ORIGINAL ARTICLE

Night shift work at specific age ranges and chronic disease risk factors

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ABSTRACT

Objectives We examined the association of night shift work history and age when night shift work was performed with cancer and cardiovascular disease risk factors among 54 724 women in the Nurses' Health Study (NHS) II.

Methods We calculated age-adjusted and socioeconomic status-adjusted means and percentages for cancer and cardiovascular risk factors in 2009 across categories of night shift work history. We used multivariable-adjusted logistic regression to estimate odds ratios (ORs) and 95% CIs for key risk factors among 54 724 participants (72% ever shift workers). We further examined these associations by age (20–25, 26–35, 36–45 and 46+ years) at which shift work was performed.

Results Ever night shift workers had increased odds of obesity (body mass index ≥30 kg/m^2; OR=1.37, 95% CI 1.31 to 1.43); higher caffeine intake (≥131 mg/day; OR=1.16, 95% CI 1.12 to 1.22) and total calorie intake (≥1715 kcal/day; OR=1.09, 95% CI 1.04 to 1.13); current smoking (OR=1.30, 95% CI 1.19 to 1.42); and shorter sleep durations (≤7 h of sleep/day; OR=1.19, 95% CI 1.15 to 1.24) compared to never night shift workers. These estimates varied depending on age at which night work was performed, with a suggestion that night shift work before age 25 was associated with fewer risk factors compared to night shift work at older ages.

Conclusions Our results indicate that night shift work may contribute to an adverse chronic disease risk profile, and that risk factors may vary depending on the age at which night shift work was performed.

What this paper adds

- Recent studies have suggested that working at night is associated with an adverse risk profile for chronic diseases.
- Adding to this data, we evaluated the effects of night shift work and timing by specific age ranges on chronic disease risk factors among 54 724 women in the Nurses' Health Study II.
- Our findings indicate that targeted lifestyle interventions for night shift workers should potentially take into account age when shift work is performed, as risk factors may vary over the course of a woman's shift work career.

INTRODUCTION

Shift work is common in many occupations in modern society, particularly in service industries including healthcare, manufacturing and transportation. According to the Current Population Survey,[1] approximately 18% of the US labour force works alternative shifts that fall outside of a traditional day shift. While studies indicate that shift work (a proxy for light exposure at night and chronodisruption) may have adverse effects on acute health-related outcomes (eg, accidents, reproductive factors, gastrointestinal malfunction and sleep),[2–5] associations between night shift work and chronic diseases are less clear and difficult to study given the need for detailed exposure assessment and long follow-up to ascertain chronic disease outcomes.[6 7] A recent study[8] of over 40 000 UK women found that working at night was associated with higher odds of smoking, obesity and being in the lowest third of socioeconomic status (SES), suggesting a more adverse risk profile for chronic diseases among shift workers.

Adding to this data, we examined the distribution of risk factors for cancer and cardiovascular disease—the most common chronic diseases and leading causes of mortality in the USA[9]—by night shift work history in the Nurses' Health Study (NHS) II, a large cohort of women with substantial shift work exposure, long-term follow-up, and a large number of reported health and lifestyle characteristics. Given the consistency of night shift work from young adulthood through older age among NHS II participants, we are in a unique position to evaluate night shift work and timing by specific age ranges in relation to chronic disease risk factors.

MATERIALS AND METHODS

NHS II was initiated in 1989 when 116 430 female registered nurses, aged 25–42 years and living in 14 US states, completed an initial questionnaire on their medical history, health and lifestyle. Since 1989, similar questionnaires have been completed biennially to update this information, with follow-up rates at approximately 90%. This study was approved by the Institutional Review Board (IRB) of Brigham and Women's Hospital (Boston, Massachusetts, USA).

