift nurses.

We used descriptive statistics to assess continuous variables [calculated as "mean ± standard deviation (SD)"] and categorical variables (calculated as "frequencies" and "percentages"). We performed one-way analysis of variance (ANOVA) to compare depression and anxiety levels in nurses according to different continuous variables. We assessed the distributions of characteristics between the different groups using the chi-square test for categorical variables. The Bonferroni correction was applied for correcting the multiple tests. Therefore, p-value <0.006 was considered statistically significant for the univariate analysis of demographic characteristics related to depression/anxiety in all nurses, and p-value <0.002 was considered statistically significant for the univariate analysis of demographic and shift work characteristics related to depression/anxiety in shift nurses.

We assessed the existence of multicollinearity by calculating the variance inflation factor (VIF) for all variables, and then performed multivariable ordered logistic regression analysis (35). If the univariate analysis revealed statistically significant variables, we decided whether to enter them into a multivariable ordinal logistic regression analysis. The goal of this analysis was to identify the main variables associated with depression and anxiety and to estimate the adjusted odds ratios (ORs) and 95% confidence intervals (CIs). According to Bonferroni correction, p-value <0.025 was considered statistically significant for the regression analysis.

RESULTS

Prevalence and Characteristics of Depression and Anxiety in Nurses

Our analysis included data from a total of 11,061 nurses from 20 hospitals in Shandong Province, China. Questionnaires with incomplete or inconsistent responses were excluded from the analysis, resulting in a completion rate of 83.00% (n = 9,181). See **Tables 1, 2** for summaries of the descriptive statistics related to the prevalence of depression and anxiety and the basic demographic characteristics of the nurses. Data from 9,181 participants were analyzed. Approximately 94.76% (n = 8,700) of the participants were women, 57.10% (n = 5,242) held primary titles, the average age was 33.24 ± 7.31 years, and the average length of service was 10.75 ± 7.61 years. The results showed that 55.85% (n = 5,128) of the nurses had some degree of anxiety (mild = 41.19%, moderate = 9.93%, severe = 4.73%), and 58.39% (n = 5,361) had some degree of depression (mild = 39.61%, moderate = 8.80%, moderately severe = 6.61%, severe = 3.37%).

Among the 9,181 nurses, 66.20% (n = 6,078) were shift nurses. As shown in **Tables 1**, **2**, the prevalence of depression and anxiety in shift nurses was statistically significantly higher than that among non-shift nurses. Among the shift nurses, 58.82% (n = 3,575) had some degree of anxiety (mild = 42.63%, moderate = 11.01%, severe = 5.18%), and 62.08% (n = 3,773) had some degree of depression (mild = 40.95%, moderate = 9.61%, moderately severe = 7.57%, severe = 3.95%).

Tables 3, **4** show the descriptive statistics of the prevalence of depression and anxiety, the basic demographic characteristics, and the characteristics of shift work in shift nurses. The average age and the average length of service of shift nurses were 31.06 ± 5.31 years and 8.42 ± 5.13 years, respectively. Among the shift nurses, 93.37% (n = 5,675) were women, 67.14% (n = 4,081) held primary titles, 53.09% (n = 3,227) worked in two shifts, and 60.50% (n = 3,677) had a schedule in which shifts were rotated in a clockwise direction.

Univariate Analysis of Demographic and Shift Work Characteristics Associated With Depression/Anxiety in Nurses

Tables 1, 2 also show the results of the univariate analysis of the depression and anxiety-related demographic characteristics in all nurses. According to the Bonferroni correction, a p-value <0.006 was considered as statistically significant in the above univariate analysis. We found that shift work significantly correlated with the levels of anxiety ($\chi^2 = 73.54$, $p < 0.001$) and depression ($\chi^2 = 123.16$, $p < 0.001$). Additionally, the number of years spent engaged in nursing significantly correlated with the levels of anxiety ($F = 5.30$, $p = 0.001$) and depression ($F = 6.30$, $p < 0.001$). The level of anxiety varied according to gender ($\chi^2 = 16.48$, $p < 0.001$), department ($\chi^2 = 65.23$, $p < 0.001$), and professional title ($\chi^2 = 37.93$, $p < 0.001$). Furthermore, the level of depression varied according to gender ($\chi^2 = 25.25$, $p < 0.001$), department ($\chi^2 = 73.49$, $p < 0.001$), and professional title ($\chi^2 = 59.27$, $p < 0.001$).

See **Tables 3**, **4** for the results of our univariate analysis of demographic and shift work characteristics related to depression and anxiety in shift nurses. According to the Bonferroni correction, a p-value <0.002 was considered as statistically significant in the above univariate analysis. Among the demographic variables, age was associated with anxiety level ($F = 5.74$, $p < 0.001$) and depression level ($F = 4.61$, $p = 0.001$) in shift nurses. Shift arrangement characteristics included the number of months engaged in shift work per year, the number of night shifts worked per month, working > 40 h/week during shift work, busyness during night shifts, and resting during night shifts, all of which correlated with levels of depression and anxiety. Physical and mental characteristics associated with depression and anxiety included physical fatigue/mental fatigue/physical discomfort during night shifts, psychological stress before/during/after night shifts, and the feeling of being refreshed after resting before/after night shifts. Personal habits during shift work associated with depression and anxiety levels included sleep quality before/after night shifts, using sleep medication before/after night shifts, food intake during shift work, and the timing of meals during shift work.

Multivariable Ordinal Logistic Regression Analysis of Demographic and Shift Work Characteristics Associated With Depression and Anxiety

Before performing the multivariable ordinal logistic regression analysis, we conducted a test for multicollinearity. We substituted dummy variables for the ordinal and nominal variables, and found that no variables had a VIF value >10. **Table 5** shows the results of the multivariable ordinal logistic regression analysis of demographic characteristics associated with depression (R^2 = 0.345) and anxiety (R^2 = 0.326) in all nurses. According to the Bonferroni correction, a p-value < 0.025 was considered as statistically significant in our regression analysis. The fully adjusted model indicated that shift work correlated with higher levels of depression and anxiety among all nurses (OR = 1.54, 95% CI: 1.40–1.69; and OR = 1.36, 95% CI: 1.24–1.50, respectively) when other demographic characteristics were held constant.

We next sought to determine the specific characteristics of shift work that affect depression (R^2 = 0.412) and anxiety (R^2 = 0.392) levels (**Table 6**). We found that in shift nurses, overtime work correlated with higher depression and anxiety levels. The ORs of depression and anxiety continuously increased with the amount of overtime work (i.e., from 1 week to 4 weeks per month), indicating that more overtime work increases the chance of depression and anxiety. Busyness during night shifts (OR = 1.44, 95% CI: 1.01–1.28) and overeating during shift work correlated with higher level of depression in shift nurses (OR = 1.25, 95% CI: 1.04–1.50).

Shift nurses often plan rest periods before and after night shifts. Therefore, we explored the effect of energy recovery after rest on depression and anxiety in shift nurses. Our results showed that the feeling of being refreshed after resting before a

TABLE 1 | Descriptive statistics and univariate analysis of demographic characteristics related to depression in all nurses ($N = 9,181$).

Variables	Total, *n* (%)	Depression, *n* (%)					$F/\chi2$[‡]	*p* value
		Normal	Mild	Moderate	Moderately severe	Severe		
Total	9,181 (100.00)	3,820 (41.61)	3,637 (39.61)	808 (8.80)	607 (6.61)	309 (3.37)		
Age, years (mean ± SD)	33.24 ± 7.31	33.58 ± 7.93	33.08 ± 6.81	33.20 ± 7.18	32.44 ± 6.49	32.58 ± 6.61	4.92	**<0.001**
Years of working (mean ± SD)	10.75 ± 7.61	11.19 ± 8.23	10.48 ± 7.16	10.67 ± 7.41	9.96 ± 6.77	10.21 ± 6.61	6.30	**<0.001**
Gender								
Male	481 (5.24)	174 (36.17)	178 (37.01)	53 (11.02)	53 (11.02)	23 (4.78)	25.25	**<0.001**
Female	8,700 (94.76)	3,646 (41.91)	3,459 (39.76)	755 (8.68)	554 (6.37)	286 (3.29)		
Education								
Associate's degree	922 (10.04)	420 (45.55)	334 (36.23)	78 (8.46)	64 (6.94)	26 (2.82)	8.58	0.379
Bachelor's degree	8,149 (88.76)	3,356 (41.18)	3,260 (40)	720 (8.84)	535 (6.57)	278 (3.41)		
Master's degree	110 (1.20)	44 (40)	43 (39.09)	10 (9.09)	8 (7.27)	5 (4.55)		
Marital status								
Unmarried	2,132 (23.22)	870 (40.81)	844 (39.59)	194 (9.1)	153 (7.18)	71 (3.33)	4.23	0.836
Married	6,861 (74.73)	2,872 (41.86)	2,719 (39.63)	598 (8.72)	438 (6.38)	234 (3.41)		
Others	188 (2.05)	78 (41.49)	74 (39.36)	16 (8.51)	16 (8.51)	4 (2.13)		
Department								
Internal medicine	2,678 (29.17)	1,063 (39.69)	1,083 (40.44)	241 (9)	182 (6.8)	109 (4.07)	73.49	**<0.001**
Surgery	1,998 (21.76)	820 (41.04)	786 (39.34)	172 (8.61)	147 (7.36)	73 (3.65)		
Emergency	498 (5.42)	193 (38.76)	187 (37.55)	62 (12.45)	39 (7.83)	17 (3.41)		
Gynecology and obstetrics	672 (7.32)	297 (44.2)	278 (41.37)	50 (7.44)	33 (4.91)	14 (2.08)		
Pediatrics	697 (7.59)	288 (41.32)	288 (41.32)	59 (8.46)	42 (6.03)	20 (2.87)		
Operating room	634 (6.91)	288 (45.43)	241 (38.01)	51 (8.04)	36 (5.68)	18 (2.84)		
Intensive care unit	573 (6.24)	200 (34.9)	240 (41.88)	56 (9.77)	53 (9.25)	24 (4.19)		
Outpatient	328 (3.57)	149 (45.43)	129 (39.33)	28 (8.54)	19 (5.79)	3 (0.91)		
Others	1,103 (12.01)	522 (47.33)	405 (36.72)	89 (8.07)	56 (5.08)	31 (2.81)		
Professional title[†]								
Primary	5,242 (57.10)	2,195 (41.87)	2,058 (39.26)	441 (8.41)	355 (6.77)	193 (3.68)	59.27	**<0.001**
Intermediate	3,471 (37.81)	1,366 (39.35)	1,424 (41.03)	328 (9.45)	241 (6.94)	112 (3.23)		
Senior	468 (5.10)	259 (55.34)	155 (33.12)	39 (8.33)	11 (2.35)	4 (0.85)		
Monthly income, CNY								
<3,000	841 (9.16)	362 (43.04)	335 (39.83)	65 (7.73)	52 (6.18)	27 (3.21)	15.25	0.228
3,000–5,999	5,190 (56.53)	2,124 (40.92)	2,067 (39.83)	450 (8.67)	365 (7.03)	184 (3.55)		
6,000–8,999	2,473 (26.94)	1,023 (41.37)	975 (39.43)	236 (9.54)	160 (6.47)	79 (3.19)		
≥9,000	677 (7.37)	311 (45.94)	260 (38.4)	57 (8.42)	30 (4.43)	19 (2.81)		
Shift work								
No	3,103 (33.80)	1,515 (48.82)	1,148 (37.00)	224 (7.22)	147 (4.74)	69 (2.22)	123.16	**<0.001**
Yes	6,078 (66.20)	2,305 (37.92)	2,489 (40.95)	584 (9.61)	460 (7.57)	240 (3.95)		

SD, standard deviation; CNY, China Yuan. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers ($p < 0.006$). [†]*Nursing professional titles can be divided into three categories: primary, intermediate and senior.*
[‡]*F for one-way analysis of variance (ANOVA) and $\chi2$ for chi-square test.*

TABLE 2 | Descriptive statistics and univariate analysis of demographic characteristics related to anxiety in all nurses ($N = 9,181$).

Variables	Total, *n* (%)	Anxiety, *n* (%)				$F/\chi2$[‡]	*p* value
		Normal	Mild	Moderate	Severe		
Total	9,181 (100.00)	4,053 (44.15)	3,782 (41.19)	912 (9.93)	434 (4.73)		
Age, years (mean ± SD)	33.24 ± 7.31	33.48 ± 7.79	33.14 ± 6.95	32.69 ± 6.83	32.98 ± 6.73	3.51	0.015
Years of working (mean ± SD)	10.75 ± 7.61	11.08 ± 8.12	10.56 ± 7.25	10.16 ± 7.00	10.49 ± 6.88	5.30	**0.001**
Gender							
Male	481 (5.24)	198 (41.16)	182 (37.84)	70 (14.55)	31 (6.44)	16.48	**<0.001**
Female	8,700 (94.76)	3,855 (44.31)	3,600 (41.38)	842 (9.68)	403 (4.63)		
Education							
Associate's degree	922 (10.04)	443 (48.05)	352 (38.18)	89 (9.65)	38 (4.12)	9.32	0.157
Bachelor's degree	8,149 (88.76)	3,569 (43.80)	3,378 (41.45)	810 (9.94)	392 (4.81)		
Master's degree	110 (1.20)	41 (37.27)	52 (47.27)	13 (11.82)	4 (3.64)		
Marital status							
Unmarried	2,132 (23.22)	935 (43.86)	880 (41.28)	236 (11.07)	81 (3.80)	9.38	0.153
Married	6,861 (74.73)	3,030 (44.16)	2,827 (41.20)	659 (9.61)	345 (5.03)		
Others	188 (2.05)	88 (46.81)	75 (39.89)	17 (9.04)	8 (4.26)		
Department							
Internal medicine	2,678 (29.17)	1,132 (42.27)	1,117 (41.71)	283 (10.57)	146 (5.45)	65.23	**<0.001**
Surgery	1,998 (21.76)	869 (43.49)	836 (41.84)	192 (9.61)	101 (5.06)		
Emergency	498 (5.42)	207 (41.57)	201 (40.36)	69 (13.86)	21 (4.22)		
Gynecology and obstetrics	672 (7.32)	321 (47.77)	275 (40.92)	46 (6.85)	30 (4.46)		
Pediatrics	697 (7.59)	296 (42.47)	309 (44.33)	64 (9.18)	28 (4.02)		
Operating room	634 (6.91)	291 (45.9)	261 (41.17)	57 (8.99)	25 (3.94)		
Intensive care unit	573 (6.24)	223 (38.92)	241 (42.06)	76 (13.26)	33 (5.76)		
Outpatient	328 (3.57)	171 (52.13)	126 (38.41)	23 (7.01)	8 (2.44)		
Others	1,103 (12.01)	543 (49.23)	416 (37.72)	102 (9.25)	42 (3.81)		
Professional title[†]							
Primary	5,242 (57.10)	2,342 (44.68)	2,133 (40.69)	506 (9.65)	261 (4.98)	37.93	**<0.001**
Intermediate	3,471 (37.81)	1,455 (41.92)	1,475 (42.49)	379 (10.92)	162 (4.67)		
Senior	468 (5.10)	256 (54.7)	174 (37.18)	27 (5.77)	11 (2.35)		
Monthly income, CNY							
<3,000	841 (9.16)	388 (46.14)	331 (39.36)	89 (10.58)	33 (3.92)	5.37	0.801
3,000–5,999	5,190 (56.53)	2,274 (43.82)	2,145 (41.33)	515 (9.92)	256 (4.93)		
6,000–8,999	2,473 (26.94)	1,084 (43.83)	1,026 (41.49)	250 (10.11)	113 (4.57)		
≥9,000	677 (7.37)	307 (45.35)	280 (41.36)	58 (8.57)	32 (4.73)		
Shift work							
No	3,103 (33.80)	1,550 (49.95)	1,191 (38.38)	243 (7.83)	119 (3.83)	73.54	**<0.001**
Yes	6,078 (66.20)	2,503 (41.18)	2,591 (42.63)	669 (11.01)	315 (5.18)		

SD, standard deviation; CNY, China Yuan. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers ($p < 0.006$). [†]Nursing professional titles can be divided into three categories: primary, intermediate and senior. [‡]F for one-way analysis of variance (ANOVA) and $\chi2$ for chi-square test.

TABLE 3 | Descriptive statistics and univariate analysis of demographic and shift work characteristics related to depression in shift nurses (*N* = 6,078).

Variables	Total	Depression, *n* (%)					$F/\chi^{2§}$	*p*value
		Normal	Mild	Moderate	Moderately severe	Severe		
Total	6,078 (100.00)	2,305 (37.92)	2,489 (40.95)	584 (9.61)	460 (7.57)	240 (3.95)		
Age, years (mean ± SD)	31.06 ± 5.31	30.73 ± 5.51	31.18 ± 5.06	31.17 ± 5.27	31.53 ± 5.37	31.77 ± 5.63	4.61	**0.001**
Years of working (mean ± SD)	8.42 ± 5.13	8.24 ± 5.28	8.41 ± 4.93	8.54 ± 4.88	8.81 ± 5.35	9.24 ± 5.66	2.97	0.018
Fatigue scores (mean ± SD)								
Physical fatigue scores	5.48 ± 2.73	4.05 ± 2.84	6.14 ± 2.26	6.74 ± 1.80	6.76 ± 2.36	6.73 ± 2.52	320.92	**<0.001**
Mental fatigue scores	2.75 ± 1.44	2.18 ± 1.37	2.87 ± 1.36	3.52 ± 1.42	3.46 ± 1.17	3.67 ± 1.22	215.08	**<0.001**
Gender								
Male	403 (6.63)	136 (33.75)	151 (37.47)	48 (11.91)	47 (11.66)	21 (5.21)	16.95	0.002
Female	5,675 (93.37)	2,169 (38.22)	2,338 (41.2)	536 (9.44)	413 (7.28)	219 (3.86)		
Education								
Associate's degree	649 (10.68)	275 (42.37)	245 (37.75)	59 (9.09)	52 (8.01)	18 (2.77)	9.90	0.272
Bachelor's degree	5,392 (88.71)	2,019 (37.44)	2,228 (41.32)	521 (9.66)	404 (7.49)	220 (4.08)		
Master's degree	37 (0.61)	11 (29.73)	16 (43.24)	4 (10.81)	4 (10.81)	2 (5.41)		
Marital status								
Unmarried	1,811 (29.80)	710 (39.2)	733 (40.47)	173 (9.55)	132 (7.29)	63 (3.48)	6.34	0.609
Married	4,167 (68.56)	1,550 (37.2)	1,718 (41.23)	403 (9.67)	321 (7.7)	175 (4.2)		
Others	100 (1.65)	45 (45)	38 (38)	8 (8)	7 (7)	2 (2)		
Department								
Internal medicine	1,851 (30.45)	690 (37.28)	768 (41.49)	175 (9.45)	139 (7.51)	79 (4.27)	33.45	0.397
Surgery	1,472 (24.22)	557 (37.84)	594 (40.35)	143 (9.71)	121 (8.22)	57 (3.87)		
Emergency	396 (6.52)	141 (35.61)	154 (38.89)	53 (13.38)	31 (7.83)	17 (4.29)		
Gynecology and obstetrics	476 (7.83)	198 (41.6)	203 (42.65)	36 (7.56)	26 (5.46)	13 (2.73)		
Pediatrics	497 (8.18)	192 (38.63)	215 (43.26)	44 (8.85)	32 (6.44)	14 (2.82)		
Operating room	359 (5.91)	142 (39.55)	144 (40.11)	39 (10.86)	20 (5.57)	14 (3.9)		
Intensive care unit	499 (8.21)	174 (34.87)	204 (40.88)	49 (9.82)	50 (10.02)	22 (4.41)		
Outpatient	32 (0.53)	11 (34.38)	12 (37.5)	4 (12.5)	4 (12.5)	1 (3.12)		
Others	496 (8.16)	200 (40.32)	195 (39.31)	41 (8.27)	37 (7.46)	23 (4.64)		
Professional title†								
Primary	4,081 (67.14)	1,613 (39.52)	1,640 (40.19)	377 (9.24)	290 (7.11)	161 (3.95)	19.19	0.014
Intermediate	1,960 (32.25)	676 (34.49)	838 (42.76)	201 (10.26)	167 (8.52)	78 (3.98)		
Senior	37 (0.61)	16 (43.24)	11 (29.73)	6 (16.22)	3 (8.11)	1 (2.7)		

(Continued)

TABLE 3 | Continued

Variables	Total	Depression, *n* (%)					$F/\chi^{2§}$	*p*value
		Normal	Mild	Moderate	Moderately severe	Severe		
Monthly income, CNY								
<3,000	556 (9.15)	226 (40.65)	230 (41.37)	44 (7.91)	34 (6.12)	22 (3.96)	15.44	0.218
3,000–5,999	3,790 (62.36)	1,474 (38.89)	1,530 (40.37)	354 (9.34)	292 (7.7)	140 (3.69)		
6,000–8,999	1,466 (24.12)	515 (35.13)	615 (41.95)	156 (10.64)	115 (7.84)	65 (4.43)		
≥9,000	266 (4.38)	90 (33.83)	114 (42.86)	30 (11.28)	19 (7.14)	13 (4.89)		
Work schedule[‡]								
Two shifts	3,227 (53.09)	1,196 (37.06)	1,363 (42.24)	316 (9.79)	239 (7.41)	113 (3.5)	24.47	0.002
Three shifts	2,649 (43.58)	1,044 (39.41)	1,054 (39.79)	238 (8.98)	196 (7.4)	117 (4.42)		
Others	202 (3.32)	65 (32.18)	72 (35.64)	30 (14.85)	25 (12.38)	10 (4.95)		
Shift rotation direction								
Clockwise	3,677 (60.50)	1,463 (39.79)	1,477 (40.17)	327 (8.89)	267 (7.26)	143 (3.89)	16.12	0.003
Counterclockwise	2,401 (39.50)	842 (35.07)	1,012 (42.15)	257 (10.7)	193 (8.04)	97 (4.04)		
Shift work experience								
0–5 years	1,946 (32.02)	801 (41.16)	779 (40.03)	165 (8.48)	139 (7.14)	62 (3.19)	24.62	0.077
6–10 years	2,218 (36.49)	821 (37.02)	916 (41.3)	223 (10.05)	168 (7.57)	90 (4.06)		
11–15 years	1,406 (23.13)	493 (35.06)	598 (42.53)	147 (10.46)	108 (7.68)	60 (4.27)		
16–20 years	384 (6.32)	145 (37.76)	150 (39.06)	36 (9.38)	34 (8.85)	19 (4.95)		
>20 years	124 (2.04)	45 (36.29)	46 (37.1)	13 (10.48)	11 (8.87)	9 (7.26)		
Months of shift work per year								
1–3 months	289 (4.75)	137 (47.4)	108 (37.37)	32 (11.07)	11 (3.81)	1 (0.35)	53.19	**<0.001**
10–12 months	4,757 (78.27)	1,742 (36.62)	1,949 (40.97)	456 (9.59)	392 (8.24)	218 (4.58)		
7–9 months	538 (8.85)	218 (40.52)	231 (42.94)	46 (8.55)	32 (5.95)	11 (2.04)		
4–6 months	494 (8.13)	208 (42.11)	201 (40.69)	50 (10.12)	25 (5.06)	10 (2.02)		
Night shifts per month								
≤4	1,267 (20.85)	561 (44.28)	486 (38.36)	106 (8.37)	67 (5.29)	47 (3.71)	52.03	**<0.001**
5–9	4,150 (68.28)	1,538 (37.06)	1,724 (41.54)	412 (9.93)	319 (7.69)	157 (3.78)		
≥10	661 (10.88)	206 (31.16)	279 (42.21)	66 (9.98)	74 (11.2)	36 (5.45)		
Interval between night shifts								
≤4 days	1,955 (32.17)	714 (36.52)	797 (40.77)	198 (10.13)	164 (8.39)	82 (4.19)	9.00	0.342
5–7 days	3,474 (57.16)	1,332 (38.34)	1,424 (40.99)	325 (9.36)	261 (7.51)	132 (3.8)		
≥8 days	649 (10.68)	259 (39.91)	268 (41.29)	61 (9.4)	35 (5.39)	26 (4.01)		