Population for analysis

In 2009, 90 482 women completed the NHS II cohort questionnaire; of these, 71 997 recalled information on primary work schedule for each prespecified age range (from ages 20 to 25, 26–35,

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36–45 and 46+ years). Thus, we have shift work information on each time period during a woman's working life, as it was recalled in 2009. Women who provided work schedule information were generally similar to women who did not provide work schedule information (eg, mean age=55.2 vs 54.2 years, mean body mass index=27.8 vs 27.7 kg/m^2, respectively). To create unambiguous exposure groups and reduce possible misclassification, we restricted the population for analysis to women whose responses to multiple questions about work schedule histories were internally consistent; thus, we excluded 16 877 women who reported a primary non-night shift schedule with ≥1 night shifts per month during the specified age range, and 396 women who reported a primary night shift schedule and no night shifts per month during the specified age range. As a result, there were 54 724 women left in our analytic sample.

Assessment of shift work

Participants reported detailed information on occupational history by age periods of their working life, including their primary shift work schedule, in 2009. Work schedule for each specific age range (20–25 years, 26–35 years, 36–45 years and 46+ years) was queried by asking women to report: 'Your primary work schedule during each age range (Consider your schedule 'day/evening' if most work hours were between 7:00–15:00, or 15:00–23:00, 'night' if 23:00—7:00; and 'early morning' if 4:00—9:00)'. Response categories were given as 'day/evenings only, nights only, early mornings only, rotating with nights, rotating with no nights, or other/didn't work'. In 2009, women also recalled, for each age range, the type of nursing occupation, years worked at occupation, full-time/part-time work, total years of rotating night shifts and average night shifts per month.

Covariates of interest

Potential cancer and cardiovascular disease risk factors were derived from the main NHS II questionnaires and were determined a priori based on evidence from published literature. We grouped potential risk factors into the following categories: modifiable, non-modifiable and health-related risk factors.

Modifiable risk factors, including body mass index (BMI, in kg/m^2), physical activity (MET-hours per week), smoking status, oral contraceptive use and postmenopausal hormone use were assessed in 2009; BMI at age 18 was assessed in 1989. Average hours of sleep over a 24-hour period were reported by age range of shift work in 2009. Dietary factors including alcohol (g/day), caffeine consumption (mg/day) and total energy intake (kcal/day) were assessed in 2007 because this was the cohort questionnaire most proximal to the reporting of shift work history. The Alternative Healthy Eating Index score (AHEI) was also assessed in 2007 and reflects adherence to a diet pattern based on foods and nutrients most predictive of disease risk; total scores range from 0 (non-adherence) to 110 (perfect adherence).[10]

Non-modifiable risk factors, including age (years), menopausal status, age at menopause (years), parity, chronotype, living alone, and allergies were assessed in 2009; age at menarche was assessed in 1989. Nurses also reported their spouse/partner's education level in 1999 (high school or less; 2 or 4-year college; graduate school; or not married/missing) as an indicator of SES.

Health-related risk factors, including medication use (ie, antihypertensives and aspirin), medical visits in the past 2 years (ie, mammography, physical examination and colonoscopy/sigmoidoscopy), and hypercholesterolaemia (blood cholesterol ≥200 mg/dL) were assessed in 2009; multivitamin use was assessed in 2007. History of diabetes, angina and high blood pressure, and family history of myocardial infarction and/or cancer, except non-melanoma skin cancer, were assessed in 1989 and information was updated subsequently on most of the biennial follow-up questionnaires.

Additional covariates assessed for secondary analyses include work stress and social support. Work stress was assessed in 1993 and 1997 with the 27-item Karasek Job Content Questionnaire,[11] which measures the psychological work load 'demands' and level of 'control' to manage the workload. Based on the job demand/control model, jobs are categorised into four classes of work stress: (1) jobs that are high demand/low control ('high strain'), (2) jobs that are low demand/high control ('low strain'), (3) jobs that are high demands/high control ('active') and (4) jobs that are low demand/low control ('passive').[12 13] In 1993, social support was assessed when participants were asked if they had a close confidant (eg, someone who they can share confidences and feelings with).

Statistical analysis

Among the 54 724 women in our analysis, 15 391 women reported never working night shifts and 39 333 women reported working night shifts at some point during their career. Women who reported a primary shift schedule with rotating night shifts or nights only (ie, permanent nights) were categorised as 'ever' night shift workers. We calculated means and proportions of self-reported occupational characteristics across prespecified age ranges at which shift work was performed (age 20–25, 26–35, 36–45 and 46+; table 1). We then estimated age-adjusted (in 5-year increments) and SES-adjusted means and percentages of cancer and cardiovascular risk factors (modifiable, non-modifiable and health-related factors) for ever vs never night shift work. To evaluate which risk factors differed significantly by shift work status, we calculated two-sided p values using PROC GLM for continuous covariates and PROC CATMOD for categorical covariates (table 2). To correct for multiple comparisons, we used the Bonferroni adjustment on the basis of the number of tested covariates. $P<\alpha_c$ (Bonferroni-corrected α) were considered statistically significant.

Next, we used multivariable-adjusted logistic regression models to estimate odds ratios (ORs) and 95% CIs for modifiable risk factors whose age-adjusted and SES-adjusted means or percentages differed significantly by shift work status, dichotomising continuous outcomes (eg, caffeine and calorie intake) along the median of never night shift workers (table 3). To determine the importance of age at which night shift work occurred, we first examined these associations overall according to night shift work (ever/never) (table 3) and then separately examined them among rotating and nights only shift work for each respective age range (tables 4 and 5). Logistic regression models were adjusted for age and SES for comparability to the Million Women Study[8] (model 1); and additional covariates that produced a 5% or greater change of the β coefficient representing the exposure effect[14] (model 2). To evaluate the association between shift work at specific ages and obesity, we additionally adjust for BMI at age 18 to provide estimates that are independent of earlier BMI (model 3). Based on the hypothesis that never night shift workers might have the least amount of chronodisruption, these women were the reference group in all analyses.

We conducted several secondary analyses. Given that psychosocial factors have been associated with adverse health effects, we adjusted for work stress (high strain, low strain, passive and

Table 1 Occupational characteristics of 54 724 women in the Nurses' Health Study II across key age periods of their working life*,†,‡

Characteristic	Age 20–25		Age 26–35		Age 36–45		Age 46+	
	Per cent	Mean(SD)	Per cent	Mean(SD)	Per cent	Mean(SD)	Per cent	Mean(SD)
Occupation held the longest	–		–		–		–	
ER	3.7		5.2		4.5		3.0	
OR	2.8		4.2		4.3		4.1	
ICU	18.2		17.0		9.4		5.6	
Other inpatient nurse	43.6		30.6		19.8		15.0	
Nursing education or admin	1.1		7.0		12.4		14.8	
Outpatient or community	3.0		9.2		14.9		16.8	
Other hospital nursing	9.5		8.2		7.5		7.7	
Nursing outside hospital	3.3		8.5		14.0		16.5	
Non-nursing employment	8.0		2.3		3.8		5.9	
Full-ime homemaker	3.1		5.5		5.3		3.6	
Retired	<1		<1		<1		<1	
Other	3.5		2.0		3.7		5.8	
Full-time work	84.0		66.5		67.2		72.7	
Primary work schedule	–		–		–		–	
Days/eves only	44.6		61.3		72.6		80.0	
Nights only	14.3		12.6		9.9		7.1	
Early mornings only	<1		1.3		2.2		2.8	
Rotating with nights	36.6		19.7		9.9		5.3	
Rotating with no nights	<1		<1		<1		<1	
Other/did not work	3.2		4.3		4.9		4.4	
Years worked at occupation held the longest		4.2 (1.4)		7.8 (2.0)		8.3 (1.6)		7.2 (2.6)
Total years of rotating night shifts§		3.0 (1.6)		5.2 (2.9)		6.0 (3.1)		5.6 (3.4)
Average night shifts per month¶		10.9 (6.1)		10.7 (6.0)		10.9 (6.0)		11.1 (6.1)
Average hours of sleep over a 24-hour period		7.1 (1.0)		6.9 (1.0)		6.9 (1.0)		7.0 (1.0)