(Continued)

TABLE 3 | Continued

Variables	Total	Depression, *n* (%)					$F/\chi^{2§}$	*p*value
		Normal	Mild	Moderate	Moderately severe	Severe		
Night shift staffing								
1	1,932 (31.79)	737 (38.15)	783 (40.53)	187 (9.68)	140 (7.25)	85 (4.4)	7.00	0.858
2 (take turns)	2,212 (36.39)	860 (38.88)	910 (41.14)	203 (9.18)	162 (7.32)	77 (3.48)		
2 (take no turns)	838 (13.79)	306 (36.52)	353 (42.12)	82 (9.79)	66 (7.88)	31 (3.7)		
≥3	1,096 (18.03)	402 (36.68)	443 (40.42)	112 (10.22)	92 (8.39)	47 (4.29)		
Psychological stress before night shifts								
No	633 (10.41)	428 (67.61)	145 (22.91)	30 (4.74)	18 (2.84)	12 (1.9)	266.25	**<0.001**
Yes	5,445 (89.59)	1,877 (34.47)	2,344 (43.05)	554 (10.17)	442 (8.12)	228 (4.19)		
Psychological stress during night shifts								
No	698 (11.48)	474 (67.91)	162 (23.21)	33 (4.73)	19 (2.72)	10 (1.43)	304.22	**<0.001**
Yes	5,380 (88.52)	1,831 (34.03)	2,327 (43.25)	551 (10.24)	441 (8.2)	230 (4.28)		
Psychological stress after night shifts								
No	2,546 (41.89)	1,336 (52.47)	889 (34.92)	181 (7.11)	99 (3.89)	41 (1.61)	451.09	**<0.001**
Yes	3,532 (58.11)	969 (27.43)	1,600 (45.3)	403 (11.41)	361 (10.22)	199 (5.63)		
Using sleep medication before night shifts								
Never/rarely	4,729 (77.81)	2,011 (42.52)	1,911 (40.41)	429 (9.07)	261 (5.52)	117 (2.47)	410.19	**<0.001**
Sometimes	1,130 (18.59)	237 (20.97)	511 (45.22)	135 (11.95)	159 (14.07)	88 (7.79)		
Often	219 (3.60)	57 (26.03)	67 (30.59)	20 (9.13)	40 (18.26)	35 (15.98)		
Using sleep medication after night shifts								
Never/rarely	4,930 (81.11)	2,074 (42.07)	2,006 (40.69)	442 (8.97)	277 (5.62)	131 (2.66)	401.41	**<0.001**
Sometimes	946 (15.56)	184 (19.45)	425 (44.93)	115 (12.16)	140 (14.8)	82 (8.67)		
Often	202 (3.32)	47 (23.27)	58 (28.71)	27 (13.37)	43 (21.29)	27 (13.37)		
Physical discomfort during night shifts								
No	1,935 (31.84)	1,116 (57.67)	630 (32.56)	93 (4.81)	69 (3.57)	27 (1.4)	515.92	**<0.001**
Yes	4,143 (68.16)	1,189 (28.7)	1,859 (44.87)	491 (11.85)	391 (9.44)	213 (5.14)		
Busyness during night shifts								
No	1,739 (28.61)	836 (48.07)	645 (37.09)	133 (7.65)	85 (4.89)	40 (2.3)	124.67	**<0.001**
Yes	4,339 (71.39)	1,469 (33.86)	1,844 (42.5)	451 (10.39)	375 (8.64)	200 (4.61)		
Feeling of being refreshed after resting before night shifts								
No	1,657 (27.26)	373 (22.51)	682 (41.16)	230 (13.88)	214 (12.91)	158 (9.54)	452.10	**<0.001**
Yes	4,421 (72.74)	1,932 (43.7)	1,807 (40.87)	354 (8.01)	246 (5.56)	82 (1.85)		

(Continued)

TABLE 3 | Continued

Variables	Total	Depression, *n* (%)					$F/\chi^{2§}$	*p*value
		Normal	Mild	Moderate	Moderately severe	Severe		
Feeling of being refreshed after resting after night shifts								
No	767 (12.62)	150 (19.56)	306 (39.9)	92 (11.99)	116 (15.12)	103 (13.43)	349.52	**<0.001**
Yes	5,311 (87.38)	2,155 (40.58)	2,183 (41.1)	492 (9.26)	344 (6.48)	137 (2.58)		
Sleep quality before night shifts								
Normal	3,996 (65.75)	1,787 (44.72)	1,599 (40.02)	299 (7.48)	223 (5.58)	88 (2.2)	350.45	**<0.001**
Poor	2,082 (34.25)	518 (24.88)	890 (42.75)	285 (13.69)	237 (11.38)	152 (7.3)		
Sleep quality after night shifts								
Normal	4,700 (77.33)	1,978 (42.09)	1,914 (40.72)	405 (8.62)	295 (6.28)	108 (2.3)	304.90	**<0.001**
Poor	1,378 (22.67)	327 (23.73)	575 (41.73)	179 (12.99)	165 (11.97)	132 (9.58)		
Food intake during shift work								
Normal	2,085 (34.30)	1,003 (48.11)	779 (37.36)	154 (7.39)	102 (4.89)	47 (2.25)	177.79	**<0.001**
More	749 (12.32)	252 (33.64)	291 (38.85)	88 (11.75)	69 (9.21)	49 (6.54)		
Less	3,244 (53.37)	1,050 (32.37)	1,419 (43.74)	342 (10.54)	289 (8.91)	144 (4.44)		
Meal timing during shift work								
Regular	2,302 (37.87)	1,068 (46.39)	896 (38.92)	172 (7.47)	123 (5.34)	43 (1.87)	168.73	**<0.001**
Early	1,008 (16.58)	372 (36.9)	393 (38.99)	98 (9.72)	88 (8.73)	57 (5.65)		
Delayed	2,768 (45.54)	865 (31.25)	1,200 (43.35)	314 (11.34)	249 (9)	140 (5.06)		
Working > 40 h/week during shift work								
Never/rarely	1,148 (18.89)	631 (54.97)	375 (32.67)	75 (6.53)	38 (3.31)	29 (2.53)	273.59	**<0.001**
1 week/month	1,160 (19.09)	461 (39.74)	496 (42.76)	100 (8.62)	78 (6.72)	25 (2.16)		
2 weeks/month	1,069 (17.59)	368 (34.42)	479 (44.81)	104 (9.73)	90 (8.42)	28 (2.62)		
3 weeks/month	638 (10.50)	219 (34.33)	267 (41.85)	70 (10.97)	62 (9.72)	20 (3.13)		
4 weeks/month	2,063 (33.94)	626 (30.34)	872 (42.27)	235 (11.39)	192 (9.31)	138 (6.69)		
Rest during night shifts								
No	1,868 (30.73)	702 (37.58)	714 (38.22)	169 (9.05)	175 (9.37)	108 (5.78)	40.36	**<0.001**
Yes	4,210 (69.27)	1,603 (38.08)	1,775 (42.16)	415 (9.86)	285 (6.77)	132 (3.14)		

SD, standard deviation; CNY, China Yuan. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers ($p < 0.002$). †Nursing professional titles can be divided into three categories: primary, intermediate and senior. ‡Other work schedules include long-term irregular shifts for a variety of reasons. §F for one-way analysis of variance (ANOVA) and $\chi 2$ for chi-square test.

TABLE 4 | Descriptive statistics and univariate analysis of demographic and shift work characteristics related to anxiety in shift nurses (*N* = 6,078).

Variables	Total	Anxiety, *n* (%)				$F/\chi^{2\S}$	*p* value
		Normal	Mild	Moderate	Severe		
Total	6,078 (100.00)	2,503 (41.18)	2,591 (42.63)	669 (11.01)	315 (5.18)		
Age, years (mean ± SD)	31.06 ± 5.31	30.79 ± 5.43	31.17 ± 5.14	31.26 ± 5.43	31.93 ± 5.37	5.74	**<0.001**
Years of working (mean ± SD)	8.42 ± 5.13	8.25 ± 5.20	8.46 ± 4.97	8.52 ± 5.33	9.31 ± 5.30	4.20	0.006
Fatigue scores (mean ± SD)							
Physical fatigue scores	5.48 ± 2.73	4.21 ± 2.85	6.23 ± 2.22	6.68 ± 2.26	6.75 ± 2.34	370.12	**<0.001**
Mental fatigue scores	2.75 ± 1.44	2.26 ± 1.40	2.95 ± 1.38	3.39 ± 1.28	3.54 ± 1.29	205.50	**<0.001**
Gender							
Male	403 (6.63)	162 (40.20)	150 (37.22)	65 (16.13)	26 (6.45)	14.69	0.002
Female	5,675 (93.37)	2,341 (41.25)	2,441 (43.01)	604 (10.64)	289 (5.09)		
Education							
Associate's degree	649 (10.68)	294 (45.3)	262 (40.37)	69 (10.63)	24 (3.70)	10.32	0.112
Bachelor's degree	5,392 (88.71)	2,198 (40.76)	2,308 (42.80)	596 (11.05)	290 (5.38)		
Master's degree	37 (0.61)	11 (29.73)	21 (56.76)	4 (10.81)	1 (2.70)		
Marital status							
Unmarried	1,811 (29.80)	772 (42.63)	766 (42.30)	206 (11.37)	67 (3.70)	17.14	0.009
Married	4,167 (68.56)	1,683 (40.39)	1,785 (42.84)	453 (10.87)	246 (5.90)		
Others	100 (1.65)	48 (48.00)	40 (40.00)	10 (10.00)	2 (2.00)		
Department							
Internal medicine	1,851 (30.45)	749 (40.46)	789 (42.63)	205 (11.08)	108 (5.83)	29.10	0.216
Surgery	1,472 (24.22)	604 (41.03)	638 (43.34)	151 (10.26)	79 (5.37)		
Emergency	396 (6.52)	156 (39.39)	168 (42.42)	55 (13.89)	17 (4.29)		
Gynecology and obstetrics	476 (7.83)	216 (45.38)	200 (42.02)	36 (7.56)	24 (5.04)		
Pediatrics	497 (8.18)	200 (40.24)	228 (45.88)	53 (10.66)	16 (3.22)		
Operating room	359 (5.91)	153 (42.62)	152 (42.34)	39 (10.86)	15 (4.18)		
Intensive care unit	499 (8.21)	195 (39.08)	205 (41.08)	70 (14.03)	29 (5.81)		
Outpatient	32 (0.53)	14 (43.75)	11 (34.38)	6 (18.75)	1 (3.12)		
Others	496 (8.16)	216 (43.55)	200 (40.32)	54 (10.89)	26 (5.24)		
Professional title[†]							
Primary	4,081 (67.14)	1,742 (42.69)	1,703 (41.73)	427 (10.46)	209 (5.12)	14.57	0.024
Intermediate	1,960 (32.25)	744 (37.96)	875 (44.64)	238 (12.14)	103 (5.26)		
Senior	37 (0.61)	17 (45.95)	13 (35.14)	4 (10.81)	3 (8.11)		

(Continued)

TABLE 4 | Continued

Variables	Total	Anxiety, *n* (%)				$F/\chi^{2§}$	*p* value
		Normal	Mild	Moderate	Severe		
Monthly income, CNY							
<3,000	556 (9.15)	243 (43.71)	229 (41.19)	63 (11.33)	21 (3.78)	16.06	0.066
3,000–5,999	3,790 (62.36)	1,588 (41.90)	1,598 (42.16)	410 (10.82)	194 (5.12)		
6,000–8,999	1,466 (24.12)	575 (39.22)	634 (43.25)	176 (12.01)	81 (5.53)		
≥9,000	266 (4.38)	97 (36.47)	130 (48.87)	20 (7.52)	19 (7.14)		
Work schedule[‡]							
Two shifts	3,227 (53.09)	1,317 (40.81)	1,407 (43.6)	343 (10.63)	160 (4.96)	16.78	0.010
Three shifts	2,649 (43.58)	1,119 (42.24)	1,100 (41.53)	290 (10.95)	140 (5.29)		
Others	202 (3.32)	67 (33.17)	84 (41.58)	36 (17.82)	15 (7.43)		
Shift rotation direction							
Clockwise	3,677 (60.50)	1,572 (42.75)	1,517 (41.26)	392 (10.66)	196 (5.33)	11.10	0.011
Counterclockwise	2,401 (39.50)	931 (38.78)	1,074 (44.73)	277 (11.54)	119 (4.96)		
Shift work experience							
0–5 years	1,946 (32.02)	853 (43.83)	806 (41.42)	213 (10.95)	74 (3.80)	20.58	0.057
6–10 years	2,218 (36.49)	901 (40.62)	952 (42.92)	244 (11.00)	121 (5.46)		
11–15 years	1,406 (23.13)	547 (38.9)	615 (43.74)	158 (11.24)	86 (6.12)		
16–20 years	384 (6.32)	158 (41.15)	163 (42.45)	39 (10.16)	24 (6.25)		
>20 years	124 (2.04)	44 (35.48)	55 (44.35)	15 (12.10)	10 (8.06)		
Months of shift work per year							
1–3 months	289 (4.75)	152 (52.60)	100 (34.60)	31 (10.73)	6 (2.08)	45.92	**<0.001**
10–12 months	4,757 (78.27)	1,916 (40.28)	2,016 (42.38)	551 (11.58)	274 (5.76)		
7–9 months	538 (8.85)	211 (39.22)	266 (49.44)	42 (7.81)	19 (3.53)		
4–6 months	494 (8.13)	224 (45.34)	209 (42.31)	45 (9.11)	16 (3.24)		
Night shifts per month							
≤4	1,267 (20.85)	602 (47.51)	484 (38.2)	122 (9.63)	59 (4.66)	34.89	**<0.001**
5–9	4,150 (68.28)	1,655 (39.88)	1,825 (43.98)	462 (11.13)	208 (5.01)		
≥10	661 (10.88)	246 (37.22)	282 (42.66)	85 (12.86)	48 (7.26)		
Interval between night shifts							
≤4 days	1,955 (32.17)	779 (39.85)	827 (42.30)	241 (12.33)	108 (5.52)	7.87	0.248
5–7 days	3,474 (57.16)	1,443 (41.54)	1,488 (42.83)	368 (10.59)	175 (5.04)		
≥8 days	649 (10.68)	281 (43.30)	276 (42.53)	60 (9.24)	32 (4.93)		
Night shift staffing							
1	1,932 (31.79)	815 (42.18)	799 (41.36)	218 (11.28)	100 (5.18)	10.58	0.306
2 (take turns)	2,212 (36.39)	916 (41.41)	953 (43.08)	220 (9.95)	123 (5.56)		
2 (take no turns)	838 (13.79)	322 (38.42)	382 (45.58)	97 (11.58)	37 (4.42)		
≥3	1,096 (18.03)	450 (41.06)	457 (41.70)	134 (12.23)	55 (5.02)		

(Continued)

TABLE 4 | Continued

Variables	Total	Anxiety, *n* (%)				$F/\chi^{2§}$	*p* value
		Normal	Mild	Moderate	Severe		
Psychological stress before night shifts							
No	633 (10.41)	455 (71.88)	138 (21.8)	27 (4.27)	13 (2.05)	276.13	**<0.001**
Yes	5,445 (89.59)	2,048 (37.61)	2,453 (45.05)	642 (11.79)	302 (5.55)		
Psychological stress during night shifts							
No	698 (11.48)	508 (72.78)	150 (21.49)	29 (4.15)	11 (1.58)	327.28	**<0.001**
Yes	5,380 (88.52)	1,995 (37.08)	2,441 (45.37)	640 (11.9)	304 (5.65)		
Psychological stress after night shifts							
No	2,546 (41.89)	1452 (57.03)	879 (34.52)	154 (6.05)	61 (2.40)	498.26	**<0.001**
Yes	3,532 (58.11)	1,051 (29.76)	1,712 (48.47)	515 (14.58)	254 (7.19)		
Using sleep medication before night shifts							
Never/rarely	4,729 (77.81)	2,167 (45.82)	1,956 (41.36)	424 (8.97)	182 (3.85)	296.25	**<0.001**
Sometimes	1,130 (18.59)	280 (24.78)	549 (48.58)	203 (17.96)	98 (8.67)		
Often	219 (3.60)	56 (25.57)	86 (39.27)	42 (19.18)	35 (15.98)		
Using sleep medication after night shifts							
Never/rarely	4,930 (81.11)	2,234 (45.31)	2,046 (41.5)	453 (9.19)	197 (4.00)	288.21	**<0.001**
Sometimes	946 (15.56)	217 (22.94)	473 (50.00)	167 (17.65)	89 (9.41)		
Often	202 (3.32)	52 (25.74)	72 (35.64)	49 (24.26)	29 (14.36)		
Physical discomfort during night shifts							
No	1,935 (31.84)	1,151 (59.48)	637 (32.92)	117 (6.05)	30 (1.55)	429.40	**<0.001**
Yes	4,143 (68.16)	1,352 (32.63)	1,954 (47.16)	552 (13.32)	285 (6.88)		
Busyness during night shifts							
No	1,739 (28.61)	867 (49.86)	677 (38.93)	152 (8.74)	43 (2.47)	98.22	**<0.001**
Yes	4,339 (71.39)	1,636 (37.70)	1,914 (44.11)	517 (11.92)	272 (6.27)		
Feeling of being refreshed after resting before night shifts							
No	1,657 (27.26)	408 (24.62)	774 (46.71)	282 (17.02)	193 (11.65)	419.09	**<0.001**
Yes	4,421 (72.74)	2,095 (47.39)	1,817 (41.10)	387 (8.75)	122 (2.76)		
Feeling of being refreshed after resting after night shifts							
No	767 (12.62)	182 (23.73)	324 (42.24)	148 (19.3)	113 (14.73)	274.22	**<0.001**
Yes	5,311 (87.38)	2,321 (43.70)	2,267 (42.68)	521 (9.81)	202 (3.80)		
Sleep quality before night shifts							
Normal	3,996 (65.75)	1,904 (47.65)	1,645 (41.17)	326 (8.16)	121 (3.03)	314.81	**<0.001**
Poor	2,082 (34.25)	599 (28.77)	946 (45.44)	343 (16.47)	194 (9.32)		

(Continued)

TABLE 4 | Continued

Variables	Total	Anxiety, *n* (%)				$F/\chi^{2\S}$	*p* value
		Normal	Mild	Moderate	Severe		
Sleep quality after night shifts							
Normal	4,700 (77.33)	2,118 (45.06)	1,971 (41.94)	445 (9.47)	166 (3.53)	231.81	**<0.001**
Poor	1,378 (22.67)	385 (27.94)	620 (44.99)	224 (16.26)	149 (10.81)		
Food intake during shift work							
Normal	2,085 (34.30)	1,051 (50.41)	798 (38.27)	173 (8.30)	63 (3.02)	133.62	**<0.001**
More	749 (12.32)	276 (36.85)	317 (42.32)	102 (13.62)	54 (7.21)		
Less	3,244 (53.37)	1,176 (36.25)	1,476 (45.5)	394 (12.15)	198 (6.10)		
Meal timing during shift work							
Regular	2,302 (37.87)	1,141 (49.57)	904 (39.27)	195 (8.47)	62 (2.69)	141.66	**<0.001**
Early	1,008 (16.58)	384 (38.10)	432 (42.86)	123 (12.20)	69 (6.85)		
Delayed	2,768 (45.54)	978 (35.33)	1255 (45.34)	351 (12.68)	184 (6.65)		
Working > 40 h/week during shift work							
Never/rarely	1,148 (18.89)	671 (58.45)	370 (32.23)	75 (6.53)	32 (2.79)	261.40	**<0.001**
1 week/month	1,160 (19.09)	503 (43.36)	512 (44.14)	113 (9.74)	32 (2.76)		
2 weeks/month	1,069 (17.59)	401 (37.51)	494 (46.21)	134 (12.54)	40 (3.74)		
3 weeks/month	638 (10.50)	234 (36.68)	289 (45.3)	77 (12.07)	38 (5.96)		
4 weeks/month	2,063 (33.94)	694 (33.64)	926 (44.89)	270 (13.09)	173 (8.39)		
Rest during night shifts							
No	1,868 (30.73)	757 (40.52)	731 (39.13)	246 (13.17)	134 (7.17)	40.10	**<0.001**
Yes	4,210 (69.27)	1,746 (41.47)	1,860 (44.18)	423 (10.05)	181 (4.30)		

SD, standard deviation; CNY, China Yuan. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers ($p < 0.002$). †Nursing professional titles can be divided into three categories: primary, intermediate and senior. ‡Other work schedules include long-term irregular shifts for a variety of reasons. §F for one-way analysis of variance (ANOVA) and $\chi 2$ for chi-square test.

TABLE 5 | Multivariable ordinal logistic regression analysis of demographic characteristics associated with depression and anxiety in all nurses (N = 9,181).

Variables	Depression		Anxiety	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**
Age (for every additional year)	1.00 (0.99, 1.02)	0.673	1.00 (0.99, 1.02)	0.442
Years of working (for every additional year)	1.00 (0.99, 1.01)	0.686	0.99 (0.98, 1.00)	0.232
Gender (ref: Male)				
Female	0.74 (0.61, 0.89)	**0.001**	0.83 (0.69, 1.01)	0.056
Department (ref: Internal medicine)				
Surgery	0.94 (0.84, 1.05)	0.251	0.92 (0.83, 1.03)	0.148
Emergency	0.99 (0.83, 1.19)	0.941	0.98 (0.82, 1.18)	0.856
Gynecology and obstetrics	0.78 (0.66, 0.91)	**0.002**	0.77 (0.65, 0.90)	**0.001**
Pediatrics	0.89 (0.76, 1.04)	0.135	0.92 (0.79, 1.08)	0.316
Operating room	0.79 (0.67, 0.94)	**0.007**	0.85 (0.72, 1.01)	0.061
Intensive care unit	1.07 (0.90, 1.27)	0.428	1.07 (0.90, 1.27)	0.466
Outpatient	0.98 (0.78, 1.22)	0.842	0.77 (0.62, 0.97)	0.026
Others	0.81 (0.70, 0.92)	**0.002**	0.81 (0.71, 0.93)	**0.003**
Professional title† (ref: Primary)				
Intermediate	1.22 (1.10, 1.36)	**<0.001**	1.24 (1.11, 1.38)	**<0.001**
Senior	0.81 (0.63, 1.04)	0.096	0.90 (0.70, 1.15)	0.396
Shift work (ref: No)				
Yes	1.54 (1.40, 1.69)	**<0.001**	1.36 (1.24, 1.50)	**<0.001**

OR, odds ratio; CI, confidence interval; ref, reference group. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers (p < 0.025).
†Nursing professional titles can be divided into three categories: primary, intermediate and senior.

night shift significantly correlated with lower levels of depression and anxiety in shift nurses (OR = 0.72, 95% CI: 0.64–0.81; and OR = 0.69, 95% CI: 0.61–0.78, respectively). Similarly, the feeling of being refreshed after resting after a night shift was associated with reduced depression and anxiety in shift nurses (OR = 0.71, 95% CI: 0.61–0.83; and OR = 0.75, 95% CI: 0.64–0.88, respectively). We investigated whether the quality of sleep before and after night shifts affected depression and anxiety levels in shift nurses. Our results showed that poor sleep quality before or after night shifts was associated with greater levels of anxiety (OR = 1.19, 95% CI: 1.06–1.34; and OR = 1.18, 95% CI: 1.04–1.34, respectively) and depression (OR = 1.19, 95% CI: 1.06–1.33; and OR = 1.29, 95% CI: 1.44–1.47, respectively) in shift nurses. Moreover, both pre- and post-shift use of sleep medication significantly correlated with greater levels of depression and anxiety.