*54 724 women reported these occupational characteristics for each age range in 2009.
†Values are crude means and SDs or percentages estimated among all work schedules (eg, day/eves, nights, early mornings, rotating with nights, rotating with no nights and other) and among women with both part-time and full-time schedules, unless otherwise indicated.
‡May not add up to 100% due to rounding.
§Values are estimated among women who reported a primary rotating with night shift schedule at the specific age range.
¶Values are estimated among women who reported a primary rotating with nights or night shifts only schedule at the specific age range.
ER, emergency room; ICU, intensive care unit; OR, operating room.

active job) and social support (eg, close confidant) (yes, no). We also adjusted for type of nursing occupation (inside hospital, outside hospital, non-nursing/other) since work demand may vary by type of nursing occupation. To assess whether associations may be explained by either shift work intensity or shift work duration, we also conducted separate models that adjusted for average number of night shifts reported per month (0, 1–2, 3–4, 5–6, 7–8, 9–10, 11–15, 16–20, 21+ night shifts per month) and total years of night shift work (0, 1–<10, 10–<20, 20+ years).

For all analyses, we report multivariable-adjusted results, which were similar to age-and-SES adjusted results. All analyses were conducted with SAS software, V.9.3 (SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

Table 1 describes occupational characteristics across age ranges that shift work was performed among 54 724 women in NHS II. Qualitatively, there were several important differences across these age ranges; specifically, as age at shift work increased, women were more likely to work in nursing careers outside of the hospital (3.3% among women aged 20–25 vs 16.5% among women aged 46+), more likely to have a primary day/evening work schedule (44.6% among women aged 20–25 vs 80% among women aged 46+), and less likely to work full-time (84% among women aged 20–25 vs 72.7% among women aged 46+). Additionally, more women worked rotating night shifts earlier in life compared to later in life (36.6% among women aged 20–25 vs 5.3%, among women aged 46+).

After adjusting estimates for age and SES and applying a Bonferonni correction, we observed several significant differences across chronic disease risk factors comparing ever vs never night shift workers (table 2). Among modifiable risk factors, ever night shift workers were more likely to have a higher BMI (28.1 vs 27 kg/m^2), higher daily caloric (1822 vs 1772 kcal/day) and caffeine intake (184 vs 167 mg/day), shorter sleep duration (67% vs 63% ≤7 h/day), and to currently smoke (7% vs 5%) compared to never night shift workers. Among non-modifiable risk factors, compared to never night shift workers, ever night shift workers were more likely to be nulliparous (19% vs 17%), live alone (13% vs 11%) and less likely to be morning chronotypes (33% vs 38%). Among health-related factors, ever night shift workers were also more likely to have a history of diabetes (8% vs 6%), angina (3% vs 2%) and high blood pressure (36% vs 33%); regularly use antihypertensive medication (34% vs 32%) and aspirin (11% vs 9%), and less likely to have had a mammography in the past 2 years (90% vs 92%), compared to never night shift workers (table 2).

In table 3, we observed that night shift workers had significantly higher odds of obesity (defined as BMI ≥30 kg/m^2; OR=1.37, 95% CI 1.31 to 1.43), higher caffeine (defined as ≥131 mg) (OR=1.16, 95% CI 1.12 to 1.22) and total calorie

Table 2 Modifiable, non-modifiable and health-related risk factors in 2009 across ever versus never night shift workers in Nurses' Health Study II (N=54 724)†

	Shift work categories			
	Never night shift work (n=15 391)‡		Ever night shift work (n=39 333)	
Characteristic	Per cent	Mean (SD)	Per cent	Mean (SD)
Modifiable factors				
Age, years		56.0 (4.3)		54.9 (4.4)
Body mass index, kg/m^2		27.0 (6.0)		28.1 (6.7)*
Physical activity, MET-hours/week§		22.7 (28.4)		23.7 (29.8)
Current average sleep over a 24-hour period, ≤7 h	63		67*	
Ever used oral contraceptives	89		89	
Ever used postmenopausal hormones	55		54	
Current smoker	5		7*	
Alcohol consumption, g/day¶		6.3 (10.3)		6.3 (10.2)
Caffeine consumption, mg/day¶		167 (136)		184 (142)*
Alternative healthy eating index score¶,††		55.3 (11.7)		55.7 (11.5)
Total Calories, in kcal/day¶		1772 (547)		1822 (562)*
Non-modifiable factors				
Age at menarche, years		12.4 (1.4)		12.4 (1.4)
Age at menopause, years‡‡		47.4 (6.2)		47.2 (6.5)
Postmenopausal	76		76	
Nulliparous	17		19*	
Morning chronotype	38		33*	
Living alone	11		13*	
Any allergy	29		30	
Health-related factors				
Family history of disease	–		–	
Myocardial infarction	44		46	
Cancer	55		57	
Health/illness	–		–	
History of diabetes (type II)	6		8*	
History of angina	2		3*	
History of high blood pressure	33		36*	
Blood cholesterol, ≥200 mg/dL	35		34	
Medication or supplements	–			
Antihypertension medication	32		34*	
Regular use of aspirin, ≥325 mg/tablet§§	9		11*	
Regular use of low dose aspirin, ≤100 mg /tablet§§	25		26	
Multivitamin use¶¶	59		60	
Medical visits in the past 2 years	–			
Mammography	92		90*	
Physical examination	93		93	
Colonoscopy/sigmoidoscopy	35		35	

†Values are means and SDs or percentages standardised to the age and socioeconomic status (SES) distribution of the study population.
‡Reference group.
§Metabolic equivalents from recreational and leisure time activities.
¶Nutrient intake was assessed in the 2007 cohort questionnaire with an embedded food frequency questionnaire (FFQ).
††Alternative Healthy Eating Index (AHEI) score measures adherence to a diet pattern based on foods and nutrients most predictive of disease risk. The total score ranges from 0 (non-adherence) to 110 (perfect adherence).
‡‡Among postmenopausal women.
§§Reported as current use within the past 2 years and defined as ≥2 tablets per week.
¶¶Assessed in 2007.
*p<0.0011 (significant after Bonferroni correction).

intake (defined as ≥1715 kcal per day; OR=1.09, 95% CI 1.04 to 1.13), less sleep (defined as ≤7 h per day; OR=1.19, 95% CI 1.15 to 1.24), and being a current smoker (OR=1.30, 95% CI 1.19 to 1.42) compared to never night shift workers. Further, odds of modifiable risk factors were generally stronger among ever nights only shift workers at any age range compared to ever rotating night workers, and varied depending on age at which night work was performed (tables 4 and 5). Our data suggests that rotating night work was significantly associated with BMI earlier in life (age 26–35) and later in life (age 46+) and smoking behaviour earlier in life (age 26–35) and mid-life (age 36–45; table 4). Nights only shift work was associated with BMI and smoking across almost all age ranges of working night only shifts; however, total calories, caffeine intake and sleep were generally not associated with night only work at any age ranges (table 5). In general, odds of risk factors were lower among women who worked rotating or night only shifts early in life (age 20–25), although this pattern was not entirely consistent.

Table 3 ORs and 95% CIs of modifiable risk factors in 2009 across ever vs never night shift work in Nurses' Health Study II (N=54 724)

Characteristic	Shift work categories	
	Never worked night shifts (n=15 391) OR (95% CI)	Ever worked night shifts (n=39 333) OR (95% CI)
Obese (body mass index ≥30 kg/m^2)	–	–
N (cases/non-cases)*	3822/11 218	12 161/26 329
Model 1†	Ref	1.37 (1.31 to 1.43)
Model 2‡	Ref	1.37 (1.31 to 1.43)
Model 3§	Ref	1.26 (1.20 to 1.32)
Caffeine intake (≥131 mg)¶	–	–
N (cases/non-cases)*	6667/6665	18 402/14 994
Model 1†	Ref	1.22 (1.17 to 1.27)
Model 2**	Ref	1.16 (1.12 to 1.22)
Total Calories (≥1715 kcal/day)¶	–	
N (cases/non-cases)*	6666/6666	17 860/15 536
Model 1†	Ref	1.14 (1.10 to 1.19)
Model 2††	Ref	1.09 (1.04 to 1.13)
Current smoker	–	–
N (cases/non-cases)*	764/14 627	2625/36 708
Model 1†	Ref	1.35 (1.24 to 1.47)
Model 2‡‡	Ref	1.30 (1.19 to 1.42)
Average sleep (≤7 h)§§	–	–
N (cases/non-cases)*	9233/5595	25 349/12 681
Model 1†	Ref	1.19 (1.15 to 1.24)
Model 2¶¶	Ref	1.19 (1.15 to 1.24)