We next examined the effects of shift-related physical and psychological factors on mental health. We found that psychological stress related to night shifts negatively impacted depression and anxiety in shift nurses according to the time period. For example, psychological stress during night shifts led to higher anxiety levels (OR = 1.51, 95% CI: 1.16–1.98), whereas psychological stress after night shifts led to higher levels of both anxiety (OR = 1.73, 95% CI: 1.54–1.94) and depression (OR = 1.51, 95% CI: 1.35–1.69). Furthermore, physical discomfort during night shifts was a risk factor for increased levels of depression and anxiety (OR = 1.62, 95% CI: 1.43–1.83; and OR = 1.46, 95% CI: 1.29–1.65, respectively). Finally, physical fatigue correlated with greater levels of depression and anxiety (OR = 1.20, 95% CI: 1.18–1.23; and OR = 1.19, 95% CI: 1.17–1.22, respectively), as was the case with psychological fatigue (OR = 1.26, 95% CI: 1.21–1.31; and OR = 1.26, 95% CI: 1.21–1.31, respectively). The ORs of depression and anxiety for psychological fatigue were greater than those for physical fatigue.

DISCUSSION

Prevalence of Depression and Anxiety Among Nurses

In this study, 55.85% of all nurses surveyed, and 58.82% of shift work nurses surveyed reported varying levels of anxiety. This prevalence was higher than that reported by health care workers in a previous Chinese study (44.6%) (36) and roughly the same as that in a Spanish study (58.6%) (37). In this study, 14.66–16.19% of nurses showed moderate to severe anxiety, which was higher than that in Japanese nurses (11.10%) (38). In addition, 58.39% of all nurses surveyed, and 62.08% of shift work nurses surveyed had varying degrees of depression, which was higher than the prevalence reported by Lai et al. in China (50.4%) (36), that reported by Awano et al. in Japan (34.90%) (38), and that reported by Luceño-Moreno et al. in Spain (46.0%) (37). The prevalence of depression among nurses in the Korean Nurses' Health Cohort was 64.80%, which was roughly the same as that in our study (25). These differences in the prevalence of depression and anxiety may be related to varying regional and social backgrounds among study populations. In the context of infection prevention and control during the COVID-19 pandemic, nurses in China had a heavier workload and increased

TABLE 6 | Multivariable ordinal logistic regression analysis of demographic and shift work characteristics associated with depression and anxiety in shift nurses (*N* = 6,078).

Variables	**Depression**		**Anxiety**	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**
Age (for every additional year)	0.99 (0.98, 1.00)	0.139	0.99 (0.98, 1.00)	0.197
Months of shift work per year (ref: 1–3 months)				
10–12 months	1.24 (0.97, 1.58)	0.088	1.22 (0.95, 1.57)	0.122
7–9 months	1.06 (0.79, 1.42)	0.699	1.24 (0.93, 1.67)	0.149
4–6 months	1.15 (0.85, 1.54)	0.364	1.13 (0.84, 1.54)	0.412
Night shifts per month (ref: ≤4)				
5–9	0.95 (0.84, 1.09)	0.476	0.95 (0.83, 1.08)	0.406
≥10	1.06 (0.88, 1.28)	0.562	0.91 (0.75, 1.11)	0.349
Psychological stress before night shifts (ref: No)				
Yes	1.09 (0.83, 1.42)	0.535	1.14 (0.87, 1.50)	0.343
Psychological stress during night shifts (ref: No)				
Yes	1.30 (1.01, 1.69)	0.046	1.51 (1.16, 1.98)	**0.002**
Psychological stress after night shifts (ref: No)				
Yes	1.51 (1.35, 1.69)	**<0.001**	1.73 (1.54, 1.94)	**<0.001**
Feeling of being refreshed after resting before night shifts (ref: No)				
Yes	0.72 (0.64, 0.81)	**<0.001**	0.69 (0.61, 0.78)	**<0.001**
Feeling of being refreshed after resting after night shifts (ref: No)				
Yes	0.71 (0.61, 0.83)	**<0.001**	0.75 (0.64, 0.88)	**<0.001**
Using sleep medication before night shifts (ref: Never/rarely)				
Sometimes	1.23 (1.04, 1.45)	**0.015**	1.23 (1.04, 1.46)	**0.017**
Often	1.54 (1.09, 2.16)	**0.014**	1.59 (1.13, 2.22)	**0.007**
Using sleep medication after night shifts (ref: Never/rarely)				
Sometimes	1.42 (1.19, 1.70)	**<0.001**	1.28 (1.07, 1.53)	**0.007**
Often	1.67 (1.17, 2.38)	**0.005**	1.35 (0.95, 1.93)	0.095
Physical discomfort during night shifts (ref: No)				
Yes	1.62 (1.43, 1.83)	**<0.001**	1.46 (1.29, 1.65)	**<0.001**
Busyness during night shifts (ref: No)				
Yes	1.14 (1.01, 1.28)	**0.030**	1.06 (0.95, 1.20)	0.300
Sleep quality before night shifts (ref: Normal)				
Poor	1.19 (1.06, 1.33)	**0.004**	1.19 (1.06, 1.34)	**0.004**
Sleep quality after night shifts (ref: Normal)				
Poor	1.29 (1.14, 1.47)	**<0.001**	1.18 (1.04, 1.34)	**0.012**
Food intake during shift work (ref: Normal)				
More	1.25 (1.04, 1.50)	**0.019**	1.10 (0.91, 1.33)	0.320
Less	1.12 (0.98, 1.29)	0.096	1.03 (0.90, 1.19)	0.644
Meal timing during shift work (ref: Regular)				
Early	1.02 (0.86, 1.20)	0.820	1.12 (0.95, 1.33)	0.181
Delayed	1.13 (0.98, 1.29)	0.084	1.13 (0.98, 1.29)	0.089
Working > 40 h/week during shift work (ref: Never/rarely)				
1 week/month	1.29 (1.09, 1.52)	**0.003**	1.27 (1.07, 1.51)	**0.007**
2 weeks/month	1.41 (1.18, 1.67)	**<0.001**	1.47 (1.23, 1.75)	**<0.001**
3 weeks/month	1.41 (1.16, 1.72)	**0.001**	1.51 (1.23, 1.84)	**<0.001**
4 weeks/month	1.60 (1.37, 1.87)	**<0.001**	1.66 (1.42, 1.94)	**<0.001**
Fatigue scores (for every additional point)				
Physical fatigue scores	1.20 (1.18, 1.23)	**<0.001**	1.19 (1.17, 1.22)	**<0.001**
Mental fatigue scores	1.35 (1.30, 1.40)	**<0.001**	1.26 (1.21, 1.31)	**<0.001**
Rest during night shifts (ref: No)				
Yes	1.03 (0.92, 1.15)	0.632	0.97 (0.87, 1.09)	0.632

OR, odds ratio; CI, confidence interval; ref, reference group. Statistically significant differences after application of the Bonferroni correction are shown as bold numbers ($p < 0.025$).

shift work pressure, which is likely to have affected their mental health (39).

Effect of Shift Work Characteristics on Depression and Anxiety

A previous study found that self-reported levels of depression and anxiety were higher in shift workers than in non-shift workers (7). In the present study, shift nurses were 1.54 and 1.36 times more likely to have greater levels of depression and anxiety, respectively, compared with non-shift nurses. A meta-analysis of longitudinal data showed that shift work enhanced the overall risk of adverse mental health outcomes (e.g., depression and anxiety) by 28% among 28,431 participants (22). Lee et al. also found that Korean nurses who engaged in shift work were 1.5 times more likely to experience more severe depressive symptoms in comparison with non-shift workers (25). A previous population-based study surveying 277,168 workers in the UK Biobank indicated that shift workers were more likely to consult a physician for treatment of feelings of depression, anxiety, emotional instability, or neuroticism (3).

Lee et al. recently conducted a meta-analysis of observational epidemiological studies. They found that shift work at night was correlated with a 40% increase in the risk of depression, which persisted in subgroup analyses by shift duration, sex, and occupation (13). Similarly, in a longitudinal study of UK households, Weston et al. discovered that shift work significantly correlated with depressive symptoms regardless of occupation, age, or sex (24). The above study was consistent with our findings in that we found no statistically significant correlation between gender, age, shift duration, or depressive symptoms in nurses. However, our finding may be because female nurses accounted for a large proportion of the shift nurses in this study, i.e., 93.37%. Therefore, the gender imbalance should be considered for our data interpretation. Future studies should seek to increase the sample size of male nurses to obtain more representative information regarding mental health outcomes in male nurses (40).

Most studies that have compared different patterns of shift work in terms of negative psychological outcomes have been highly dependent on general demographic factors. Thus, further investigation is needed regarding differences in shift work characteristics, personal factors, and the environmental characteristics of shift work (41). In this study, we sought to address gaps in previous work by exploring individual factors and characteristics of the shift work environment. We found that the number of night shifts worked, the lengths of shifts, the work schedule and the shift rotation direction did not influence depression and anxiety among shift nurses. These findings are supported by Øyane et al. (18), Berthelsen et al. (42), and Lin et al. (16). Some possible reasons for the above results were as follows. First, we may have not collected the most important variables among shift-related variables, such as night shift handover time, shift adaptability, circadian rhythm changes during shifts, etc., which need to be supplemented in future studies. Second, circadian rhythm changes during shifts may fully mediate the relationship between the above variables and anxiety/depression, leading to the possibility that these variables may not directly affect mental health (6, 7).

Berthelsen et al. (42) and Natvik et al. (43) found that the number of h worked per week did not correlate with an increased incidence of anxiety or depression. However, other studies focused on extended working h (overtime) have found a positive linear correlation between the additional h worked as a result of overtime and anxiety or depression (8, 44). Our findings are consistent with the above studies, in which we found a positive dose-response relationship between the number of overtime weeks per month and anxiety or depression. Furthermore, we found the proportion of nurses who worked at least some overtime each month to be as high as 81.11%. These results suggest that overtime work may be not conducive to the maintenance of physical and mental health in shift nurses. Nursing managers should seek to understand the reasons why nurses engage in overtime work as well as the negative impacts on mental and physical health, and thus make changes to the workplace to limit this type of work practice.

Altered sleep patterns caused by shift work have been linked with irritability, depressed mood, anxiety, and nervousness (45, 46). A prospective study of shift workers found that changes in mental health, including symptoms of depression and anxiety, were modulated by sleep after engaging in shift work for 1 year (47). Based on the above findings, we explored the effects of sleep and energy recovery at different times relative to shift work on depression and anxiety in nurses. Shift nurses often plan sleep or rest periods before and after night shifts to ensure that they have an adequate energy level for working and are restored after the experience of shift work. Our present data indicate that shift nurses who self-reported poor sleep quality before or after night shifts may have an increased risk of anxiety or depression. At the same time, we found that nurses who self-reported that their energy levels returned to normal after pre- or post-night shift sleep may be at reduced risk of anxiety or depression. Our results are supported by a study by Booker et al. who found that disordered sleep as a result of shift work led to more severe symptoms of depression and anxiety (48). It is possible that poor sleep quality and low energy levels lead to reduced enthusiasm regarding shift work. Such negative emotions could accumulate, leading to increased symptoms of depression and anxiety, and ultimately decreased work efficiency (49). Our data indicate that nurses who used sleep medications during sleep before or after night shifts were more likely to report higher levels of anxiety or depression. However, we know that nurses with higher anxiety/depression may be more likely to take sleep medications. Given the cross-sectional nature of this study, the direction of potential causality may not be known. Therefore, longitudinal data may need to be collected to further explore the relationship. In addition, nursing managers may benefit from evaluating the sleep quality and sleep drug use of shift nurses, and aim to provide a good sleep environment and sleep hygiene advice for night nurses. These measures could reduce the negative effects of sleep problems on levels of depression and anxiety in shift nurses.

Our results suggest that night shift busyness may be a factor for increased risk of depression and anxiety severity among nurses, and that busy night shifts are a possible cause of fatigue (50). Previous studies have shown that shift-related fatigue is significantly connected with depression and anxiety in nurses (51, 52). In this study, we discriminated mental fatigue from physical fatigue, and found that both factors may increase the risk of depression and anxiety in shift nurses. Therefore, from the perspective of nursing management, reducing the work burden of shift nurses and helping them lower the degree of physical and mental fatigue will likely reduce the severity of symptoms of depression and anxiety. After exploring the relationship between psychological stress at different time periods of shifts and the mental health of shift nurses, we found that psychological stress before night shifts, psychological stress during night shifts, and psychological stress after night shifts may be all risk factors for depression and anxiety in shift nurses. Previous studies have shown a significantly positive correlation between stress levels in shift nurses and symptoms of depression and anxiety (37, 52). Further studies are needed to determine the causes of psychological stress in shift nurses during night shifts to reduce the impact of this stress on their mental health (e.g., depression and anxiety).

Limitations and Strengths

First, although this was a multi-center study, it had a cross-sectional design. Thus, we were able to conduct correlational analyses but not causal inferences. Further studies with a longitudinal design may support our results. Second, the data in this study were subjective, which may have led to partial recall bias. Future studies with objective measurements are needed to strengthen our findings. Despite the above shortcomings, we have contributed to the field by exploring the detailed relationships between shift-related variables at different time periods and depression and anxiety in shift nurses. In addition to the frequency and direction of rotation of shift schedules, we also examined psychological stress, dietary changes, and fatigue levels during night shifts.

CONCLUSION

The characteristics of shift work such as overtime work and busy night shift work may be not conducive to the mental health of shift nurses. Moreover, psychological stress and fatigue during night shifts appear to enhance symptoms of depression and anxiety. Physical discomfort and fatigue during night shifts may have negative impacts on mental health. Efforts to decrease depression and anxiety in shift nurses may be carried out from the perspective of reducing the workload, reducing sources of stress during night shifts, and guiding nurses to relax and relieve fatigue.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because the data from the Nurses' Health Cohort Study of Shandong needs time for data clearing and establishment of guidelines. We are planning on opening this data to the public in the future. Requests to access the datasets should be directed to YC, caoyj@sdu.edu.cn.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Scientific Research of Shandong University Qilu Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YL and YW: methodology, formal analysis, data curation, software, writing-original draft, and visualization. RL and XL: writing-review and editing and project administration. XG, LL, and JL: investigation. YC: conceptualization, resources, supervision, project administration, and funding acquisition. All authors contributed to the article and approved the submitted version.

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Mobile phone sleep self-management applications for early start shift workers: A scoping review of the literature

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Poor sleep has significant impacts on both mental and physical well-being. This is especially the case for shift workers who rely on good sleep practices to manage the disruption caused by their working conditions. In recent years there has been a proliferation of sleep-focused mobile phone applications, some of which may be suitable for use by shift workers. There is limited evidence however, on whether these applications are sufficient in managing the sleep needs of the early start shift working population (i.e., those whose work schedules begin pre-dawn). This scoping review aims to identify and discuss peer-reviewed literature on mobile sleep applications used by early start shift workers for sleep-self management. Four databases (Scopus, EBSCOhost, CINAHL and PsycInfo) were searched for relevant literature using a pre-determined search string. The initial search using the term *early start shift work* returned no papers, however a broadened search on shift work in general found 945 papers for title and abstract screening, of which 21 were deemed eligible for full text screening. Two of these papers met the inclusion criteria for this review. The results highlight, firstly, the paucity of research on the use of mobile phone applications for sleep self-management amongst early start shift workers, and secondly, the need for further research on the effectiveness of mobile applications for sleep self-management amongst shift workers in general. A working definition of early start shift work that can be used to stimulate research in this understudied population of shift workers is also proposed.

KEYWORDS

shift work, sleep self-management, sleep technology, mobile app, well-being

Introduction

Shift work is an increasingly important employment scheduling practice in a modern society that demands service across all 24 h of the day. Broadly defined, shift work refers to any schedule of work that occurs outside normal daytime working hours. Shift work hours typically consist of either regular nights and evenings or rotating shifts between day and evening hours, although other varieties of shift work also exist. In Australia, approximately 1 in 6 employees works regular shift work hours (1), with equivalent figures reported in European Union member states (2) and the United States of America (3).

Shift work increases risk for multiple health problems if it is not appropriately managed. 'Shift work disorder', for example, is characterized by symptoms of insomnia and excessive sleepiness and affects approximately a quarter of the shift working population (4). Shift workers are also at increased risk of cardiovascular disease, diabetes, and gastrointestinal disorders (5). Poorer mental health outcomes are also reported in some shift working populations (6). Misalignment of endogenous circadian rhythms with external clock time and reduced sleep time are two possible mediators of the association between shift work and poorer mental health (5). This may be particularly the case for "early start shift workers," that is, shift workers who begin their work in the pre-dawn period (i.e., before sunrise). From a circadian perspective, this group experience chronic phase misalignment between their endogenous circadian rhythm and typical wake time on workdays (sometimes referred to as *social jetlag* (7). This group are also expected to be sufficiently alert to perform their work duties at a time when their circadian drive for wake is typically at its lowest point in the 24-h circadian cycle. Early start shift workers also experience reduced hours of sleep due to the unusually early bedtime required to achieve a minimum of 7 h sleep at night. Examples of shift workers who typically start work in the pre-dawn period include garbage collectors, bakers, short-haul airline pilots, and some factory workers. In a previous study by our group, we found that racehorse trainers, who also typically start work in the pre-dawn period, reported elevated levels of depression and anxiety (8). Daytime dysfunction due to poor sleep was found to be a potentially important causative factor in their higher levels of psychological distress. Strategies for managing the detrimental effects of poor sleep on health are an essential tool in the shift worker's arsenal of protective behaviors.

The self-management of sleep behavior is an increasingly important strategy for limiting the negative health outcomes associated with compromised sleep. Self-management is especially important for shift workers who commonly experience sleep that is less than optimal in both length and quality (9). With specific reference to early start shift workers, a study of short-haul airline pilots found that those who started their shift before 5 am had significantly reduced sleep hours and higher levels of fatigue than their counterparts who started work later in the day (10). Self-management of health is defined as an "ongoing… process with a focus on self-identified needs or problems that require continual monitoring" (11) p. 1783); it may or may not involve interactions with health care providers. Rapid advances in personalized health-supporting technologies have accelerated the adoption of self-management strategies in both clinical practice and individual efforts to support health, including sleep [e.g., (12)]. Evidence of the useability and effectiveness of these technologies in shift working populations is mixed (13), for example, found that an m-Health app targeting health behavior change in shift workers was rated by users as "slightly to moderately useful" but did not improve sleep quality as intended. Still, increasingly sophisticated, yet user-friendly and affordable technologies mean that technology-mediated self-management of sleep behavior is accessible to a wider demographic than has ever been the case before. Current technologies permit powerful and independent data gathering and use in-built algorithms to facilitate the evaluation of sleep-related phenomena.

Smartphone technologies are particularly suited to the widespread adoption of health self-management strategies. Internationally, the median level of smartphone ownership among advanced economies in 2019 was 76% (14). A more recent consumer survey by Deloitte in Australia reported that 92% of Australians aged 18–75 years owned a smartphone device in 2021 (15). The delivery of sleep health information *via* this medium is therefore accessible to a large proportion of the population. Greater access to smartphones by large sections of the community has led to a proliferation of smartphone apps, including those that encourage self-management of health and well-being. Such growth offers new and more accessible options for health behavior change (16). A large number of smartphone apps specifically designed to support sleep health are available in the major digital marketplaces (e.g., App Store, Google Play) (11) identified just under 2,000 apps that were designed for this purpose. The vast majority consisted of relaxation/meditation sounds or alarm clocks. Apps that offered more than these basic functions varied greatly in quality, content, and functionality. Importantly, none of the apps were designed specifically to support the unusual sleep patterns of shift workers.

The aim of this scoping review was to ascertain the breadth of research available on the use of mobile phone sleep applications for sleep self-management amongst early start shift workers. Preliminary searches yielded no results for the term "early start shift work. As such, the review sought to identify the existing peer-reviewed literature regarding the utilization of mobile sleep applications for the general shift working population. While such studies reflect the results and experiences of shift workers which may at times fall outside of the definition of "early start" shift work, we believe that implications can be drawn from this evidence to support the facilitation of similar studies with a more specific subset of the shift working population—early start shift workers. Further, in light of a lack of consensus on the term "early start shift work," this scoping review proposes a working definition of this term to aid future research and interventions in broadening understanding of the specific needs of this minority working demographic.

Methods

Design

A scoping review methodology was employed and guided by the framework of (17) to ensure a rigorous approach to the investigation.

Search strategy

Four databases were the subject of a comprehensive search (Scopus, EBSCOhost, CINAHL, and PsycInfo) using the following search string: ("sleep* app*" OR "sleep* technolog*" OR "sleep* management*" OR "Computer and sleep" OR "Computer therapy and sleep" OR "Digital sleep companion" OR "Digital sleep app*" OR "Sleep behavio* change and technolog*" OR "Sleep monitor* and digital technolog*"). These specific databases and search terms were selected due to their likelihood of yielding the broadest range of search results possible.

An initial search was conducted in 2019 by one reviewer (IR) and re-run with the support of a research librarian to ensure accurate results. An additional search was run in 2021 to check for updates to the literature. The initial search in 2019 elicited 1,030 peer reviewed journal papers and the 2020–21 search yielded a further 360 papers. Additional qualifiers using Boolean phrases (AND "shift worker*" AND "well-being" OR "well-being" OR "mental health") were used to seek out literature more specific to the research question, but such phrases yielded no additional results. All papers from the 2009–19 search were added to Endnote, where using the automated and manual deduplication procedure, 430 papers were eliminated. The remaining papers (600) were uploaded to Covidence where 15 were eliminated for being duplicates. The 360 papers from the 2020–21 search were manually screened for duplication and none were eliminated. In total, 945 papers were moved forward to title and abstract screening from which 942 were excluded and 21 progressed to full text screening. After full text screening with consideration for the inclusion and exclusion criteria, a total of 2 papers met the requirements for this scoping review. Twelve of the excluded studies were assessed as being outside of scope (e.g., review paper, mobile phone technology required concomitant use of a wearable device), five of the studies were excluded due to the wrong population being studied (e.g., not shift workers, sleep disorder patients), and a further two studies were excluded because they were not peer-reviewed publications (e.g., expert opinion).

Article screening

Articles were included in the review if they met the following criteria: 1) were published in English between 2009 and 2021. 2) the study population were shift workers. 3) the study involved the use or analysis of mobile phone sleep applications.

The following review techniques were employed: 1) only full text peer-reviewed articles were selected. 2) inclusion criteria were limited by date and language. 3) one reviewer (IR) screened and selected the articles, and an additional two secondary reviewers (BB, SH) screened the selection of articles. 3) a secondary reviewer re-ran the search string in all databases to confirm the number of results. 4) a single reviewer (CL) extracted the findings from the studies selected. 5) the PRISMA protocol was followed to guide the development of the scoping review (see Figure 1).

Data extraction

Using Microsoft Excel, a database was created to manage the articles that made it past the title and abstract screening. Key details from the articles were listed including, title, author(s), year of publication, country of origin, journal of publication, study design, target groups and outcomes. The database was developed and maintained by one reviewer (CL) who extracted the relevant data, and a secondary reviewer (BB) who screened the data and confirmed the inclusion of the selected articles.

Results

Characteristics of studies

Two studies met the inclusion criteria for the scoping review. These studies originated from the Republic of Korea (18) and The Netherlands (19), respectively. Both conducted research on the use of mobile sleep applications for shift workers, the first focusing on nurses and the second on airline pilots. The study on nurses employed a qualitative descriptive analysis approach while the study on pilots was a randomized controlled trial. See Table 1 for the extracted data from these studies.

Study findings

The two included studies investigated the use of mobile phone sleep applications among shift workers, albeit in different ways and in different shift working populations. 18 measured various aspects of sleep (e.g., sleep onset latency, total sleep time, wakefulness during the sleep period) among shift working nurses using the *Sleep Time* app (Azumio Inc.). A sleep diary was used alongside the app for comparison. While the primary outcome of this study was that both sleep onset latency and time in bed were significantly lower on night shift compared to day shift, and sleepiness scores were significantly higher immediately after waking in the night shift group, the outcome most relevant to the current review was the high level of agreement between

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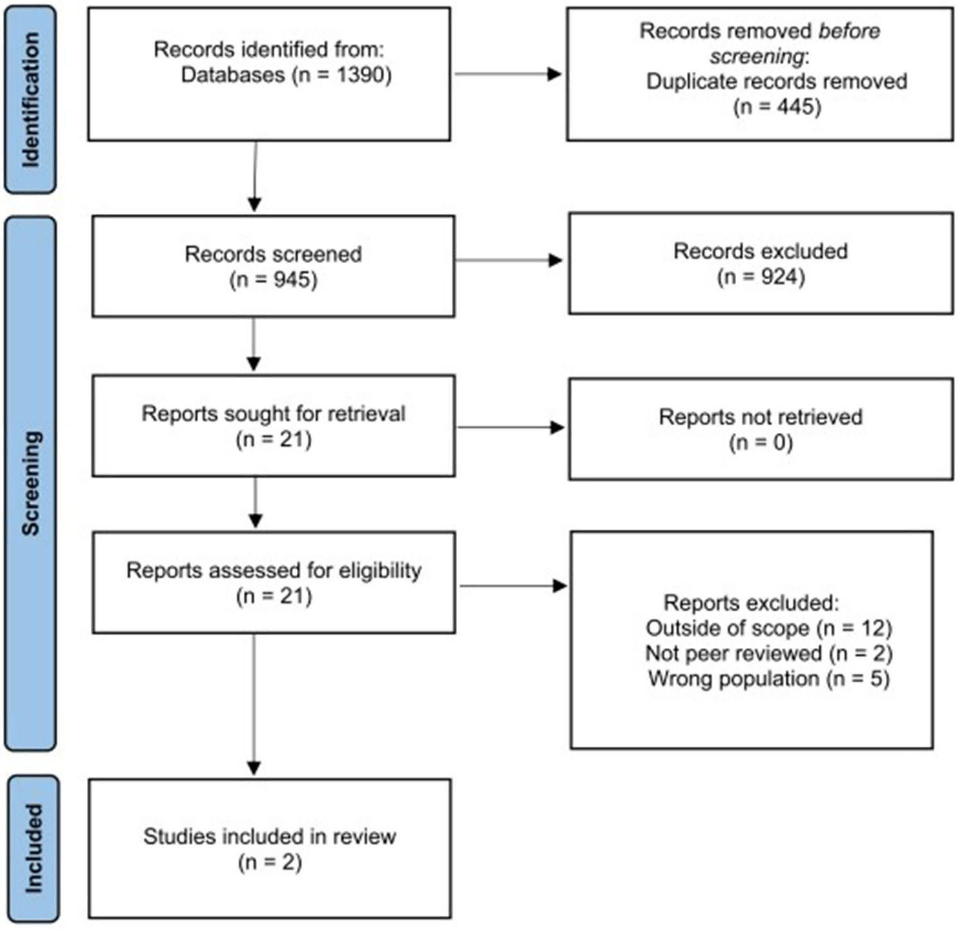

FIGURE 1
PRISMA diagram showing the flow of selection and exclusion of articles through the different stages of the review.

TABLE 1 Overview of studies included in the scoping review.

Author(s), Year, Country	Sample	Study design	Study aim	Key findings
Joo et al. (18) (Republic of Korea)	Nurses ($N = 20$)	Quantitative descriptive analysis	To study the sleep latency and post-sleep wakefulness of shift working nurses	Time in bed was significantly lower for night shift nurses than day Sleep latency was significantly lower after night shifts than day Sleepiness scores were significantly higher immediately after waking up among night shift nurses
van Drongelen A et al. (19) (The Netherlands)	Pilots ($N = 502$)	Randomized controlled trial	To evaluate the effects of mHealth interventions to improve the health perception of airline pilots	After 6 months the intervention group showed significant improvement on fatigue Offering tailored advice through mHealth is an effective way to support airline staff who work irregular hours and experience circadian disruption

self-reported and app-assessed sleep parameters (r = 0.78 to 0.99). This level of agreement supports the usefulness of objective sleep data collected *via* a mobile phone app as a viable assessment method.

(19) investigated the effectiveness of a health advice intervention on fatigue delivered *via* mobile phone (*MORE Energy* app) to 502 international airline pilots. The health advice was tailored to pilots' flight schedules and personal characteristics (including chronotype) and targeted preventive actions for reducing fatigue, including circadian- and sleep-related behaviors (e.g., optimal timing of exposure to daylight and sleep) and improving fitness and nutrition. The results showed that after 6 months of app use, fatigue was significantly lower among the intervention group compared to a control group of pilots who received generic health advice on the targeted preventive measures. Specific areas of improvement were sleep quality (but not sleep length or sleep latency), healthy snacking behavior, and strenuous physical activity. High levels of app use compliance were required to receive the maximum benefit for reducing fatigue, although moderate improvements were seen even with lower levels of compliance.

Discussion

This scoping review aimed to investigate previous research on the use of mobile phone applications for sleep self-management amongst early start shift workers. An initial search on this specific employment group failed to locate any studies so we broadened the search to include the general shift working population. Only two studies met study inclusion criteria—one that used an app to investigate sleep among shift working nurses (18) and one that investigated the effectiveness of an app to deliver a fatigue management intervention among international airline pilots (19).

The two included studies make different contributions to the current investigation: 18 showed that sleep data collected *via* the *Sleep Time* mobile phone app were as accurate as self-report sleep diaries for measuring the amount of time spent in bed and the amount of time taken to fall asleep (sleep onset latency). Objective and automated assessment of these sleep characteristics *via* an app may be useful for improving compliance with their measurement, particularly over longer time frames when compliance rates can decline [e.g., (20)]. For shift workers, long-term compliance with the measurement of sleep behavior may be necessary for a comprehensive assessment of how different work schedules and behavior changes affect sleep. The app-based assessment of other sleep characteristics (e.g., total sleep time and the amount of time spent awake after sleep onset) showed less consistency of measurement with the self-report diary. The accuracy of sleep diaries for measuring important sleep characteristics is mixed [e.g., (20, 21)], especially when sleep is compromised [e.g., (22)] or when daytime naps are used [e.g., (23)], both of which may apply in shift working populations. Nevertheless, sleep diaries are often the only viable method available for the self-management of sleep. An automated app that can be used in place of a sleep diary is likely to increase compliance in the long-term and may yield more complex and useful sleep-related information as algorithms continue to improve.

The randomized controlled trial by 19 showed that health advice delivered to shift workers *via* a mobile phone app can successfully initiate and sustain health behavior change. The effectiveness of the app may be attributed to careful tailoring of health advice to the specific characteristics of the user. Generic advice on sleep can be found in many public health forums (e.g., www.sleepfoundation.org) and may be ineffective at producing similar levels of change if it is not tailored to the needs of the target audience [see also, (24)]. Regular engagement with the app also enhanced positive outcomes among users in the van Drongelen, Boot et al. study. To increase long-term compliance, apps should actively encourage engagement through feedback, goal setting, and rewards. These are important considerations in the design of mobile phone apps for facilitating health behavior change [see also, (25)].

The fact that only two studies met inclusion criteria for the review was unexpected, especially after search criteria were broadened to include general shift workers and not just limited to early start shift workers. While the shortage of returned studies may be partially attributed to the search terms used and inclusion/exclusion criteria (see Limitations), this scoping review indicates that there is limited research in this space. Mobile phone apps for sleep are in plentiful supply; however, as reported by (11) few meet minimum expected standards of quality, functionality, and validation for sleep self-management, and even fewer would meet these criteria in a specialist population like shift workers. Application of minimum standards and evidence-based design recommendations [e.g., (11, 16, 25)], are needed. Further, app developers should employ a codesign approach [for instance, see (26)], designing apps *for shift workers with shift workers*, when creating specialist sleep apps. This is particularly the case when designing for specialist workers, such as early start shift workers. This may lead to greater uptake and use of mobile phone apps about sleep self-management and contribute to the body of research in this space.

The complete absence of studies returned from the initial search for early start shift work was also unexpected. As a descriptive term, *early start shift work* appears to be unrecognized in the literature as a way to describe shift work schedules that begin prior to dawn; however, there does not seem to be an alternative description in common use that could apply to this understudied population of shift workers. This group appear to have many unique characteristics that are not shared with other shift workers—rising before dawn when the circadian drive for wake is low, and the associated misalignment of phase between circadian and homeostatic sleep processes, are prominent differences. Another distinctive feature of this group is that early start shift workers have difficulty obtaining sufficient sleep on a regular basis due to the unusually early bedtime required, as is the need to be physically and cognitively alert at times of the day that are biologically prejudicial to such activity. For example, the horse-racing, air traffic control and nursing professions include early start shift workers. In these contexts, errors or lapses in judgement at work may adversely affect the health and well-being of the early start shift worker, and the health and safety of others with whom they work, e.g., people in proximity to horses, airline passengers, and patients. Classifying early start shift workers into the same category as other shift working populations may be disadvantageous to research and policy on the safety and well-being considerations for this minority population of shift workers.

To stimulate research in this understudied population of shift workers we propose a working definition of early start shift work as *a work schedule that starts in the pre-dawn period, that is, before the first light of day*. Light is the most powerful zeitgeber for the endogenous circadian system (27), so appropriately timed exposure to light in the morning is necessary for ensuring a stable 24-h pattern of sleep and wake [see also, (28)]. Tying the definition to morning light schedules instead of 24-h clock time would therefore appear to be an important consideration. From a circadian science perspective at least, clock time is less important than 24-h (circadian) biological time in managing sleep/wake cycles. The proposed definition also has the advantage of being flexible with regards to local time which can vary greatly due to seasonal and latitudinal variations in light/dark cycles. This is especially relevant to shift workers whose work duties are performed mostly in outdoor settings (e.g., horse racing staff and garbage collectors). The proposed working definition may have limited application around the winter solstice in higher northern hemisphere latitudes where dawn occurs later in the morning, meaning that most of the working population would be classified as early start shift workers at these times.

Limitations

The limitations for this review concern the selected search terms and exclusion criteria. Firstly, inclusion of *smartphone* as a search term may have increased the number of studies returned from the literature search. While we believe most of the relevant literature was captured in our search using terms such as *app*, *technology*, and *digital*, inclusion of *smartphone* in the search may have been a useful addition. Secondly, studies that employed wearables such as smartwatches, wristbands, and rings in their collection of sleep data were excluded due to the limited availability of these devices in the initial reference period of 2009–2019, and concerns over the application of review findings to the wider population of shift workers. The recent proliferation of wearable technologies in general use, and the enhanced functionality in sleep-related applications such devices afford, means that any update to the current literature review should include research on these devices.

Conclusion

The findings of this review highlight a paucity of published research on the use of mobile phone applications for sleep self-management amongst early start shift workers. Further research is needed, therefore, on applications appropriate to this subgroup of shift workers whose unique working conditions require specific interventions and support. The appropriate timing and use of light in both the early morning and evening hours is one example of support that is specifically relevant to this group. To stimulate such research, we have proposed a working definition of early start shift work as *a work schedule that starts in the pre-dawn period, that is, before the first light of day*. This definition emphasizes alignment with light/dark cycles and is therefore more consistent with circadian science principles than traditional definitions that emphasize clock time.

We also note that, while a large number of mobile phone applications that target sleep self-management already exist in the digital marketplace, few, if any, are designed specifically for use by shift workers. There is clearly a need, therefore, for a more evidence-based and context-specific approach to the development of mobile phone sleep applications for this group. We recommend that applications are co-designed in partnership with shift workers as the optimal strategy for fulfilling this need.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

BB, HD, and AAM conceived and designed the review. CL collated the study results. BB wrote the manuscript which was reviewed and revised by HD, AAM, and CL. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Concurrent trajectories of self-rated health and working hour patterns in health care shift workers: A longitudinal analysis with 8-year follow-up

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Background: The association between health and working hours is hypothesized to be reciprocal, but few longitudinal studies have examined changes in both health and working hour patterns over time. We examined combined trajectories of self-related health and two working hour patterns (working <35 h/week and working night shifts) and the extent to which these trajectories were predicted by employees' lifestyle and mental health.

Methods: Participants of this cohort study with a 8-year follow-up were 5,947 health care shift workers. We linked self-reports of health from three repeated surveys with objective pay-roll based data on working hours. Using group-based multi-trajectory analysis we identified concurrent trajectories for self-rated health and working hour patterns. We examined their associations with baseline lifestyle-related factors (smoking, at-risk alcohol use, obesity, and physical inactivity) and mental health (sleep problems and psychological distress) using multinomial regression analysis.

Results: Three combined trajectories of self-rated health and working <35 h/week and four combined trajectories of self-rated health and night work were identified. Unhealthy lifestyle and poor mental health were associated with trajectories of moderate and declining health. Sleep problems were linked with working <35 h/week. Younger age and good mental health were associated with a combined trajectory of good health and continued night shift work.

Conclusion: Trajectories of suboptimal and declining health are associated with trajectories of reducing working hours and leaving night work, and are more common in employees with unhealthy lifestyle, sleep problems, and psychological distress.

KEYWORDS
night work, health, working hours, multi-trajectory analysis, shift work (MeSH)

Introduction

Long working hours (1, 2) and shift work (3–5) may contribute to health problems, but health problems may also affect the choice of working hours and patterns (6, 7). For example, people with health problems are more likely to work part-time (8, 9) and may be less likely to work night shifts, particularly in health care sector (10). Age also affects preference for working long hours and night shifts. Older employees have found to prefer work either shorter shifts or day shifts over longer working hours and nights (11, 12) and it has been suggested that younger and older employees respond differently to long working hours or night work (13, 14), particularly in the long term (15, 16).

However, evidence is limited as most research has relied on study designs where either health or working hour characteristics have been measured on at one point in time only. Due to advances in longitudinal modeling, it would be possible to analyze repeat data on both health and working hour patterns simultaneously. Person-centered approaches, such as growth mixture modeling with longitudinal data, can identify patterns of development and divide participants into qualitatively different latent groups without prior assumptions (17). These latent groups, i.e., developmental trajectories, cannot be directly observed from the data. Providing latent groups, i.e., developmental trajectories, the models are composed of two elements: the probability of group membership and the probability of the observed data given group membership (18). With this method, it is possible to take into account the concurrent development in more than one factor, and approximate the proportion of individuals following specific simultaneous trajectories of working hours and health and examine the antecedents of these trajectories. The trajectories of self-rated health have sparsely been examined before. A Swiss study found slowly declining trajectories not influenced by age, gender, or socioeconomic status (19). A previous study from partly the same cohort as in the current study, achieved somewhat contradicting results showing that a small proportion of employees actually improved their health after transition to retirement. The likelihood of this trajectory was higher in women and in higher socioeconomic status (20). One previous study identified trajectories of working hours and found that female sex, age, lifestyle risk factors, and health problems were associated with short and varying working hours (21). The study did not account for simultaneous changes in self-rated health, and used subjective evaluations on working hours. Thus, little is known about concurrent changes in self-rated health, objectively measured working hours and night work, or the lifestyle determinants of these combined trajectories.

We aimed to examine the concurrent changes in self-rated health and two working hour patterns: working <35 weekly hours and working night shifts. Moreover, we investigated how sex, age, lifestyle factors (smoking, at-risk alcohol use, low physical activity, and obesity), mental health (sleep problems and psychological distress) at baseline were associated with the different identified concurrent trajectories of self-rated health and working hour patterns among shift working health care employees.

Methods

Study population

Participants were drawn from the Finnish Public Sector cohort study (22, 23), and they were employees of ten towns, four hospital districts, and two other health care organizations. They were followed up with questionnaire surveys at 2 to 4-year intervals in 2008–2016. Survey responses were linked to records of the participating organizations' registers of payroll-based daily working hour data including information on age and sex, obtained from the shift scheduling program Titania® for each participant. Titania® is an administrative software used at workplaces with shift work. The scheduling program includes both the planned and actual working hour data [for details, see reference (24)]. These were identified based on the starting and ending times of daily working hours using the classification of work shifts in which night shift was determined as $\geq$ 3 h of work between 23:00 and 06:00 h as previously described (25). Titania® data on annual average weekly working hours and night work on the preceding year to each survey were also linked to survey data. The participants had period-based work contracts organized as day work or shift work, where working hours are planned and balanced for every 3 weeks (total planned working hours 114 h and 45 min). Detailed information is given elsewhere (26), but in general, working hours in the period-based work are mostly irregular. Of the participants, 94% were in shift work and 6% in day work. Day workers may also work occasionally (by demand) other than day shifts.

The self-reported data analyzed in the current study included responses to three questionnaire surveys administered in 2008, 2012, and 2015–2016 (average response rate 70%). The baseline was the response given in 2008. Participants with data on self-rated health and working hour patterns for at least in 2008 and 2015–2016 were included in the analysis. This resulted in an analytical sample of 5,947 participants, as described in Figure 1. Ethics approval is from the Ethical Committee of the Helsinki and Uusimaa hospital district (HUS/1210/2016).

Survey-based measures

To assess self-rated health, we used a single-item measure "How do you rate your health?" with response options; 1 = poor; 2 = fairly poor; 3 = average; 4 = fairly good; 5 = good.

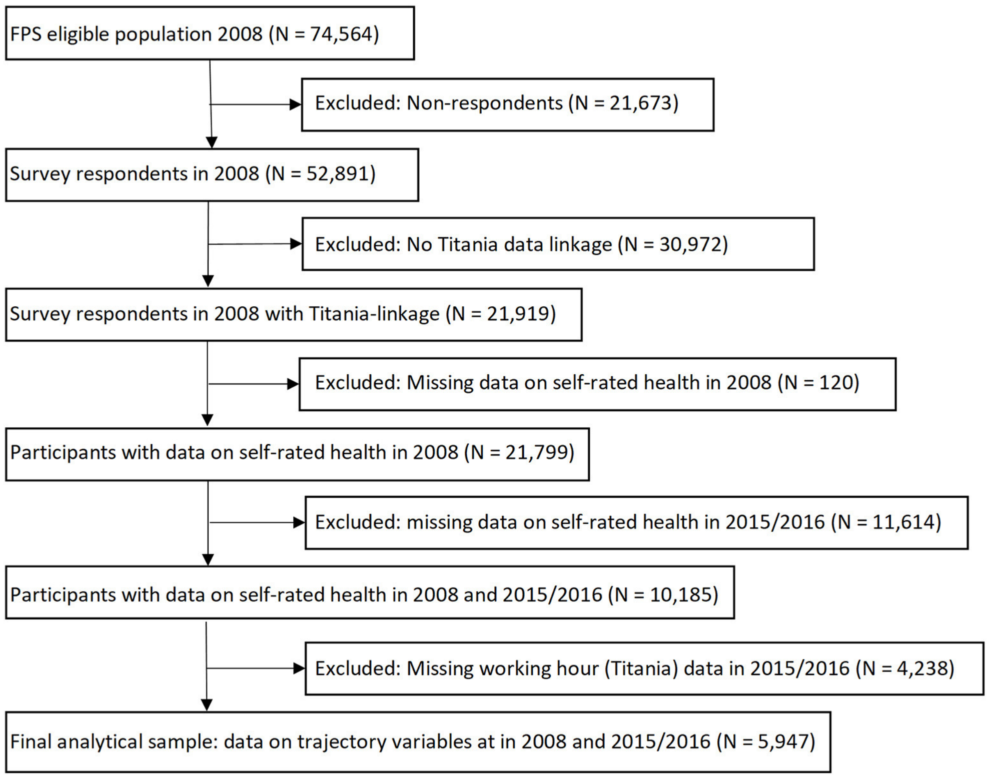

FIGURE 1
Flow chart of the study participants.

The question is widely used and recommended as a standard indicator of health in surveys (27).

Self-reported lifestyle risk factors included smoking, at-risk alcohol use, obesity, and physical inactivity. Smoking was classified into current smoker, never smoker, or ex-smoker (28). Alcohol use was elicited by questions on weekly consumption. One drink was approximately equivalent to one unit or one glass of alcoholic drink or 12 g of alcohol. Alcohol use was dichotomized into no use or moderate use (a maximum of 140 g or 11 units for women and 280 g or 23 units for men) vs. alcohol use greater than this (29). Body mass index (BMI = weight in kilograms divided by height in meters squared) was dichotomized as less than 30 (non-obese) and 30 or more, indicating obesity (30). Participants were categorized as being physically inactive if they reported <2 metabolic equivalent task hours per day (~30 min of walking) and active if more than this (31).

Mental health -related variables were sleep problems, and symptoms of depression and anxiety. We used the Jenkins Sleep Scale to measure common sleep problems during the last month (32, 33). Four items evaluated: the difficulty to fall asleep, wake up at night, difficulty to stay asleep, and wake up exhausted in the morning. Each item is rated on a scale from zero to five, where 0 = never, 1 = 1–3 nights/month, 2 = about 1 night/week, 3 = 2-4 nights/week, 4 = 5-6 nights/week, and 5 = nearly every night. The total score is a sum of all four items' scores from zero (no sleep problems) to 20 (most sleep problems). Participants with a score 4 or higher were coded as having sleep problems (1 = case, 0 = non-case). We used the 12-item General Health Questionnaire (GHQ-12) to measure psychological distress, that is, symptoms of depression and anxiety (34). In GHQ-12, respondents rate the extent to which they are affected by each of the 12 symptoms of distress (0 = not at all, 0 = as much as usual, 1 = slightly more than usual, 1 = much more than usual). Participants with a rating of 1 in at least 4 items of the total measure were coded as cases of psychological distress (1 = case, 0 = non-case).

Register-based measures

The average weekly (from Monday 00:00 to Sunday 24:00) working hours during the year immediately preceding the survey (= the start date for the year was the date preceding the survey response) were calculated for each survey year. Calendar weeks without work, that is on paid or non-paid leave, were excluded. Those working <35 h per week were coded as cases (=1), and those working more than that as non-cases (=0). The cut-off of 35 h was chosen based on 35 h being the overall mean of the working hours during the years of this study. Only 12% of the study population had a formal part-time job contract. Of them, 23% worked ≥35 h per week, and 77% less than that. Of those with full-time contract, 42% worked ≥35 h per week, and 58% less than that.

In a similar manner, proportion (%) of night shifts from all shifts during the year preceding the survey years were also calculated. Those working >1% of their shifts in night shifts were coded as working night shifts (=1) and those with <1% as working no/minimal number of night shifts (=0). Age was treated as continuous variable and sex was coded as 1 = men, 2 = women.

Statistical analysis

We used group-based multi-trajectory analysis (18) to identify trajectories of health and working hours separately for (1) self-rated health and working <35 h/week; and (2) self-rated health and night work. Self-rated health was treated as continuous variable and working hour patterns were dichotomous variables. Group-based multi-trajectory modeling is a form of finite mixture modeling to distinguish and describe subpopulations (clusters) existing within the studied population (18). We used a censored ("regular") normal model of group-based multi-trajectory analysis with linear distribution. The goodness of model fit was judged by running the procedure several times with the number of trajectory clusters starting from one up to five. The Bayesian Information Criterion, Akaike Information Criterion and average posterior probability were used as criteria to confirm the goodness of fit. We used multinomial regression analyses to determine the extent to which baseline health and lifestyle-related factors were associated with the identified clusters.

Multi-trajectory analysis was performed with Stata/IC Statistical Software: Release 17 (StataCorp, College Station, Texas, USA). The additional freely available Stata module 'traj' was required to conduct group-based trajectory analysis (Jones and Nagin 1999; 2013). SAS software package (version 9.4; SAS Institute, Inc, Cary, North Carolina) was used for regression analyses.