*N's vary due to missing data among modifiable risk factors.
†Adjusted for age (5 years), education level of the nurse's spouse/partner (≤ high school, 2-year or 4-year college, graduate school or not married/missing).
‡Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week) and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
§Adjusted for model 2 covariates plus body mass index at age 18 (<18.5, 18.5 to <20, 20 to <22.5, 22.5 to <25, 25 to <27.5, ≤27.5 kg/m^2).
¶Assessed in 2007 and median value based on never night shift workers.
**Adjusted for model 1 covariates plus total calories (quintiles, kcal/day) and smoking status (never, past, current smoker).
††Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (quintiles, mg), smoking status (never, past, current smoker), chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
‡‡Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (quintiles, mg), alternative healthy eating index (quintiles) and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
§§Average hours of sleep over a 24-hour period.
¶¶Adjusted for model 1 covariates plus chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).

In models that additionally adjusted for work stress, social support, type of nursing occupation and total years of night shift work, results did not substantially change (data not shown). Higher levels of average night shifts per month were significantly associated with an increased risk of obesity (eg, multivariable OR (95% CI) for 1–2 nights/month vs 0 nights/month=1.13 (0.70 to 1.83); 3–4 nights/month vs 0 nights/month=1.38 (0.85 to 2.22), 5–6 nights/month vs 0 nights/month=1.65 (1.02 to 2.66), 7–8 nights/month vs 0 nights/month=1.85 (1.15 to 2.99), 9–10 nights/month vs 0 nights/month=1.85 (1.14 to 3.00), 11–15 nights/month vs 0 nights/month=2.25 (1.39 to 3.64), 16–20 nights/month vs 0 nights/month=2.28 (1.39 to 3.75), 21+ nights/month vs 0 nights/month=3.42 (1.95 to 6.03); p-trend<0.0001). Furthermore, the increased risk of obesity was present across age categories among rotating and night only shift workers.

DISCUSSION

In this study of US female nurses, women were more likely to report a primary rotating night-shift schedule, full-time work and a nursing occupation within a hospital setting earlier in life compared to later in life. We also found that night shift workers tended to have a more adverse risk profile for chronic diseases compared to never night shift workers, and risk factors varied depending on age at which night work was performed.

Epidemiological studies, including previous studies in the NHS cohorts,[15–17] have observed differences in several established cancer and cardiovascular risk factors among those with versus without a history of shift work, including a higher BMI,[18–24] dietary intake[25] and smoking,[21 26–29] as well as shorter duration of sleep.[30 31] Exact mechanisms between shift work and these key risk factors are not well established. Several putative mechanisms have been suggested, including increased circadian rhythm disruption and disturbed sociotemporal patterns[5 18 32 33]; both can lead to behavioural changes in dietary intake, smoking and duration of sleep. These key risk factors may lead to unfavourable metabolic disturbances contributing to increased obesity among night shift workers. In line with our results, a recent study[8] that examined characteristics of 41 652 women in the Million Women Study, a cohort with 13.2% of participants reporting night shift work, found that women with a history of night shift work had a higher BMI and were more likely to be current smokers compared to those without a history of night shift work (mean BMI=27.3 vs 26.6 kg/m^2; percent smokers=8.6% vs 6.2%, respectively). This study did not assess the association between night shift work and daily caffeine or total calorie intake.