Results

Of the 74,564 adults in the eligible population, 52,891 (71%) participated in the baseline survey (T1), 30,569 (58%) were successfully linked to Titania register, and 5,947 (19%) had data also 8 years later, at T3, and were included in the analytical sample (Figure 1). The 5,947 employees were predominantly women (93%). Mean age was 43.6 years (SD = 8.6) in 2008. The majority, 56%, were nurses; 26% personal care workers; 9% head nurses/physicians; 6% cleaners and helpers; and 2% were clerical support workers. Participants' occupational position remained largely unchanged during the follow-up.

A total of 81% rated their health as "good" or "rather good" at baseline (mean = 1.78, SD = 0.81). Self-rated health decreased during follow-up, the corresponding figures being 76% (mean = 1.90, SD = 0.86) in 2012, and 73% (mean = 1.99, SD = 0.89) in 2016. A total of 46% worked <35 weekly working hours at baseline. In 2012 and 2016, the corresponding percentages were 40 and 44%, respectively. A total of 38% worked night shifts at baseline. The percentage working night shifts decreased during the follow-up, being 33% in 2012 and 30% in 2016.

A three-cluster model was chosen for working <35 weekly hours, and a four-cluster model for working night shifts (Table 1). The three concurrent trajectories of self-rated health and working <35 h/week were (Figure 2).

TABLE 1 Goodness of fit of group-based trajectory analysis models: the chosen models are shown in bold.

Model	Smallest group		BIC	AIC	APP
	N	%			
Working <35 h/week					
1-cluster model	5,947	100	−34,880.6	−34,863.9	
2-cluster model	2,158	36.3	−32,534.3	−32,500.9	0.93/0.94
3-cluster model	**1,617**	**27.3**	**−32,074.2**	**−32,024**	**0.91/0.84/0.82**
4-cluster model	Did not converge				
Working night shifts					
1-cluster model	5,947	100	−34,094.2	−34,077.5	
2-cluster model	2,004	33.7	−30,311.2	−30,277.8	0.99/0.99
3-cluster model	1,332	22.4	−28,955.1	−28,904.9	0.91/0.93/0.96
4-cluster model	**774**	**13.0**	**−28,062.8**	**−27,995.9**	**0.93/0.92/0.90/0.94**
5-cluster model	Did not converge				

BIC, Bayesian Information Criterion; AIC, Akaike Information Criterion; APP, Average Posterior Probability.

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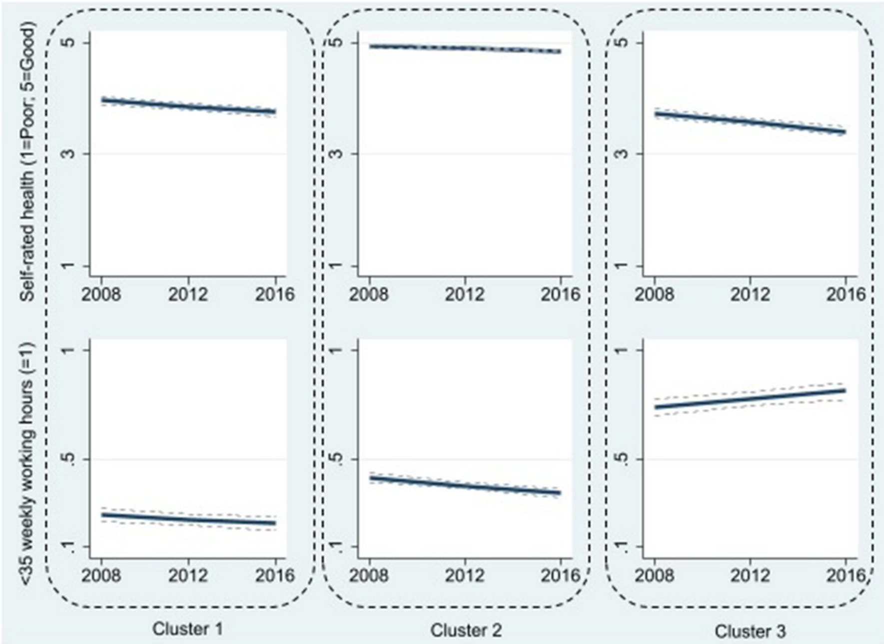

FIGURE 2
Three clusters of trajectories of self-rated health and working <35 weekly working hours. Cluster 1 (38%): Fairly good but declining self-rated health, and low and decreasing probability of <35 weekly working hours; Cluster 2 (35%): Sustained optimal self-rated health, and moderate but decreasing probability of <35 weekly working hours; Cluster 3 (27%): Fairly good but declining self-rated health, and high and increasing probability of <35 weekly working hours. 95% confidence intervals are shown as dotted lines, albeit they are poorly visible due to being very narrow at times.

1. Cluster 1 (38%): Fairly good but declining self-rated health, and low and decreasing probability of <35 weekly working hours.
2. Cluster 2 (35%): Sustained optimal self-rated health, and moderate but decreasing probability of <35 weekly working hours.
3. Cluster 3 (27%): Fairly good but declining self-rated health, and high and increasing probability of <35 weekly working hours.

Table 2 shows the associations of lifestyle and mental health -related factors and cluster membership (self-rated health and working <35 weekly hours) based on multinomial regression analysis. Cluster 1 "Fairly good but declining self-rated health, and low and decreasing probability of <35 weekly working hours" was used as a reference cluster.

Cluster 2 was characterized by better self–rated health but higher probability of <35 weekly working hours than in the reference cluster, was more probable with less lifestyle risk factors ($OR_{currentsmoking}$ = 0.61, 95% CI 0.50–0.74; $OR_{ex-smoking}$ = 0.77, 95% CI 0.65–0.92; $OR_{obesity}$ = 0.41, 95% CI 0.33–0.50; $OR_{lowphysicalactivity}$ = 0.59, 95% CI 0.50–0.70), less sleep problems (OR = 0.51, 95% CI 0.43–0.61), and less psychological distress (OR = 0.46, 95% CI 0.39–0.55). Employees in Cluster 2 were younger than those in Cluster 1 (OR = 0.93, 95% CI 0.92–0.94).

Compared to Cluster 1, Cluster 3 was characterized by similar fairly good but declining self–rated health, but a higher and increasing probability of <35 weekly working hours. Cluster membership in Cluster 3 was more probable in women (OR = 1.69, 95% CI 1.28–2.22) and younger employees (OR = 0.96, 95% CI 0.95–0.97). Clusters 1 and 3 did not differ by lifestyle factors, but employees in Cluster 3 had a higher likelihood of sleep problems (OR = 1.17, 95% CI 1.00–1.37) than those in Cluster 1.

The four concurrent trajectories of self-rated health and working night shifts were (Figure 3).

1. Cluster 1 (41%): Fairly good but declining self-rated health, and no night work.
2. Cluster 2 (25%): Sustained optimal self-rated health, and no night work.
3. Cluster 3 (13%): Sustained optimal self-rated health, and high but slightly decreasing probability of night work.
4. Cluster 4 (21%): Fairly good but declining self-rated health, and high but decreasing probability of night work.

TABLE 2 Lifestyle and mental health -related factors associated with cluster membership (self-rated health and working <35 weekly hours).

	Cluster 2: Sustained optimal self-rated health, and moderate but decreasing probability of <35 weekly working hours, $n = 2{,}083$		Cluster 3: Fairly good but declining self-rated health, and high and increasing probability of <35 weekly working hours, $n = 1{,}555$	
	OR	**95% CI**	**OR**	**95% CI**
Men	1		1	
Women	1.23	0.97–1.56	**1.69**	**1.28–2.22**
Age/1 year	**0.93**	**0.92–0.94**	**0.96**	**0.95–0.97**
Non-smoking	1		1	
Ex-smoking	**0.77**	**0.65–0.92**	0.98	0.82–1.17
Smoking	**0.61**	**0.50–0.74**	1.06	0.88–1.27
No at-risk alcohol use	1		1	
At-risk alcohol use	0.87	0.68–1.12	0.91	0.72–1.16
Non-obese	1		1	
Obese	**0.41**	**0.33–0.50**	1.12	0.95–1.33
≥ 2 MET hr/day	1		1	
<2 MET hr /day	**0.59**	**0.50–0.70**	1.03	0.88–1.20
No sleep problems	1		1	
Sleep problems	**0.51**	**0.43–0.61**	**1.17**	**1.00–1.37**
No psychological distress	1		1	
Psychological distress	**0.46**	**0.39–0.55**	1.16	0.99–1.35

Multinomial regression (reference=Cluster 1 'Fairly good but declining self-rated health, and low and decreasing probability of <35 weekly working hours', n = 2,124).
Odds ratio (OR) with 95% confidence intervals (CI). Statistically significant ($p < 0.05$) estimates are bolded.

Table 3 shows the associations of lifestyle and mental health -related factors and cluster membership (self-rated health and night shifts) based on multinomial regression analysis. Cluster 2 "Sustained optimal self-rated health, no night work" was used as a reference cluster.

Cluster 1, characterized by poorer and declining self-rated health than in the reference cluster, but similar minimal levels of night work' was more probable among older employees (OR = 1.05, 95% CI 1.04–1.06), in those with more lifestyle risk factors ($OR_{currentsmoking}$ = 1.96, 95% CI 1.55–2.48; $OR_{ex-smoking}$ = 1.38, 95% CI 1.14–1.67; $OR_{obesity}$ = 2.81, 95% CI 2.22–3.57; $OR_{lowphysicalactivity}$ = 1.74, 95% CI 1.46–2.08), sleep problems (OR = 2.17, 95% CI 1.79–2.63), and psychological distress (OR = 2.24, 95% CI 1.86–2.70).

Cluster 3, characterized by similar optimal self–rated health, but contrary to the reference cluster, employees worked night shifts, was more probably among younger employees (OR = 0.95, 95% CI 0.94–0.96) and those who smoked ($OR_{current}$ = 2.16, 95% CI 1.62–2.87; $OR_{ex-smokers}$ = 1.31, 95% CI 1.02–1.69), but also those with a lower likelihood of at-risk alcohol use (OR = 0.47, 95% CI 0.31–0.73) and psychological distress (OR = 0.74, 95% CI 0.56–0.99).

Cluster 4, characterized by both poorer self–rated health and higher probability of night work, was associated with a higher likelihood of lifestyle risk factors ($OR_{currentsmoking}$ = 3.13, 95% CI 2.45–4.01; $OR_{ex-smoking}$ = 1.36, 95% CI 1.09–1.70; $OR_{obesity}$ = 3.23, 95% CI 2.49–4.17; $OR_{lowphysicalactivity}$ = 1.45, 95% CI 1.19–1.78), sleep problems (OR = 1.93, 95% CI 1.55–2.41), and psychological distress (OR = 1.99, 95% CI 1.61–2.45).

Discussion

This study examined the combined trajectories of self-rated health and objectively measured working hour patterns over an 8-year follow-up among 5,947 shift working healthcare employees. Moreover, we examined lifestyle and mental health -related factors that predicted each trajectory. For self-rated health and working <35 hours/week, three distinctive clusters emerged: (1) "Slightly declining good health, and slightly increasing working time"; (2) "Sustained good health, and moderate but slightly increasing working time"; and (3) "Fairly good but declining health, short and decreasing working hours".

The identified concurrent trajectories of health and patterns of working hours add to the earlier research on healthy worker effect (35). Our results corroborate the previous findings that working hour patterns are modified by health (1–7). A total of 27% of participants belonged to the cluster characterized by declining health and shortening weekly working hours. This is in line with earlier findings that declining health is often associated with working fewer hours (8, 9). However, this is not the case for all employees: 38% worked standard hours despite declining

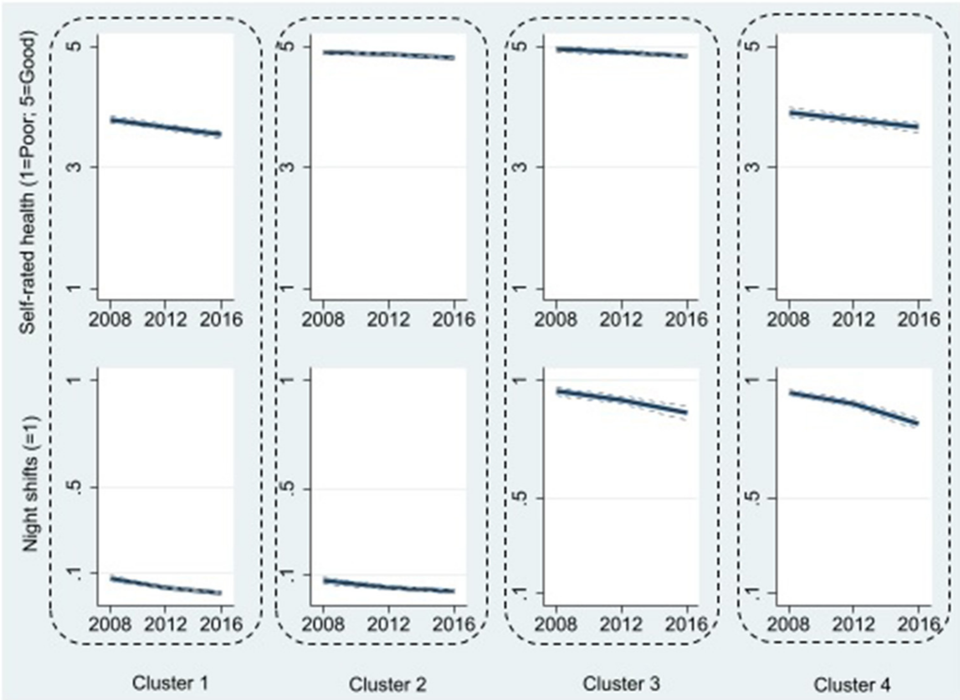

FIGURE 3
Four clusters of trajectories of self-rated health and working night shifts. Cluster 1 (41%): Fairly good but declining self-rated health, and no night work; Cluster 2 (25%): Sustained optimal self-rated health, and no night work; Cluster 3 (13%): Sustained optimal self-rated health, and high but slightly decreasing probability of night work; Cluster 4 (21%): Fairly good but declining self-rated health, and high but decreasing probability of night work. 95% confidence intervals are shown as dotted lines, albeit they are poorly visible due to being very narrow.

health. Congruent to earlier studies, lifestyle risk factors were predictive of poorer self-rated health (36). However, sleep problems were the only risk factor linked with high and stable probability short weekly working hours. Previous research has shown significant differences between individuals in sleepiness (37), which may affect their suitability to shift work.

For self-rated health and night shift work, four distinctive clusters emerged: (1) "Fairly good but declining health, no night work"; (2) "Sustained good health, no night work"; (3) "Sustained good health with night work"; and (4) "Fairly good but declining health with night work". In both trajectories including night work, the trend was decreasing. We did not identify trajectories, or trajectory clusters, characterized by increasing trend in night work. A total of 66% of participants belonged to the two clusters characterized by good health, but a minimal amount night work. Also here, lifestyle risk factors were predictive of poorer health. Those who continued working night shifts despite declining health, had a higher probability of poor lifestyle and mental health as compared to those also having declining health, but not working night shifts. In turn, those who remained in optimal health and consistently worked night shifts for the entire follow-up of 8 years, were characterized by younger age, lower likelihood of at-risk alcohol use, and lower likelihood of psychological distress.

The association with younger age was expected as earlier studies have shown that younger and older employees might respond differently to night work (13, 14). However, few longitudinal studies on the association between night shift work and lifestyle factors exist. Night shift work has been previously associated with poor sleep patterns, higher body mass index and smoking (38–41). The results on physical activity have been mixed (40, 42), but a previous study originating from the same Finnish public sector cohort as used in this study, showed an increased probability of physical activity in employees with night shifts (43).

Our findings support the hypothesis of the healthy worker effect in night work (35), that is, those who have health problems might be less likely to work night shifts or move from night work to day work (10). We identified a distinct cluster characterized by employees with suboptimal health selected to daywork, and another district cluster characterized by employees with sustained optimal health selected to night work. Between these clusters, there were employees characterized by decreasing trend in both probability of night shift work and in health. This cluster

TABLE 3 Health and lifestyle -related factors associated with cluster membership (self-rated health and night work).

	Cluster 1: Fairly good but declining self-rated health, and no night work, $n = 2,443$		Cluster 3: Sustained optimal self-rated health, and high but slightly decreasing probability of night work, $n = 755$		Cluster 4: Fairly good but declining self-rated health, and high but decreasing probability of night work, $n = 1,183$	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Men (=ref)	1		1		1	
Women	1.03	0.78–1.36	0.90	0.65–1.26	0.81	0.60–1.10
Age/1 year	**1.05**	**1.04–1.06**	**0.95**	**0.94–0.96**	1.00	0.99–1.01
Non-smoking	1		1		1	
Ex-smoking	**1.38**	**1.14–1.67**	**1.31**	**1.02–1.69**	**1.36**	**1.09–1.70**
Smoking	**1.96**	**1.55–2.48**	**2.16**	**1.62–2.67**	**3.13**	**2.45–4.01**
No at-risk alcohol use	1		1		1	
At-risk alcohol use	0.96	0.75–1.24	**0.47**	**0.31–0.73**	0.91	0.67–1.22
Non-obese	1		1		1	
Obese	**2.81**	**2.22–3.57**	1.29	0.92–1.80	**3.23**	**2.49–4.17**
≥ 2 MET hr/day	1		1		1	
<2 MET hr /day	**1.74**	**1.46–2.08**	0.96	0.75–1.23	**1.45**	**1.19–1.78**
No sleep problems	1		1		1	
Sleep problems	**2.17**	**1.79–2.63**	1.07	0.81–1.42	**1.93**	**1.55–2.41**
No psychological distress	1		1		1	
Psychological distress	**2.24**	**1.86–2.70**	**0.74**	**0.56–0.99**	**1.99**	**1.61–2.45**

Multinomial regression (ref=Cluster 2 'Sustained optimal self-rated health, no night work', n = 1,381).
Odds ratio (OR) with 95% confidence intervals (CI). Statistically significant ($p < 0.05$) estimates are bolded.

can be described as comprising those among whom the adverse effects of continuing night work are best illustrated. Our findings support earlier research findings showing that older employees prefer shorter shifts and day shifts (11), and that the benefits to improved sleep quality are most pronounced among aging employees transferring from shift work to daywork (25).

Depending on the multi-trajectory model, 35–38% of participants had a sustained optimal health status. For the majority (62–65%), the health trajectory was declining. However, as the sample consisted of employed working-aged individuals, self-rated health status was not poor in any of the clusters. There were, however, no clusters where health would improve in line with less working hours or less night shifts. Some earlier studies have examined the trajectories of self-rated health in varying populations, and in found similarly shaped trajectories (44, 45).

The study is the first to examine the concurrent changes in self-rated health and objectively measured working hour patterns. The use of objective data on working hours is a strength and adds validity to our findings, as subjective estimates on working hours are prone to recall or reporting bias. Our findings may be of specific interest for the health care sector struggling with aging employees, personnel turnover and shortage, and both physically and psychosocially demanding work (46, 47), as they support other studies on shift work and health proposing that employees over 50 years should be offered an opportunity to move away from shift work to avoid health problems (48, 49).

Two main limitations of this study are data attrition (linkage to working hour records was available for 21,919 out of 52,891 respondents but due to missing data at follow-up the final analytic sample included only 5,947 participants) and generalizability given that 93% were women, 56% nurses and all were working in the healthcare sector. The loss to follow-up, particularly in survey responses in 8 years from 2008 to 2015/2016, may partly be due to employees changing employers, or having left the labor market either temporarily or permanently. The possible health-related selection out of the labor market suggests that our estimates may be underestimates of the true effect. That is, without any health-related selection to another employer or out of the labor market, the differences in trajectories would be even more pronounced, and subsequent associations with lifestyle and mental health stronger. Moreover, we only had an opportunity to measure self-rated health and working hour patterns in three timepoints. However, the follow-up time on 8 years was rather long. The cohort included predominantly women working in public health care sector in Finland. Therefore, the results may not be generalizable to male-dominated private sector employees in shift work. Finally, as the trajectories are approximations of the true development, we cannot rule out that some people were misclassified and the group where they were placed does not describe the true development of their health and working time patterns. However, as the reliabilities in each trajectory group were satisfactory (average posterior probability ranged from 0.82 to 0.94), a classification error is an unlikely source of major bias in our results.

To conclude, the results of this study indicate that suboptimal and declining health is linked with sub-standard working hours and potential transition away from night shifts, which may indicate the healthy worker effect. These results may partly explain, why some studies have struggled to find associations between working hour patterns and sickness absence.

Data availability statement

The datasets presented in this article are not readily available because linked working hour data records require separate permission from the data owners. Statistical syntax for the analysis of the present study is available from the corresponding author. Anonymized questionnaire data from the FPS study can be shared upon request to the corresponding author. Requests to access the datasets should be directed to jenni.ervasti@ttl.fi.

Ethics statement

The studies involving human participants were reviewed and approved by Ethical Committee of the Helsinki and Uusimaa Hospital district (HUS/1210/2016). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

JE, LP, and AR designed the study. AK managed the data. JE performed data analysis and wrote the first draft. All authors participated in interpreting the data and critically reviewing the paper.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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The association between circadian rhythm of cortisol and shift work regularity among midwives—A multicenter study in Southeast China

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Objective: This article aims to explore the association between the trends of cortisol rhythm and the regularity of shift work among midwives.

Methods: Midwives from six Southeast Chinese hospitals were recruited through cluster sampling in a multi-center cross-sectional study. Urine samples were collected half an hour after waking up, at 11:00, 19:00, and 23:00 on two consecutive days in a longitudinal cohort. The urinary cortisol was assayed by the chemiluminescence method.

Results: A total of 86 midwives were included in this study, contributing 688 cortisol samples. The midwives displayed a circadian rhythm in cortisol secretion, with zeniths in the morning and nadirs in the evening. The trend of the first day was repeated on the second day. Although the total working hours per week of the two groups, namely the regular shift group ($N = 43$) and the irregular shift group ($N = 43$), were the same, significant main effects of groups ($F = 62.569$, $p < 0.001$), time ($F = 45.304$, $p < 0.001$), and group-by-time interaction ($F = 226.695$, $p < 0.001$) were indicated through linear mixed models. The main effect of day was not statistically significant, with $F = 0.105$ and $p = 0.746$. The fluctuation range of cortisol curve in the group with irregular schedules was slightly lower than that in the group with regular schedules.

Conclusion: Our results may indicate that cortisol was more inhibited in midwives with irregular shift patterns than those with regular shift patterns. It is necessary to further study the relationship between cortisol rhythm and patterns of midwives' shifts in future so as to lay a foundation for hospital managers to develop a more reasonable scheduling system for midwives with the further purpose to minimize their occupational fatigue and ensure the safety of mothers and infants.

KEYWORDS

midwives, cortisol, circadian rhythm, shift regularity, linear mixed-effects models

Introduction

Biological rhythm refers to one of the periodic phenomena of life activities, existing in almost all living organisms. In physiological circumstances, when an individual is not exposed to stress, hormonal secretion is regulated by the circadian rhythm. Cortisol, usually assayed from saliva, serum, urine, or hair (1), is a corticosteroid hormone that influences memory consolidation in humans (1) and is a parameter widely accepted by science as the best indicator of stress.

The cortisol release follows a circadian rhythm, which is high in the morning and low at bedtime (2). This circadian rhythm is established between 2 and 9 months after birth (3). This typical secretion pattern is crucial to the functions of all other systems of the human organism (4).

The European Union (EU) defines stress as "a set of neuroendocrine, immunological, and emotional processes and responses" (5) and indicates that stress associated with the workplace is the second most common work problem after musculoskeletal disorders. High and sustained levels of stress can increase the risk of cardiovascular disease, increase susceptibility to infections and mental disorders, and affect the task performance of health professionals (6).

Midwives play an important role in ensuring and promoting the health of pregnant women and newborns (7). Delivery rooms are a place of great pressure, so midwives need to closely observe the labor process, continuously monitor fetal heart, carefully identify critical and abnormal situations, and immediately give effective intervention when necessary. Therefore, their professional skills and abilities for stress are highly required. In recent years, China's universal three-child policy has led to the possibility that some elderly women may give birth to a second or third child. As a result, complications before and during pregnancy have increased, so has the pressure on midwives (8). Shift work is very common in delivery rooms. Some midwives have relatively fixed internals between night shifts or fixed forms of night shifts, while some fluctuate greatly, some attend night shift work in turn, and still some permanent night shift work. They experience fatigue, stress, and burnout due to their workloads. Midwives have reported moderate-to-severe levels of exhaustion on 22–50% of all shift days (9).

There is considerable evidence that acute stressors increase cortisol excretion, for example, a year-long longitudinal study in Germany concluded that waking cortisol was significantly higher among physicians who performed shift work (10).

However, whether irregular shifts increase cortisol disruption is not well understood. In this study, it was hypothesized that irregular shifts could further deepen the effects on cortisol rhythms based on the knowledge that midwives experience changes in stress biomarkers after long-term exposure to stress of daily work. We considered urine cortisol as an indicator to analyze the characteristics of cortisol rhythm of midwives in delivery rooms within 48 h and explore the relationship between cortisol rhythm and scheduling.

Materials and methods

Study design and participants

This study was designed as a cross-sectional survey and adhered to STROBE guideline. A descriptive and cross-sectional study was conducted from January 2020 to March 2020 in six Chinese hospitals by means of cluster sampling.

The inclusion criteria were as follows: (1) midwives who were on night shift continuously in 3 months before investigation; (2) midwives who were professionally qualified in labor rooms; (3) midwives who had no mental or physical ailments that could prevent them from their work; (4) midwives who had a regular lifestyle; (5) midwives who had no major life events in 6 months before investigation; (6) midwives who had more than 1 year of midwifery experience in labor rooms; (7) midwives who had not smoked, drunk coffee or tea 12 h before urine samples were collected; (8) midwives who participated in this study voluntarily.

The exclusion criteria were as follows: (1) midwives who were absent from work due to illness for more than 15 days in the last 3 months; (2) midwives who smoked or had ever smoked for more than 5 years; (3) midwives who had an abuse of alcoholic beverages or had ever had such a history for more than 5 years; (4) midwives who were using medications that influence the hypothalamic–pituitary–adrenal (HPA) axis (for example glucocorticoids, steroids, beta-blockers, antidepressants, melatonin, or any other psychoactive drugs); (5) midwives who were medically diagnosed with neurological or psychiatric illness; (6) midwives who had such health-related problems as diabetes, high blood pressure, or cancer; (7) midwives who were in menstrual or ovulation period, pregnancy, or lactation; (8) midwives who were diagnosed with acute diseases or in an acute attack stage of chronic diseases.

Outcome measurements

After the distribution of urine packs, midwives were informed to collect their urine samples at eight time points. The subjects collected their urine according to the specific time intervals they were told to follow. Urine samples were collected on two consecutive working days, four times a day, namely, half an hour after waking up, at 11:00, 19:00, and 23:00. Thus, urine samples were obtained from each subject at four intervals within two consecutive days, which were classified as T_1, T_2, T_3, and T_4 on the first day and T_1, T_2, T_3, and T_4 on the second day.

About 2 mls of all urine samples was taken and centrifugated at 3000 rotational speed per minute (rpm) for 8 min and then

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was stored in a refrigerator at −80°C for further testing. After that, each portion of centrifugate was tested for the level of cortisol by ELISA kits (The brand of Access Cortisol: Beckman Coulter, Catalog number: 33600. Testing instrument: Access) and chemiluminescence method.

Data collection

Urine samples and data were collected from midwives working in the six hospitals involved in this study. Informed consent was obtained from the nursing departments of these hospitals prior to the investigation. A project work group was established to develop a unified survey and questionnaire to carry out the investigation through unified methods. The researchers trained six charge nurses in the maternity wards of the sample hospitals and presented the study protocols. After unified training and assessment, the charge nurses then explained in detail the objective of the study, questionnaire filling method, and the method of urine specimen collection to the subjects who met the inclusion criteria. The subjects were asked to wrap their urine samples in a separate black plastic bag and store them temporarily in a refrigerator at 4°C. Researchers visited each sample hospital once or twice a day and sent urine samples collected in ice packs to laboratories for unified testing until all urine samples were collected and tested.

A questionnaire was conducted 1–3 days before the urine test. In the baseline questionnaire, each midwife was asked "Is your night shift regular?" Irregular shifts were defined as the intervals between night shifts or the forms of night shift (e.g., night shift before mid-night, night shift after mid-night, and overnight shift) which were not fixed in the month prior to the survey. Otherwise, it was defined as a regular one. The head nurses classified participants based on their schedules for the month preceding the survey. Participation was voluntary and anonymous. The head nurses assisted in distributing the questionnaires and reminded the midwives to complete them. The questionnaires were sealed for confidentiality and given to the head nurses when completed.

Data analysis

Statistical analysis was performed by SPSS statistical software (version 26.0, SPSS Inc., Chicago, IL, USA). Data that conformed to the normal distribution were expressed as mean ± standard deviation, and the differences between groups were compared through the independent-samples test. For quantitative data that did not conform to the normal distribution, the median (interquartile range) was used, and the differences between groups were compared through the Wilcoxon rank sum test. The categorical variables were presented as numbers (n) and percentages (%), and the differences between groups were compared with the chi-square test. Fisher's exact test was performed for categorical variables with small, expected numbers. The distributions of the cortisol

TABLE 1 Demographic data of study participants.

Variation		Regular shift group ($n = 43$)	Irregular shift group ($n = 43$)	Total	$z/\chi^2/t$	p
Age		29(26,36)	29(26,32)	29(26,34)	0.757	0.449
Marital status	Unmarried	17	16	33	0.049	0.825
	Married	26	27	53		
Level of education	Junior college	18	21	39	0.422	0.516
	Bachelor's degree or above	25	22	47		
Years of working in delivery room	≤10 year	31	33	64	—*	0.078
	11–20 year	7	10	17		
	≥21 year	5	0	5		
Working hours per week (hour)		40(35,47)	39(35,48)	39(35,47)	0.636	0.525
Night shift days per month (day)		4(2,6)	4(2,5)	4(2,5.25)	0.226	0.821
Body mass index (BMI)		21.56 ± 2.54	20.35 ± 2.38	20.80 ± 2.49	1.714	0.090
Physical activity	Inactive	13	13	26	0.003	1.000
	Active	30	30	63		
The main forms of night shift	16:00–24:00	11	10	21	—*	0.694
	0:00–8:00	16	12	28		
	16:00–8:00 at next day	12	17	29		
	8:00–16:00 and 0:00–8:00 at next day	4	4	8		

*Fisher's exact test.

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levels were skewed to the right, so we transformed the data into logarithm with its base of 10. The log-transformed data were then normally distributed. Linear mixed-effects models (LMMs) were used to test changes in outcomes over time, and age was used as a moderating factor. A two-tailed significance test was applied for all comparisons, and $P = <0.05$ indicated statistical significance.

Results

General demographic

Of the 100 participants, nine did not attend the night shifts and five were excluded due to incomplete data. The actual samples ($n = 86$) were composed of 50% regular night shift group ($n = 43$) and 50% ($n = 43$) irregular night shift group. We surveyed the subjects' ages, education, marital status, and so on. Table 1 shows the characteristics of the study samples: A total of 86 midwives were with a median age of 29 (26, 34) years, averaging almost 39 (35, 47.13) h of work per week, and 4 (2, 5.25) night shift days per month. Regarding health-related behaviors, no midwives smoked or had risky alcohol use. The majority (69.77%) were engaged in regular physical activity, and the majority (77.9%) had normal body mass index. There was no statistical difference in basic characteristics and lifestyle between the two groups.

Cortisol rhythm

Raw cortisol data are shown in Table 2, and the logarithmic distribution of the cortisol of the midwives in the two groups for two consecutive days is shown in Figure 1, suggesting a significant change of cortisol release over time.

The average logarithm of day was the highest half an hour after waking up and then declined gradually over the day, reaching their lowest point at 23:00. Half an hour after waking up the next day, the cortisol level was close to that of the first day, and the changing trend of the first day was repeated. Midwives with regular shifts had a greater range of cortisol changes. The p-values for the changes in time, group, day, and group*time were calculated by linear mixed model. The analysis considered time, group, day, and group*time as fixed effects, subjects' numbers as random effects, and their ages as a covariate.

A design of 2 (regular night shift/irregular night shift) × 4 (four duration points) was carried out to assess the differences of the two groups across time. We found significantly lower cortisol levels in regular shift midwives than those in irregular shift midwives ($F = 62.569$, $p < 0.001$). The changes of cortisol levels of midwives over time were obvious, with $F = 45.304$ and $p < 0.001$. The group-by-time interaction was also obvious, with $F = 226.695$ and $p < 0.001$. The main effect of day was not statistically significant, with $F = 0.105$ and $p = 0.746$. The estimates of fixed effects are shown in Table 3.

TABLE 2 Cortisol levels between the two groups [$P_{50}(P_{25}, P_{75})$].

	Regular shift group ($n = 43$)	**Irregular shift group ($n = 43$)**
T_1 on the first day	19.05 (14.13,28.84)	25.7 (16.6,45.71)
T_2 on the first day	17.78 (13.18,25.7)	22.91 (16.98,39.81)
T_3 on the first day	14.45 (9.12,17.78)	23.99 (15.49,34.67)
T_4 on the first day	6.46 (3.02,12.88)	21.88 (14.45,38.02)
T_1 on the second day	16.6 (12.02,24.55)	28.18 (18.2,50.12)
T_2 on the second day	16.6 (10.72,27.54)	25.12 (19.5,45.71)
T_3 on the second day	12.3 (9.12,16.22)	26.3 (17.78,44.67)
T_4 on the second day	5.5 (3.72,12.3)	28.84 (16.98,40.74)

Main effect derived from the comparison between the groups

The main effect from the comparison between the two groups was that the mean logarithmic cortisol of the regular group was 0.33 (0.25–0.41) lower than that of the irregular group, which was statistically significant ($P < 0.001$).

Main effect derived from the comparison of eight time points

Further analysis through pairwise comparison was carried out to test whether the differences between the adjacent time points were significant, as shown in Table 4. The logarithm of cortisol began to decline ($p < 0.001$) at 19:00, and it dropped to its lowest level ($p < 0.001$) at 23:00.

Discussion

In this study, the aim was to examine the impact of shift work regularity on circadian rhythm of cortisol. We used cortisol and its variations to reflect the daily stress experienced by midwives in hospital delivery rooms. The midwives' urinary cortisol levels varied based on different shift schedules for the two groups though their overall working hours were the same and their night shift days were approximate. Linear mixed models found that time, group, and time*group were statistically significant.

Further comparison showed that the cortisol of midwives began to decrease gradually half an hour after waking up in the morning, till to the lowest point at 23:00 on the first day. Compared with that lowest point, it rose obviously 30 min after waking up in the next day, and the trend of the first day was repeated until another trough appeared at 23:00. The

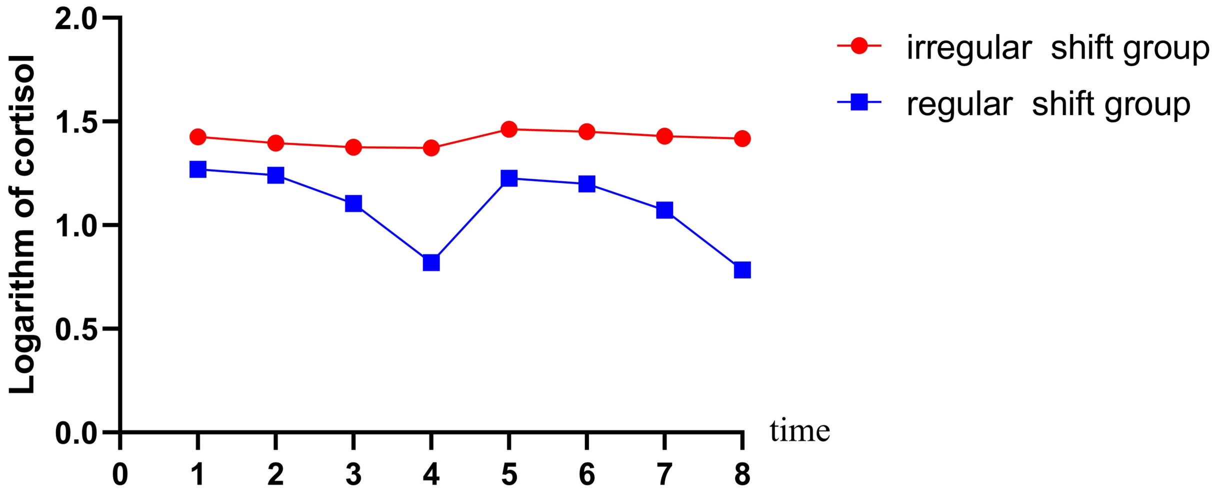

FIGURE 1
Diurnal pattern of cortisol secretion according to shift work at baseline. 1 = 30 min after waking on the first day; 2 = 11:00 on the first day; 3 = 19:00 on the first day; 4 = 23:00 on the first day; 5 = 30 min after waking on the second day; 6 = 11:00 on the second day; 7 = 19:00 on the second day; 8 = 23:00 on the second day. The blue line represents cortisol pattern for midwives with regular shifts (*N* = 43). The red line represents cortisol pattern for midwives with irregular shifts (*N* = 43).

TABLE 3 Estimates of fixed effects.

Parameter	Estimate (95% CI)	*p*
Intercept	0.85(0.62,1.09)	
[group = 1]	0.60(0.49,0.71)	<0.001
[time = 1]	0.45(0.39,0.52)	<0.001
[time = 2]	0.42(0.36,0.49)	<0.001
[time = 3]	0.28(0.22,0.35)	<0.001
[day = 1]	0(− 0.03,0.02)	0.746
Age	0(− 0.01,0.01)	0.629
[time = 1] * [group = 1]	−0.41(−0.5, −0.32)	<0.001
[time = 2] * [group = 1]	−0.4(−0.49, −0.31)	<0.001
[time = 3] * [group = 1]	−0.27(−0.36, −0.18)	<0.001

*Group = 1: irregular shift group.
Time = 1: 30 min after waking.
Day = 1: the first day.

TABLE 4 Pairwise comparisons of time effect.

	Adjusted difference (95% CI)	*P*
T_1 vs. T_2	0.03(−0.01,0.06)*	0.155
T_2 vs. T_3	0.08(0.04,0.11)*	<0.001
T_3 vs. T_4	0.15(0.1,0.19)*	<0.001

*Linear mixed-effects model adjusted for age, day, and subject as a random effect.
T_1 = 30 min after waking; T2 = 11:00; T_3 = 19:00; T_4 = 23:00.

fluctuation range of cortisol curve was slightly lower in the group of midwives with irregular work schedules. Our data confirmed that the variations of cortisol of midwives in the two groups were different, indicating that irregular schedules exerted more impact on the circadian rhythms than regular schedules among midwives on shift.

According to the latest research findings, cortisol, as a health biomarker of circadian rhythm, has been extensively investigated (11).

The cortisol release is typically in line with circadian rhythm, which is believed to grow within the first hour after waking up and reach its pinnacle around 30–45 min after waking up. It gradually dwindles during the day and falls to the minimum at mid-night (11, 12). Such circadian rhythm was verified through the logarithmic distribution of the 86 midwives' cortisol for two consecutive days in our study.

It is well known that both acute and chronic stress imply changes in cortisol. The circadian disruption induced by shift work would impair the functioning of the hypothalamic–pituitary–adrenal (HPA) axis which regulates the biological response to stressful stimuli (1). Immediate release of cortisol is an adaptive response to acute stress, but repeated or long-lasting stress may have negative effects on human bodies, that is, failure to exhibit an expected biomarker's circadian cycle or to recover after a stressor (13). Saliva cortisol level flat mirror is the foundation of HPA axis dysfunction (14).

Our study found that midwives with irregular shifts had relatively high cortisol levels at all the four points of the day (including waking up in the morning and going to bed in the evening), and their cortisol tendency from the morning to the evening was relatively stable compared with that of midwives with regular shits. Since the cortisol response was positively related to work stress, it was further confirmed that they had problems of great pressure and easy fatigue in work.

As a special medical group, midwives shoulder the double pressure of ensuring the health of delivery women and newborns. They often must deal with various special situations related to predelivery, delivery, and postpartum and are faced with many occupational risks, such as potential unsafe factors during labor, sharp instrument injury, and maternal and infant blood and body fluid exposure. The work of midwives demands constant attention, focused memory, and decision-making, and they often need to make quick decisions in emergency. For example, whether the fetus has intrauterine asphyxia, whether an emergency C-section is needed. Does the maternal labor progress stagnate? Whether the delivery women may face such situations as amniotic fluid embolism, postpartum hemorrhage, diffuse intravascular hemorrhage, and other life-threatening emergency. Individuals who work overnight or in shifts often experience circadian disruption and sleep restriction. The previous assessment of the psychological behavior scale of midwives in China found that the job burnout of midwives was at a high level (15).

It is reported that the stress of nursing teams has been evaluated worldwide with pressure scales (4). Since the scale assessment is highly subjective, we speculate that objective laboratory indicators can be referred as biomarkers of midwives' stress intensity in future, but presently, there are few studies on markers of stress in midwives. It has been found that the morning salivary cortisol concentration of emergency nurses was well correlated with the modified Mental Health Professional Stress Scale (PSS); therefore, the morning salivary cortisol sample can be applied to reflect self-perceived stress (16).

In the past, some epidemiological studies on shift work and cortisol have produced inconsistent results. For example, it was reported during shift work in emergency rooms, the salivary cortisol levels were increased (17). Sanaa found that the experimental group of nurses with night shifts had significantly higher levels of cortisol than the control group of nurses with day shifts only (18).

A similar result was found by Muhammad (19). These above-mentioned studies supported the idea that shift work can alter the cortisol patterns. However, a Canadian study among paramedics did not find any relationship between shift work and cortisol secretion (20). Those studies involved medical personnel outside obstetrics. We consider that the conclusion may be related to the nature, working environment, and working content of the specific night shift, which needs to be further analyzed in a unified and standardized way.

The sampling methods and sampling timing may affect the detection results, for example, the serum cortisol sampling time conducted in a hospital is relatively fixed, resulting in a "cortisol awakening response" (21) which is conceptualized as "a sharp increase in cortisol levels across the first 30–45 min following morning awakening" and cannot be accurately captured. In our study, we designed a urine sample of cortisol that can be easily sampled and administered by midwives at home. The first sample of the day was taken 30 min after waking up in the morning, just at the theoretical peak of cortisol secretion, so there was no specific time for collection. On the contrary, this is the time when most midwives are ready to leave home for work, which means they are about to be counted as working status and are psychologically ready to face the stress of the day.

On the other hand, those studies only reported whether they were engaged into shift work and aimed at medical personnel outside the obstetrics. We believe that the conclusion of the correlation between cortisol and shift work may be related to the nature, environment, and content of the specific night shift, which needs further analysis. The nature and pressure of midwives' work are different from those of nurses, so it is necessary to study separately the pressure status of midwives and to analyze accurately their stress index and help midwifery managers to carry out accordingly manpower management and occupational fatigue protection. There were few previous studies on the variation trend of midwives' shifts and cortisol levels, so the conclusion of our study can provide innovative reference for the management of the allocations of midwife human resources and the obstetrical midwifery technical forces. Given the nature of natural childbirth, it is not possible to completely avoid shift work for midwives, and it is necessary to reasonably adjust the number of shifts to minimize disruption to their circadian rhythms. Previous large sample data from the research hospital showed that the number of natural newborns during the day was nearly the same with that during the night (22). This study found that even working for the same hours with midwives with regular shifts each week, midwives with irregular shifts had higher cortisol level, which indicated that their work pressure was higher. This may be an area requiring further research and improvement in future.

Cumulative epidemiological evidence suggested that shift work could exert harmful effects on human health. Several chronic health conditions have been identified related to it (23).

According to a handful studies with respect to recovery of cortisol circadian rhythm after shift work, it would be more desirable to allow sufficient time for rest between shifts (24). The time from shift work to full recovery can cover at least 2 days in the case of frequent interruption of normal circadian rhythms, and even 3–4 days if they were severely disrupted (25). Midwives in the United States whose work shifts are longer than 12 h have higher rates of excessive daytime sleepiness than midwives whose work shifts are not longer than 12 h (26). Structural changes for midwives to ensure personal and patients' safety include changing the workflow, environment, or institutional policies. This study found no statistical significance of the main effect of the number of days, considering that it was related to the small number of days studied, but it is also possible that the regularity of the shift only affects the level of cortisol change within 24 h. Therefore, it is recommended to extend the days for study in future to explore the characteristics of cortisol changes within several days after the regular/irregular group midwives just complete the night shifts and to determine which shift cycle and shift form of midwives are more desirable for their circadian rhythm. It is also suggested that a relatively stable interval between shifts be maintained to help the midwives to restore their circadian rhythms after work at night and get sufficient rest at intervals of work.

Conclusion

From the research, it is clear that irregular shifts can be stressful to many midwives. The evidence from available research on shift work and cortisol circadian rhythm would provide meaningful information to future interventions regarding work schedule management. It was reported that the cortisol status may influence overall health condition as well as such indispensable work skills as attention (27). Midwives need to be very focused to observe labor process and handle it decisively in their jobs. Therefore, to improve the quality of their work, to protect their physical and mental health, and to ensure the safety of mothers and infants, hospitals need to intervene in their managements to develop a physiologically more appropriate and adaptive shift schedule to fully restore midwives' circadian rhythm and prevent possible disruption after their night work. In the meantime, accurate, valid, and non-invasive methods need to be applied to understand and monitor the midwives' levels of work stress. According to the test results, early warning intervention may be given. This study provides a new basis for protecting midwives' physical and mental health and the safety of mothers and infants.

Strengths

This was a multi-center study on six Chinese hospitals, which was representative to some extent. Urine cortisol was collected and measured at eight time points for two consecutive days to obtain reliable trends of its variation. To the authors' knowledge, the relationship between shift regularity and cortisol rhythm had been rarely reported in the literature, so this study provided an innovative basis for a more rational dispatch of midwives.

Limitations

First, the influence of additional stress sources outside the workplace was not evaluated. Second, we did not record in detail the accurate amount of job of each participant during their shifts.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Human Subjects Ethics Committee of Fujian Provincial Maternity and Children's Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

X-mJ: study design, quality control, and manuscript revision. X-xH: data collection, data analysis, manuscript drafting, and manuscript revision. Q-XZ and X-QC: data interpretation and data collection. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Night shifts in interns: Effects of daytime napping on autonomic activity and cognitive function

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Objective: Night shifts have adverse cognitive outcomes that might be attenuated by daytime napping. The neurovisceral integration model suggests that resting vagally mediated heart rate variability (vmHRV) is linked with cognitive function. This study investigated the relationship between resting vmHRV and cognitive function after different nap durations in interns after shift work.

Methods: A total of 105 interns were randomly allocated to one of three groups (non-nap, $n = 35$; 15-min nap, $n = 35$; 45-min nap, $n = 35$) to perform cognitive tests and resting vmHRV at 12:00, 15:00 and 18:00. Information processing (digit symbol substitution test; DSST), motor speed (finger tapping test; FTT), response selection (choice reaction time; CRT), and attention shifts (shifting attention test; SAT) were assessed. Resting vmHRV was assessed at baseline and during each cognitive task across groups.