Table 4 Odds ratios and 95% CIs of modifiable risk factors in 2009 across age ranges of rotating night shift work (as recalled in 2009) in Nurses' Health Study II

	Rotating night shift work categories at age ranges*				
Characteristic	Never worked night shifts (N=15 391) OR (95% CI)	Ever worked rotating night shifts at age 20–25 (N=20 022) OR (95% CI)	Ever worked rotating night shifts at age 26–35 (N=10 761) OR (95% CI)	Ever worked rotating night shifts at age 36–45 (N=5392) OR (95% CI)	Ever worked rotating night shifts at age 46+ (N=2885) OR (95% CI)
Obese (body mass index ≥30 kg/m^2)	–	–	–	–	–
N (cases/non-cases)†	3822/11 218	5510/14 129	3412/7101	1764/3508	977/1839
Model 1‡	Ref	1.00 (0.96 to 1.05)	1.22 (1.16 to 1.28)	1.08 (1.01 to 1.15)	1.15 (1.06 to 1.26)
Model 2§	Ref	1.06 (1.02 to 1.11)	1.25 (1.19 to 1.32)	1.05 (0.98 to 1.13)	1.12 (1.02 to 1.22)
Model 3¶	Ref	1.01 (0.96 to 1.06)	1.19 (1.12 to 1.26)	1.02 (0.94 to 1.10)	1.11 (1.00 to 1.23)
Caffeine intake (≥131 mg)**	–	–	–	–	–
N (cases/non-cases)†	6667/6665	9451/7694	5110/4020	2565/1945	1399/ 989
Model 1‡	Ref	1.10 (1.05 to 1.14)	1.09 (1.04 to 1.14)	1.08 (1.01 to 1.16)	1.18 (1.07 to 1.29)
Model 2††	Ref	1.08 (1.04 to 1.13)	1.05 (0.99 to 1.10)	1.04 (0.97 to 1.12)	1.16 (1.06 to 1.27)
Total Calories (≥1715 kcal/day)**	–	–	–	–	–
N (cases/non-cases)†	6666/6666	9272/7873	4949/4181	2508/2002	1374/1014
Model 1‡	Ref	1.09 (1.05 to 1.14)	1.05 (1.00 to 1.10)	1.09 (1.02 to 1.17)	1.20 (1.09 to 1.31)
Model 2‡‡	Ref	1.06 (1.02 to 1.11)	1.03 (0.98 to 1.08)	1.09 (1.01 to 1.16)	1.15 (1.05 to 1.26)
Current smoker	–	–	–	–	–
N (cases/non-cases)†	764/14 627	1130/18 892	747/10 014	433/4959	220/2665
Model 1‡	Ref	0.96 (0.89 to 1.04)	1.17 (1.07 to 1.28)	1.26 (1.12 to 1.42)	1.10 (0.94 to 1.28)
Model 2§§	Ref	0.98 (0.91 to 1.07)	1.19 (1.08 to 1.30)	1.23 (1.09 to 1.39)	1.03 (0.88 to 1.20)
Average sleep (≤7 h)¶¶	–	–	–	–	–
N (cases/non-cases)†	9233/5595	12 948/6432	6937/3449	3517/1682	1986/796
Model 1‡	Ref	1.13 (1.08 to 1.17)	1.04 (0.99 to 1.09)	1.03 (0.96 to 1.10)	1.33 (1.21 to 1.45)
Model 2***	Ref	1.13 (1.08 to 1.17)	1.04 (0.99 to 1.09)	1.03 (0.96 to 1.10)	1.33 (1.22 to 1.46)

*The number of women in ever rotating night shifts by age range does not include nights only shift work and women can be in multiple age ranges when night shift work was performed.
†N's vary due to missing data among modifiable risk factors.
‡Adjusted for age (5 years), education level of the nurse's spouse/partner (≤high school, 2-year or 4-year college, graduate school or not married/missing), primary night only shift work at age 20–25, 26–35, 36–45, 46+ (yes, no at each age-range).
§Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week) and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
¶Adjusted for model 2 covariates plus body mass index at age 18 (<18.5, 18.5 to <20, 20 to <22.5, 22.5 to <25, 25 to <27.5, ≤27.5 kg/m^2).
**Assessed in 2007 and median value based on never night shift workers.
††Adjusted for model 1 covariates plus total calories (quintiles, kcal/day) and smoking status (never, past, current smoker).
‡‡Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (mg), smoking status (never, past, current smoker), chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
§§Adjusted for model 1 covariates plus physical activity (quintiles met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (quintiles, mg), alternative healthy eating index (quintiles), and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
¶¶Average hours of sleep over a 24-hour period.
***Adjusted for model 1 covariates plus chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).