Results: Compared with the non-nap control, the 15-min and 45-min naps improved all outcome measures (including subjective sleepiness and cognitive performance) at 15:00, with some benefits maintained at 18:00. The 15-min nap produced significantly greater benefits on the FTT at 15:00 after napping than did the 45-min nap. Resting vmHRV was significantly correlated with DSST and SAT performance. In addition, FTT performance was the only significant predictor of DSST performance across different nap durations.

Conclusion: Our results demonstrate links between daytime napping (in particular, a 15-min nap) and improved cognitive control in relation to autonomic activity after shift work in interns. These results indicated that autonomic activity when awake plays a crucial role in DSST and SAT performance and facilitated the understanding of differences in neurocognitive mechanisms underlying information processing after different nap durations.

KEYWORDS

night shifts, daytime napping, autonomic activity, cognitive function, intern

Introduction

In China, the population of shift workers is approximately 80 million (1). With the busy work schedule and the increasingly tense work environment, Chinese healthcare shift workers are facing tremendous mental pressure and risk. Shift work involving circadian disruption may disturb the sleep/awake cycle. Altered sleep/wake rhythms of interns working night shifts has been associated with decreased vigilance and psychological stress (2), which is not only associated with various negative health outcomes such as obesity, cardiovascular disease, and cancers (2–9), but also potentially related to medical errors and adverse patient-related outcomes (2, 10–13). Schernhammer ES (8) found that night shifts improved the risk of colorectal cancer in the nurses. Other research also showed that night shifts were the important risk factor for breast cancer (9). Medical errors among healthcare shift workers during night shifts is well documented. Trauma residents made more cognitive errors using a simulated laparoscopic exercise due to sleep loss (12). Rothschild JM also observed that increasing rates of nighttime surgery complications were performed by attending physicians who had slept less than 6 h the previous night (13). Night shift work can lead to alterations in cognition, such as alterations in alertness, reaction times, and information processing (14).

Regarding psychological health and performance, one important cognitive process is information processing measured by the digit symbol substitution test (DSST). The DSST has been considered a "direct measure of the rate of information processing of visual figures" (15). Research has consistently observed the relationship between sleep, DSST performance, and sleep disorders, such that worse sleep quality and cognitive decline among older adults and long sleep durations (>9 h) were associated with 7-year neurocognitive decline in middle-aged to older adults (16). There are different interrelated components involved in and considered critical for good DSST performance: motor speed, relational selection, and attentional shift. To identify and assess different cognitive components that contribute to performance in the DSST, we isolated these cognitive components using a cognitive test battery that included the finger tapping test (FTT), choice reaction time (CRT), and shifting attention test (SAT) to measure motor speed, response selection, and attentional shift, respectively.

It is crucial to provide strategies that attenuate the adverse effects of shift work to ensure medical professionals' safety and health, especially their cognitive performance. Napping prior to a night shift or during the work shift has been shown to improve alertness and performance and decrease accident rates (17, 18). During shift work, naps of 20 to 50 min in duration have been associated with improvements in reaction time and restoration of performance to that seen at the start of the shift. Napping early in the night shift can improve objective measures of alertness (17). To avoid sleep inertia that sometimes occurs when waking from a nap, naps should not be longer than 50 min and can be as short as 10 to 15 min (17, 19). Naps as brief as 15 and 20 min have been shown to improve alertness following normal nocturnal sleep (20, 21). Brief naps during the night shift have also been observed to be beneficial (17). A comparison between two nap opportunities (15 vs. 45 min) following normal sleep was examined in the current study. Takahashi et al. (22) showed significantly improved alertness 30 min after the 15-min nap and comparable improvements for the two nap conditions 3 h after napping. Tietzel and Lack (23) found that 10-min nap in the afternoon was at least as recuperative as a 30-min nap in terms of improved alertness and cognitive performance for an hour following the napping after restricted nocturnal sleep. While longer naps (1 to 2 h) have been shown to be more restorative than brief naps for at least 3 h after napping (24, 25) following a night of total sleep loss. However, it is important to find the limitations of these studies. Previous studies measured the effects of different nap conditions during the 3-h time course even only 1-h time course. There is clearly a need to examine the effects of different nap conditions over an extended postnap period. Therefore, the purpose of our study was to examine the effects of different nap durations on performance after nap during long time course (i.e., 6 h). The study arranged tests at 15:00 and 18:00 after nap. Additionally, a comparison between these two nap durations (15 vs. 45 min) was examined in our study. These two durations (15 vs. 45 min) of nap opportunities were chosen in our study because, based on previous studies, a comparison between 15 and 45-min nap durations was only examined following normal sleep (22). Considering that following restricted sleep among interns, the benefits of nap durations must be weighted against their practical disadvantages. The practical aim of our study was to provide information that would allow a more informed decision regarding the most effective nap duration for improving cognitive performance in interns.

Research has shown that resting vagally mediated heart rate variability (vmHRV) may predict performance in a cognitive task (26). Some theoretical models have provided a foundation on a number of conceptual approaches linking autonomic activity and cognitive function. The polyvagal theory emphasizes the importance of the vagus nerve in regulating social behaviors and suggests that high resting vmHRV is associated with improved emotion perception (27). Another relevant model is the neurovisceral integration model (28) that indicates HRV as an essential index of adaptability and emphasizes the relationship between cognitive function and HRV (29). HRV has an effect on cognitive performance because of its ability to influence activity in prefrontal neural structures (30, 31), especially the high frequency (HF) component of the HRV, which is an index of parasympathetic control and vagal tone (32). According to the neurovisceral integration model, vmHRV plays an important role as an indicator of functional activity in the prefrontal cortex, a key area that drives cognitive control, as the heart and brain are connected *via* the vagus nerve. HRV is a non-invasive measure of beat-to-beat temporal changes in heart rate (27). vmHRV is an important index of neurovisceral integration and organismic self-regulation (33). Evidence supports the notion that resting vmHRV not only contributes to the parasympathetic nervous system and cardiac regulation but also is associated with the brain's integrative system for self-regulation in cognitive tasks (26, 28, 34, 35). Further investigation that vagal activity is associated with different cognitive tasks in the extent of different nap durations is warranted.

We investigated whether different nap durations have effects on cognitive function and whether this relationship is associated with resting vmHRV. We examined cognitive function, including information processing, motor speed, response selection, and attention shifts, measured by the DSST, FTT, CRT, and SAT in interns. In particular, the study aimed (1) to compare the differential effects of not napping, a 15-min nap, and a 45-min nap on cognitive performance, (2) to assess resting vmHRV following different nap durations during cognitive task performance, and (3) to explore the different cognitive components that contribute to performance in the DSST. We hypothesized that daytime napping, especially a 15-min nap, would benefit cognitive performance to a greater extent than non-nap conditions and that the variability in resting vmHRV during cognitive tasks would depend on the particular cognitive component and the effect of nap conditions.

Materials and methods

Participants

A total of 108 interns from the Air Force Medical University First Affiliated Hospital were recruited as volunteers. On-call interns were responsible for admitting patients throughout the night until the primary team returned at approximately 7 am and generally worked until approximately 12 pm the next day. During the night shifts, interns assist the superior doctor to deal with medical emergency, such as shock, pain, bleeding, and other medical problems. The mainly work of interns is responsible for learning treatment strategies and procedures, which needs cognitive demands, such as attention, vigilance, and information processing. They were healthy, did not have a history of psychiatric or medical disorders, and did not smoke or drink caffeine during the experiment. The interns were informed about all potential risks of the study and were supervised through the study. The participants provided written informed consent. The study was approved by the ethical committee of the Air Force Medical University.

Questionnaire

Before entering the protocol, interns completed questionnaires about their sleep status and daily habits. These questionnaires were the Pittsburgh Sleep Quality Index (PSQI) (36) and the morningness–eveningness questionnaire (37). The PSQI provided an index of the average sleep quality over the last month. Individuals with scores >5, indicating poor sleep quality, were excluded from the experiment. The morningness–eveningness questionnaire was designed to determine the circadian chronotype. Extreme morning (>70) and extreme evening (<31) chronotypes were excluded from the experiment.

Design and procedure

Out of 108 possible permutations of order for 3 conditions, 36 orders were selected at random. Interns were randomly arranged an order such that each nap condition happened an approximately equal number of times in each position order.

Assessment of subjective ratings

The participants completed the Stanford Sleepiness Scale (SSS) for the assessment of subjective sleepiness (38). The scale ranged from "1" as "very alert" to "7" as "very sleepy". Based on the aim of the study, the participants completed the self-rated sleepiness scale before the cognitive tests at 12:00, 15:00, and 18:00.

Cognitive performance

All tests were administered to the 15-min and 45-min groups before and after napping. The cognitive tests includes the DSST, FTT, CRT, and SAT. Motor speed measured by the FTT, response selection measured by the CRT, shifting of attention measured by the SAT, and information processing measured by the DSST were the four cognitive components. Table 1 provides a detailed presentation of the cognitive tests.

Electroencephalography recording

EEG was collected and analyzed using Scan 4.3 from a 32-channel array (10/20 system) with an Ag–AgCl electrode cap (NeuroScan Inc., Compumedics, Australia). EEG was collected from channels C3, C4, F3, F4, O1, and O2, and A1 and A2 were used as references. Bipolar horizontal and vertical electrooculography (EOG) electrodes placed 1 cm from the outer canthus of each eye were recorded at a 500-Hz sampling rate, and electromyography (EMG) was recorded *via* a bipolar channel. The skin-electrode impedance was maintained below 5 kΩ. A 50-Hz notch filter was used for the recording with bandpass

TABLE 1 Description of different cognitive tests.

Tests	Cognitive components	Details of the tests	Duration of test	References
Digit Symbol Substitution Test (DSST)	Motor speed, relational selection, attentional shift, working memory, and visual scanning efficiency	Each item in the parametric DSST included the presentation of a reference set of digit symbol pairs in the upper row at the top of each screen. A series of numbers from 1 to 9 corresponded to different symbols. At the middle of the screen, the symbols were presented in random order. Subjects were required to indicate a reference set of digit symbol pairs in the upper row *via* digit button press. DSST was performed for 3 min.	90s	(39)
Finger Tapping Test (FTT)	Motor speed	Subjects were instructed to watch the screen. Each subject selected his or her most flexible finger for the repeated tapping of the button for 10 s until a red light appeared. The test was repeated six times. The first three times were done on the right hand and next three on the left hand.	10s	(40)
Choice Reaction Time (CRT)	Selection response	Three stimuli of red, yellow, and green plots were randomly presented, and the test–retest reliability for the accurate rate in CRT was $r = 0.80$.The CRT required 3 min to complete.	90s	(41)
Shifting Attention Test (SAT)	Attentional shift	SAT was involved in one reference set in the first row and two different figures in the second row. The subjects were instructed to match the geometric objects either by shape or color. Three figures were presented on the screen, such that one reference was set on top and two different figures at the bottom. The top reference set was either a square or a circle. The bottom figures were square and circle. All figures were either red or blue (mixed randomly). Participants were instructed to match one of the bottom figures to the top reference set. Figures were matched by shape or color randomly. The SAT took 90 s to complete.	90s	(42–44)

filtering ranging from 0.1 Hz to 100 Hz. If the participants obtained slow-wave sleep (SWS) during the 15-min or 45-min nap, then they were allowed to continue sleeping until the SWS period ended. The participants were awakened only from sleep stage 1 or 2. The participants who entered rapid eye movement (REM) were excluded from the data analysis. The sleep recordings were scored using the 1968 International Criteria of Rechtschaffen and Kales (45).

Physiological measures

Psychophysiological data were collected using a three-electrode differential biological amplifier (KF2 dynamic multi-parameter physiological detector, Beijing Baomai Technology Company, China). R-waves series were automatically detected by KF2 dynamic multi-parameter physiological detector software and visually examined by skilled technicians. Incorrectly detected R-peaks were manually edited. Ectopic beats were corrected using the automatic medium filter provided by KF2 dynamic multi-parameter physiological detector software. Frequency domain measures of HRV were calculated using the classical power spectral estimation method. To remove abnormal RR intervals and obtain RR1 intervals, three-spline interpolations were performed. A sampling rate of 2 Hz was applied for the recording, and an RR2 interval was obtained. Frequency domain measures were obtained by performing fast Fourier transform. Analysis of the power spectra was performed on low frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.40 Hz) heartbeats. The LF and HF measures were expressed in normalized units (LFnu and HFnu). LFnu and HFnu are ratio indexes that eliminate interference factors from LF and HF and reflect the relative activity of the sympathetic nervous system and parasympathetic nervous system. The LFHRV and HFHRV measures had skewed distributions and were transformed by taking the natural logarithm (46). From these variables, we derived the HF normalized units (HFnu = (HFHRV [ms^2]/HFHRV [ms^2] + LF HRV [ms^2]) $\times$ 100). Because the LF normalized units are mathematically reciprocal to HFnu, we computed only the HFnu index, which is often thought to reflect vagal modulation.

Procedure

Figure 1 shows that our study consisted of three sessions (session 1, session 2, and session 3). In session 1, the participants were instructed to take a 15-min nap. In session 2, the participants were required to take a 45-min nap. In session 3, the participants did not nap.

Before the study, the participants were informed that the cognitive tests would be conducted five times to reduce practice effects. The participants completed the SSS and cognitive tests at 12:00. Before the baseline cognitive tests, the participants were instructed to sit quietly for 2 min, during which time, their "resting" heart rates were obtained. Thereafter, the participants underwent baseline cognitive testing with heart rate monitoring. They were then randomly assigned to the non-nap group (n = 35), 15-min nap group (n = 35) or 45-min nap group (n = 35). At 13:00, the participants in the 15-min nap and 45-min nap groups were taken to two sound-attenuated bedrooms for the naps. The two nap groups were required to sleep for up to 15 and 45 min. EEG was recorded throughout both nap conditions to monitor sleep.

At the end of the nap period, all the participants exited their respective bedrooms, and the electrodes were removed. They then watched videos until the testing session. At 15:00 and 18:00, all the participants repeated the above baseline assessments and cognitive tests with heart rate monitoring.

At 12:00, the participants completed a battery of tests (i.e., the SSS, FTT, CRT, DSST, and SAT). Prior to the baseline tests, the participants were assessed vmHRV in the rest condition was calculated. Afterwards, they performed the baseline cognitive tests with vmHRV monitoring throughout. The participants were assigned to the non-nap group, 15-min nap group, or 45-min nap group. At 13:00, the participants had an uninterrupted nap (15-min and 45-min nap) or remained awake with access to movies. EEG was recorded throughout the 15-min nap and 45-min nap. At the end of the nap, the electrodes were removed. After a period of free time, they were retested with the above baseline assessments and cognitive tests with vmHRV monitoring at 15:00 and 18:00.

Statistical analysis

IBM SPSS Statistics (version 21.0, SPSS, Inc., an IBM company, Chicago, IL, USA) was used for all analyses. Sleep data from the 15-min nap and 45-min nap groups were analyzed using descriptive statistics. Statistical analyses were carried out for each variable (i.e., the SSS, DSST, SAT, FTT, CRT, and HRV).

For all variables, 2-way repeated-measures ANOVA comprising 3 levels on the factor nap length (non-nap, 15-min nap, and 45-min nap) and 3 levels on the factor time (12:00, 15:00 and 18:00) was performed. For cognitive performance and HRV variables, simple within-subjects planned contrasts were then performed. The overall main differences between nap groups and times were not relevant to testing the aims of this study. The interest was in the relative changes from before to after nap between the non-nap group and other nap lengths, as investigated by examining the interaction effects between nap lengths and testing time. Factors influencing performance on the DSST performance were assessed by means of linear or non-linear hierarchical regression, as appropriate. To confirm that there were no differences in cognitive performance at 12:00 (baseline) among the three nap groups, we used one-way ANOVA with nap condition (non-nap, 15-min nap, and 45-min nap) as the between-participant factor and cognitive performance at 12:00 as the dependent variable. To assess the relative importance of HRV variables for cognitive performance, we utilized a hierarchical linear regression approach. In Model 1, cognitive performance was the independent variable, and test session was the dependent variable. In Model 2, we added the HRV factors as independent variables. By comparing Models 1 and 2, we measured the explanatory gain of HRV factors over and above individual differences in cognitive performance. All comparisons were adjusted by Bonferroni correction. Tests were calculated with an alpha of 0.05.

Results

Out of the original 108 interns, data from 3 were excluded. Two interns in 15-min nap group did not enter Stage 1 (S1), Stage 2 (S2) or SWS; while one intern terminated heart rate monitoring at 15:00. 105 interns (23–25 years old; mean ± standard error of mean: 24.3 ± 0.4) were included in final analyses. These interns were either in the non-nap group (n = 35; 35 males; mean ± SD: 24.1 ± 0.4 years), 15 min nap group (N = 35; 35 males; mean ± SD: 24.6 ± 0.3 years) or 45 min nap group (n = 35; 35 males; mean ± SD: 24.2 ± 0.4 years). EEG was recorded throughout both nap conditions to monitor sleep.

Sleep data

The participants who napped achieved physiological sleep during the 15-min and 45-min nap opportunities, as defined by the 1968 International Criteria of Rechtschaffen and Kales (45). In the 15-min nap group, the participants slept an average of 13.96 ± 1.21 min (mean ± SD), with 2.85 ± 1.01 min in stage 1 (S1), 7.26 ± 3.14 min in stage 2 (S2), and 1.98 ± 1.24 min in SWS. In the 45-min nap group, the participants slept an average of 43.18 ± 2.12 min, with 8.56 ± 2.33 min in stage 1 (S1), 22.64 ± 6.55 min in stage 2 (S2), and 5.85 ± 2.07 min in SWS.

TABLE 2 Two-way ANOVA interaction effects and planned within-subjects contrasts for condition (non-nap vs. other nap condition) by time (pre-nap vs. post-nap time) for all dependent variables.

Variable	ANOVA	Condition	Planned contrasts	
			Time	
	F		F	
			12:00 (baseline) vs. 15:00	12:00 (baseline) vs. 18:00
FTT	13.97**	Non-nap vs 15-min nap	42.73***	9.33**
		Non-nap vs 45-min nap	41.36***	6.27*
CRT	17.96**	Non-nap vs 15-min nap	50.89***	30.62***
		Non-nap vs 45-min nap	47.41***	16.04***
SAT	3.62**	Non-nap vs 15-min nap	16.25***	3.00
		Non-nap vs 45-min nap	10.25**	1.16
DSST	2.88*	Non-nap vs 15-min nap	5.33*	0.01
		Non-nap vs 45-min nap	4.46*	0.09
HFnu(FTT)	2.68*	Non-nap vs 15-min nap	8.97**	1.24
		Non-nap vs 45-min nap	1.30	2.05
HFnu(CRT)	17.96**	Non-nap vs 15-min nap	0.001	0.20
		Non-nap vs 45-min nap	0.15	1.77
HFnu(SAT)	5.57**	Non-nap vs 15-min nap	8.02**	0.57
		Non-nap vs 45-min nap	2.62	0.48
HFnu(DSST)	3.98**	Nonnap vs 15-min nap	15.12***	0.35
		Non-nap vs 45-min nap	10.76**	0.01

ANOVA refers to analysis of variance. FTT, Finger Tapping Test; CRT, Choice Reaction Time; DSST, Digit Symbol Substitution Test; and SAT, Shifting Attention Test; HFnu, high-frequency normalized units. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Assessment of subjective ratings

In the non-nap group, the participants showed a high level of sleepiness indicated by a significant increase in their SSS scores after a main effect "nap condition" was obtained [$F_{(2, 101)} = 5.10$, $p = 0.02$]. A significant main effect of "time of day" [$F_{(2, 101)} = 6.89$, $p < 0.01$] was observed. No significant "nap condition × time of day" interactions were observed [$F_{(2, 101)} = 1.13$, $p = 0.34$). In the 15-min nap group, the main effects of "nap condition" [$F_{(2, 101)} = 4.59$, $p = 0.03$] and "time of day" [$F_{(2, 101)} = 6.13$, $p < 0.01$] were also observed with lower SSS scores after napping, suggesting a high level of alertness. The "nap condition × time of day" interaction was not significant [$F_{(2, 101)} =1.08$, $p = 0.38$]. However, in the 45-min nap group, no significant differences were found as the main effects of "nap condition" [$F_{(2, 101)} = 1.01$, $p = 0.06$] and the "time of day" [$F_{(2, 101)} = 1.63$, $p = 0.08$] were not significant, and the "nap condition × time of day" interaction was not significant [$F_{(2, 101)} =1.12$, $p = 0.36$].

Cognitive performance and resting vmHRV

No significant differences were found in cognitive performance and resting vmHRV (12:00 baseline) among the 15-min nap, 45-min nap, and nonnap groups [FTT: $F_{(2, 101)} = 0.24$, $p = 0.79$; CRT: $F_{(2, 101)} = 0.66$, $p = 0.52$; SAT: $F_{(2, 101)} = 0.15$, $p = 0.87$; DSST: $F_{(2, 101)} = 0.73$, $p = 0.49$; HFnu (FTT): $F_{(2, 101)} = 0.24$, $p = 0.79$; HFnu (CRT): $F_{(2, 101)} = 2.61$, $p = 0.08$; HFnu (SAT): $F_{(2, 101)} = 0.27$, $p = 0.76$; HFnu (DSST): $F_{(2, 101)} = 2.33$, $p = 0.11$]. The results of 2-way interactions (nap condition × time of day) and simple planned contrasts against the non-nap group for all outcome measures are presented in Table 2. For the 15-min nap group, a significant planned contrast of interaction effects with the non-nap group was found with better performance for all cognitive outcome variables at 15:00 and better performance of FTT and CRT at 18:00 after the 15-min nap. In the 45-min nap group, the results also showed better performance for all cognitive outcome variables at 15:00 and better performance of FTT and CRT at 18:00 after the 45-min nap.

Figure 2 shows the changes in reaction time from the 12:00 baseline to the 15:00 and 18:00 times for all nap groups for the measures of (A) FTT, (B) CRT, (C) SAT, (D) DSST, (E) HFnu (FTT), (F) HFnu (CRT), (G) HFnu (SAT), and (H) HFnu (DSST). This method of illustration provides the relative changes following different nap durations from 12:00 to both 15:00 and 18:00. Figure 2 shows the change in the mean reaction time in the cognitive tasks across all nap groups over time. It presents the general increase in reaction time in the non-nap group and

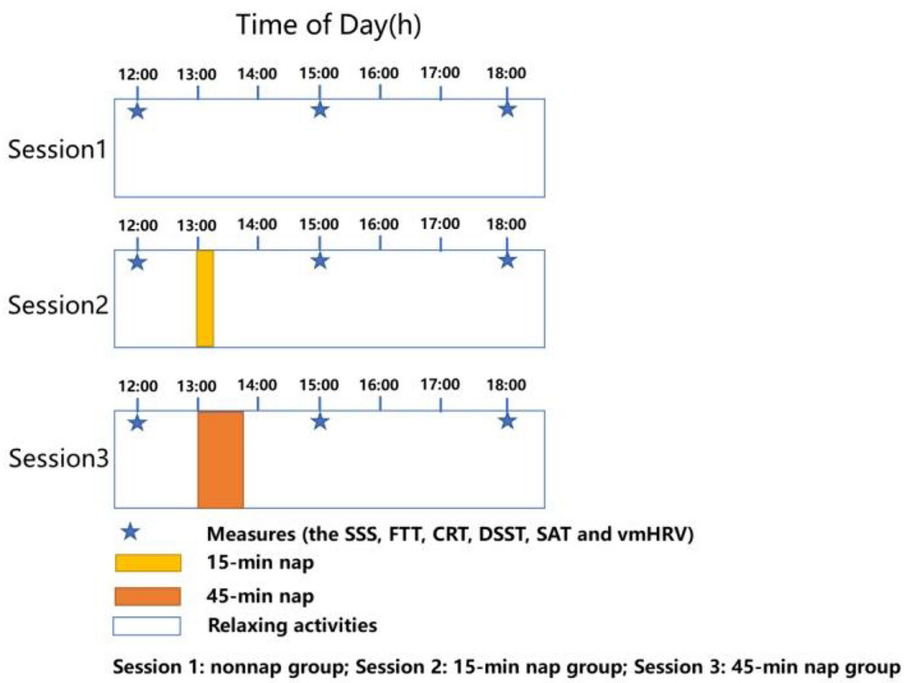

FIGURE 1
Protocol design.

a decrease in reaction time following 15-min and 45-min naps, with a regression back toward the non-nap group at 18:00 after both the 15-min and 45-min naps.

Resting vmHRV analyses revealed significant planned contrasts of the interaction effects between the non-nap group and 15-min nap group were HFnu (SAT) at 15:00 and HFnu (FTT) and HFnu (DSST) at 18:00. In the 45-min nap group, the only significant planned contrast of the interaction effects was HFnu (DSST) at 18:00.

Post hoc examination of nap conditions

Improvements in cognitive performance were evident following the 15-min and 45-min naps in this study. These improvements are graphically indicated in Figure 2 as a relatively reduced reaction time after the nap at 15:00 and subsequently increased values. *Post hoc* 2-way repeated-measures ANOVAs were performed, with 2 levels of the factor nap group (non-nap and 15-min nap) and 3 levels of the factor time (12:00, 15:00 and 18:00). In the event of a significant interaction effect, simple within-subjects planned contrasts were then performed to compare the non-nap and 15-min nap groups between the 12:00 baseline and the 2 subsequent test times, with Bonferroni adjustments due to the exploratory nature of this analysis. As presented in Table 3, significant interactions between the non-nap and 15-min nap groups were observed between 12:00 and 15:00 for all cognitive outcome variables and between 12:00 and 18:00 for FTT and CRT performance. The same analysis for the non-nap vs. 45-min nap comparison also found significant interaction effects across the three test times. The interaction between the 2 nap groups (non-nap and 45-min nap) and time (12:00 and 15:00) approached significance for all cognitive outcome measures. A significant interaction between the 2 nap groups (non-nap and 45-min nap) and time (12:00 and 18:00) was found for FTT and CRT performance.

Similarly, repeated-measures ANOVA of resting vmHRV revealed a significant main effect of HFnu (FTT), HFnu (SAT) and HFnu (DSST), with 2 levels of the factor nap group (non-nap and 15-min nap) and 3 levels of the factor time (12:00, 15:00 and 18:00). In the event of a significant interaction effect, planned contrasts were performed to compare the interaction effects of changes in the non-nap and 15-min nap groups between 12:00 and each post-nap testing period, with Bonferroni-adjusted criteria. Significant interactions between the non-nap and 15-min nap groups were observed between 12:00 and 15:00 for FTT, SAT and DSST performance. In addition, as shown in Table 4, the analysis of the non-nap vs. 45-min nap comparison found significant interaction effects across the three test times. Significant interactions between the non-nap and 45-min nap

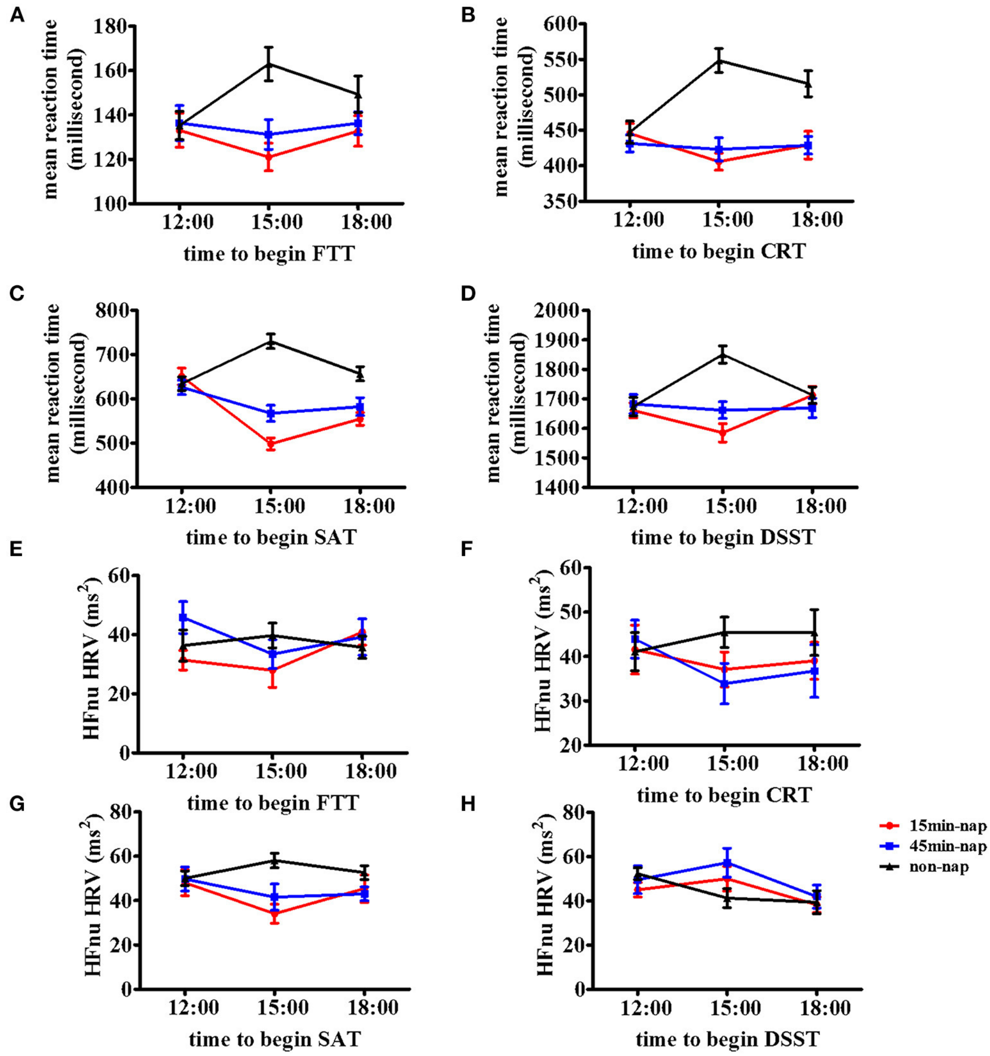

FIGURE 2
Mean and stand deviations of cognitive tests and resting vmHRV of the time course in the three nap groups. Means and standard deviations are shown for four outcome metrics of the cognitive tests and resting vmHRV among three nap groups (non-nap, 15-min nap, and 45-min nap). Time course of the **(A)** FTT performance, **(B)** CRT performance, **(C)** SAT performance, **(D)** DSST performance, **(E)** HFnu (FTT), **(F)** HFnu (CRT), **(G)** HFnu (SAT), and **(H)** HFnu (DSST) in participants under nonnap group (lines with triangle), 15-min nap group (lines with square), or 45-min nap group (lines with circle).

groups were observed only between 12:00 and 15:00 for HFnu (DSST).

Comparison of the 15 and 45-min nap conditions

The relative benefits of cognitive performance following the 15 and 45-min naps were compared with *post hoc* analyses. For all outcome measures, 2-way repeated-measures ANOVAs were performed with the factors nap group (15-min nap and 45-min nap) and time (12:00, 15:00, and 18:00). In the event of an overall significant interaction term, planned contrasts were performed to compare the simple interaction effect of changes in the 15 and 45-min nap groups between 12:00 and each post-nap testing period, with Bonferroni-adjusted criteria. As shown in Table 5, the 15-min nap produced significantly greater benefits at 15:00 after napping than did the 45-min nap for FTT performance. While all the other comparisons up until 18:00 tended to favor the performance of the 15-min nap group, none of these interaction effects were statistically significant. The same analysis on resting vmHRV after the 15-min and 45-min naps showed no significant interaction effects across the three test sessions.

TABLE 3 Two-way ANOVA and planned within-subjects contrasts for condition (non-nap vs. 15-min nap) by time for the dependent variables.

Variable	ANOVA	Condition	Planned contrasts	
			Time	
	F		F	
			12:00 (baseline) vs. 15:00	12:00 (baseline) vs. 18:00
FTT	21.74***	Non-nap vs. 15-min nap	42.73***	9.33**
CRT	29.14***	Non-nap vs. 15-min nap	50.89***	30.62***
SAT	16.05***	Non-nap vs. 15-min nap	16.25***	3.00
DSST	4.86**	Non-nap vs. 15-min nap	5.33*	0.01
HFnu(FTT)	5.49**	Non-nap vs. 15-min nap	8.97**	1.24
HFnu(CRT)	0.16	Non-nap vs. 15-min nap	–	–
HFnu(SAT)	7.69***	Non-nap vs. 15-min nap	8.02**	0.57
HFnu(DSST)	7.34**	Non-nap vs. 15-min nap	15.12***	0.35

ANOVA refers to analysis of variance. FTT, Finger Tapping Test; CRT, Choice Reaction Time; DSST, Digit Symbol Substitution Test; and SAT, Shifting Attention Test; HFnu, high-frequency normalized units. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

TABLE 4 Two-way ANOVA and planned within-subjects contrasts for time (pre-nap vs. post-nap time) by condition (non-nap vs. 45-min nap) for the dependent variables.

Variable	ANOVA	Condition	Planned contrasts	
			Time	
	F		F	
			12:00 (baseline) vs. 15:00	12:00 (baseline) vs. 18:00
FTT	20.63***	Non-nap vs. 45-min nap	41.36***	6.27*
CRT	20.01***	Non-nap vs. 45-min nap	47.41***	16.04***
SAT	3.80*	Non-nap vs. 45-min nap	10.25**	1.16
DSST	4.47*	Non-nap vs. 45-min nap	4.46*	0.01
HFnu(FTT)	2.59	Non-nap vs. 45-min nap	–	–
HFnu(CRT)	0.67	Non-nap vs. 45-min nap	–	–
HFnu(SAT)	4.67*	Non-nap vs. 45-min nap	2.62	1.48
HFnu(DSST)	5.72*	Non-nap vs. 45-min nap	10.76**	0.01

ANOVA refers to analysis of variance. FTT, Finger Tapping Test; CRT, Choice Reaction Time; DSST, Digit Symbol Substitution Test; and SAT, Shifting Attention Test; HFnu, high-frequency normalized units. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Regression analyses with parasympathetic activity during cognitive tasks

Next, the study evaluated the importance of resting vmHRV for cognitive performance across different nap durations at 12:00 (baseline), 15:00, and 18:00 with hierarchical linear regression. Two linear regression models were built to predict resting vmHRV variables for FTT, CRT, SAT, and DSST performance. The method of analysis was to estimate a separate hierarchical linear regression for different cognitive tasks due to the differences in independent variables. Regarding FTT performance, Model 1 included FTT performance across the three nap groups for the three test sessions. In Model 2, we added HFnu during FTT performance. Model 1 was significant, $F_{(3, 101)} = 26.27$, $p < 0.001$, adjusted $R^2 = 0.47$, which demonstrated that different nap lengths had a strong impact on FTT performance in the three test sessions. There was no significantly predicted performance in Model 2 [$F_{(6, 98)} = 14.61$, $p = 0.12$, adjusted $R^2 = 0.52$]. Regarding CRT performance, Model 1 included CRT performance across the three nap groups for the three test sessions. In Model 2, we added HFnu during CRT performance. Model 1 was significant [$F_{(3, 101)} = 26.53$, $p < 0.001$, adjusted $R^2 = 0.52$], which suggested that different nap

TABLE 5 Two-way ANOVA and planned within-subjects contrasts for time (pre-nap vs. post-nap time) by condition (15-min vs. 45-min) for the dependent variables.

Variable	ANOVA	Condition	Planned contrasts	
			Time	
	F		F	
			12:00 (baseline) vs. 15:00	12:00 (baseline) vs. 18:00
FTT	6.38*	15-min nap vs. 45-min nap	8.91**	2.51
CRT	2.99	15-min nap vs. 45-min nap	–	–
SAT	0.78	15-min nap vs. 45-min nap	–	–
DSST	1.30	15-min nap vs. 45-min nap	–	–
HFnu(FTT)	1.13	15-min nap vs. 45-min nap	–	–
HFnu(CRT)	1.10	15-min nap vs. 45-min nap	–	–
HFnu(SAT)	0.28	15-min nap vs. 45-min nap	–	–
HFnu(DSST)	0.11	15-min nap vs. 45-min nap	–	–

ANOVA refers to analysis of variance. FTT, Finger Tapping Test; CRT, Choice Reaction Time; DSST, Digit Symbol Substitution Test; and SAT, Shifting Attention Test; HFnu, high-frequency normalized units. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

lengths had a strong impact on CRT performance in the three test sessions. There was no significantly predicted performance in Model 2 [$F_{(6, 98)} = 13.00$, $p = 0.83$, adjusted $R^2 = 0.50$]. The same analysis of predictive resting vmHRV variables regarding SAT performance revealed that Model 1 was significant [$F_{(3, 101)} = 9.25$, $p < 0.001$, adjusted $R^2 = 0.26$], which demonstrated that different nap lengths had a strong impact on SAT performance in the three test sessions. Model 2 also significantly predicted performance, $F_{(6, 98)} = 10.69$, $p < 0.001$, adjusted $R^2 = 0.45$, $R^2 = 19.1\%$), with HFnu as a significant predictor ($p < 0.001$). Furthermore, the analysis of predictive resting vmHRV variables regarding DSST performance showed that Model 1 was significant [$F_{(3, 101)} = 22.08$, $p < 0.001$, adjusted $R^2 = 0.46$], which suggested that different nap conditions had a strong impact on DSST performance in the three test sessions. Model 2 also significantly predicted performance [$F_{(6, 98)} = 13.76$, $p = 0.03$, adjusted $R^2 = 0.51$, $R^2 = 6.5\%$], with HFnu as a significant predictor ($p < 0.001$).

Regression analyses between DSST performance and other cognitive tasks

To identify predictors of DSST performance, regression analyses were undertaken. The effect of the predictor variables would not be identical across the three nap groups at the three times. Thus, the method of analysis was to estimate a separate regression for each group to identify indicator variables and the key predictor variables. Variables such as motor speed, relational selection, and attentional shift influenced DSST performance across the three nap groups. In the 15-min nap group, the multiple R value for the equation was $R = 0.32$ ($p = 0.48$) at 12:00. After the 15-min nap (15:00), the regression equation included FTT (beta = 5.98; $p < 0.001$), CRT (beta = 0.09; $p = 0.24$), and SAT (beta = 0.18; $p = 0.55$) scores. The multiple R value for the equation was $R = 0.71$ ($p < 0.001$). At 18:00 in the 15-min nap group, the regression equation included FTT (beta = 4.79; $p < 0.001$), CRT (beta = 0.02; $p = 0.76$), and SAT (beta = 0.04; $p = 0.22$) scores. The multiple R value for the equation was $R = 0.724$ ($p < 0.01$). In the other groups, there were no significant effects related to DSST performance. In the 45-min nap group, the multiple R values for the equation were $R = 0.18$ ($p = 0.87$) at 12:00, $R = 0.42$ ($p = 0.12$) at 15:00, and $R = 0.15$ ($p = 0.91$) at 18:00. In the non-nap group, the multiple R values for the equation were $R = 0.42$ ($p = 0.12$) at 12:00, $R = 0.13$ ($p = 0.93$) at 15:00, and $R = 0.20$ at 18:00 ($p = 0.81$).

Discussion

This study provides insights into the effects of different nap durations associated with cognitive performance and HRV in interns. The participants were interns after a nightshift. We investigated the consequences on cognitive demands and fluctuations in autonomic activity after differing durations of daytime naps in interns. We present evidence that naps as brief as 15 min are considered one of the best strategies for sleep management, especially among interns, and are an effective method for improving information processing, motor speed, response selection, and attention shifting. Resting vmHRV during cognitive task performance was associated with SAT and DSST scores. Our results provide evidence of a potential role for parasympathetic activity during cognitive task performance in interns.

Based on the study, interns can limit fatigue and improve cognitive performance through naps. Strategies to improve circadian adaptation and relieve the stress include exogenous melatonin, hypnotics after work, bright light exposure, and virtual reality (VR). Melatonin (at a dose 1.8 to 3.0 mg) promote sleep quality during the day after night shifts (47). Although the effect of melatonin in improve circadian alignment has been confirmed (48), the chronic use and healthy safety for interns need further research. Hypnotics including temazepam (49), triazolam (50), and zolpidem (51) taken after night shift could improve sleep quality not cognitive performance. As one adaptation strategy, research has found that bright light exposure facilitates circadian adaptation, mood, and cognitive performance during the night shift (52, 53). Light exposure between 2500 to 10000 lux ranged from 5 sections of 15 min each to 6 h (52, 54), but the improvement of performance in daytime was not seen (55). Chaojin Chen (55) provided evidence to confirm the use of virtual reality (VR) technology to reduce stress among anesthesiologists during night shifts. The limitation of using VR technology was another extra qualified anesthesiologist arranged to take over the subjects' work during the VR immersion to make sure the safety of patients. However, it may not achieve because extra anesthesiologists are not always present. Therefore, daytime napping could be one effective and impractical strategy to improve circadian adaptation for interns.

Previous studies have shown an inverted U-shaped association between napping lengths and cognitive performance (56). For example, non-nap and long-nap groups (90 min) were associated with worse cognitive performance, and moderate nap lengths were associated with better cognitive performance (56). Omar Boukhris and colleagues found that a 90-min daytime nap opportunity was better than 40 min for attention and negative mood states in fourteen healthy adults (57). Compared with a non-nap group, the results of a previous study revealed that a 30-min nap significantly improved alertness and cognitive performance in thirteen healthy males (58). However, 4 weeks of nap restriction or practice was not effective in achieving better performance in either group, such that restricting naps in nap+ participants (who napped at least once a week) did not reduce the cognitive benefits they derived from naps and increasing naps in nap- individuals (who rarely or never napped) did not enhance nap-related perceptual learning (59)· The contradictions among these results could be related to the nap lengths and individual differences. Our findings support and extend results from studies with cognitive tests, such as the DSST, CRT, SAT, and FTT, carried out in non-nap, 15 and 45-min nap groups. In this study, cognitive performance was significantly improved after 15-min naps and 45-min naps. Cognitive performance was significantly decreased in the non-nap group. It is noteworthy that more beneficial effects were observed after a 15-min nap than after a 45-min nap, which suggested that 15-min naps were associated with better cognitive performance.

This study examined the impact of different nap durations on cognitive performance in the context of autonomic activity. Previous studies on resting vmHRV provided support for the theoretical and neuroimaging links between vmHRV and cognitive task performance (60). Behavioral evidence has shown that higher resting vmHRV predicted better performance in a wide range of cognitive tasks (61). Similarly, research has demonstrated that vmHRV was also associated with executive function—a recent meta-analysis of functional magnetic resonance imaging (fMRI) investigations showed that higher resting vmHRV was associated with better performance on a battery of tasks involving executive function (34). To test this model, researchers have proposed that the relationships between vmHRV during the task and cognitive performance are specific to the task. In this sense, better task performance is linked to decreased or increased vmHRV depending on the characteristics of different tasks (62). For example, high resting vmHRV was associated with better performance in executive function and working memory tasks than low resting HRV, whereas there were no differences in simple tasks. High resting vmHRV is also associated with goal-oriented tasks that require more self-regulatory effort (62–64). Individuals with higher resting vmHRV showed a more adaptive vagal response in a given situation (62, 65). These reports support that the varying levels of resting vmHRV are associated with in-task vmHRV and task performance, such that it could index the degree to which executive brain areas are flexible depending on task demands (65). Nevertheless, the differences observed in the present study among the resting vmHRV values across the cognitive tasks appear unusual based on the traditional interpretation. Based on the traditional interpretation, the extent of our study examined the differences among the resting vmHRV values in relation to the cognitive tasks following different nap durations. We found that HFnu suppressed the resting vmHRV in the FTT and CRT, and HFnu increased stimulation of the resting vmHRV in the DSST and SAT in 15-min nap and 45-min nap groups with faster mean reaction times. Meanwhile, HFnu showed suppression of the resting vmHRV in the DSST and SAT and increased the stimulation of the resting vmHRV in the FTT and CRT in the non-nap group with slower mean reaction times. Our findings indicated an increased stimulation of sympathetic and vagus systems depending on the different cognitive components that were engaged. The findings agree with Hansen (45), who suggested that a high resting vmHRV group showed better performance, including reaction time and accuracy parameters in executive tasks. They also showed that cognitive tests can alter HRV, and the effects on high resting vmHRV were specific to executive tasks (66). Other studies have also indicated that behavior, which is sensitive to executive function, during the tests leads to an increase in the resting vmHRV (28, 29). According to different cognitive components associated with executive and non-executive function, the results indicated that participants with high resting vmHRV had faster mean reaction times on executive tasks such as the DSST and SAT, whereas those with low resting vmHRV had faster mean reaction times on non-executive tasks including the FTT and CRT; these findings suggested that the FTT and CRT are less related to prefrontal activation than the DSST and SAT.

In addition, our study provided evidence for the cognitive mechanisms underlying DSST performance across the different nap duration conditions. DSST performance recruits different interrelated abilities, such as motor-based skills, response selection (67), and shifting of attention (68). We performed regression analyses to evaluate the contribution of the different components to DSST performance. In previous studies, motor speed was considered a component of the DSST measured by the FTT and showed significant impairments in an Asperger disorder (AD) group (15), while motor speed was negligibly affected in the normal group (69). According to the regression analysis in our study, FTT was significantly relevant to DSST performance across the different nap durations in the three time sessions, which suggested that motor speed was an important factor influencing DSST performance. Response selection measured by the CRT made little contribution to DSST performance. Traditional cognitive components that are considered critical for determining good performance in the DSST are motor speed, relational selection, and attentional shift. We found that attentional shift measured by the SAT had no significant contribution to DSST performance. However, this finding was inconsistent with a previous study (68), which showed that attentional shift is one of the significant predictors of DSST performance. We speculate that nap durations influence this process, especially the adverse effect of non-naps on DSST performance. Furthermore, successful DSST performance does not depend only on motor speed, response selection and attentional shift, but there is evidence that this process may also require working memory and visual scanning efficiency (70). Working memory and visual scanning efficiency appear essential to DSST performance. Working memory has an important influence on attentional shift, which has supervisory functions, such as error monitoring and activating task-appropriate schema (71). Visual scanning efficiency indicates that participants consult the code key frequently during the test administration (72). The principal scanning operations in the performance of the DSST involve at least two saccades: from the test item to the code key and from the code key to the test item, which suggests that appropriate saccadic eye movements do not rely on memory.

Conclusion

Studies of the effects of different nap durations on cognitive performance in the context of autonomic nervous system (ANS) activity are few. This study demonstrated that a brief nap can serve as a countermeasure against cognitive impairment and that autonomic activity while awake played a crucial role in DSST and SAT performance across the different nap durations. Motor speed was a significant predictor of DSST performance in relation to the effects of daytime napping. Furthermore, the unexplored domains of the central nervous system and the relationship of the ANS with cognitive performance, which promotes associative cognitive processes during napping, should be considered in future studies. In addition, considering that taking brief naps has critical practical implications, daytime napping has potential benefits for hospital staff.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by First Affiliated Hospital of Air Force Medical University (KY20213076-1). The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization: LW and XS. Methodology, formal analysis, and writing—original draft preparation: JF and LW. Software: XY and XCZ. Validation: JF, YW, and XS. Investigation: JF, LW, ZS, SW, LZ, XL, XBZ, and CL. Data curation: JF, LW, YP, YT, and XS. Writing—review and editing: JF and ZL. Visualization: LW and ZL. Project administration: LW and YW. Funding acquisition: YW, ZL, and XS. Resources: ZL. Supervision: LW and XY. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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