Interestingly, we found that higher intensity of night shift work was associated with an increased risk of obesity, suggesting that increasing average number of night shifts worked per month (possibly indicative of more severe circadian disruption) might be an important risk factor for obesity among shift workers. This is also reflected in the stronger ORs for obesity we observed among women who reported night only shift work as their primary work schedule (table 5), compared to those with rotating night shift work as their primary work schedule (table 4). Additional studies are warranted to confirm our finding, and to also explore the role of individual chronotype in these associations; that is, whether a shift schedule that is in line with a person's chronotype (eg, night work carried out by evening types) may less severely affect obesity and related outcomes than a shift schedule opposing chronotype (eg, early morning work schedules for morning types).

While it appears plausible that the age at which an individual performed shift work may modulate the effects of shift work on health outcomes, no other prior study, to our knowledge, has examined this particular aspect of shift work among women. Previous data from the NHS cohorts indicate that longer durations of shift work are associated with higher cancer and CVD risk, whereas shorter durations do not appear to increase these risks.[15–17 34 35] This data could provide indirect evidence for a higher risk associated with shift schedules worked earlier in life since duration could simply be an indicator of exposure earlier in life. However, in our current study, although adverse risk profiles appeared to vary slightly depending on the age at which a woman worked night shifts, and were stronger among women with night work only, versus those with rotating night shift worker, no clear pattern emerged in support of this.

Table 5 Odds ratios and 95% CIs of modifiable risk factors in 2009 across age ranges of night only shift work (as recalled in 2009) in Nurses' Health Study II

	Night only shift work categories at age ranges*				
Characteristic	Never worked night shifts (N=15 391) OR (95% CI)	Ever worked night only shifts at age 20–25 (N=7847) OR (95% CI)	Ever worked night only shifts at age 26–35 (N=6915) OR (95% CI)	Ever worked night only shifts at age 36–45 (N=5442) OR (95% CI)	Ever worked night only shifts at age 46+ (N=3909) OR (95% CI)
Obese (body mass index≥30 kg/m^2)	–	–	–	–	–
N (cases/non-cases)†	3822/11 218	2734/4933	2576/4175	2071/3237	1597/2221
Model 1‡	Ref	1.30 (1.23 to 1.38)	1.33 (1.25 to 1.41)	1.13 (1.05 to 1.22)	1.38 (1.28 to 1.50)
Model 2§	Ref	1.30 (1.23 to 1.38)	1.33 (1.25 to 1.42)	1.07 (0.99 to 1.15)	1.23 (1.12 to 1.33)
Model 3¶	Ref	1.16 (1.09 to 1.24)	1.28 (1.20 to 1.38)	1.05 (0.97 to 1.14)	1.20 (1.09 to 1.32)
Caffeine intake (≥131 mg)**	–	–	–	–	–
N (cases/non-cases)†	6667/6665	3524/3085	3153/ 2619	2488/2061	1797/ 1437
Model 1‡	Ref	1.01 (0.95 to 1.06)	1.06 (0.99 to 1.12)	1.01 (0.94 to 1.09)	1.09 (1.00 to 1.19)
Model 2††	Ref	1.00 (0.94 to 1.06)	1.03 (0.97 to 1.10)	1.00 (0.93 to 1.08)	1.08 (0.99 to 1.18)
Total Calories (≥1715 kcal/day)**	–	–	–	–	–
N (cases/non-cases)†	6666/6666	3479/3130	3016/2756	2351/2198	1697/1537
Model 1‡	Ref	1.03 (0.98 to 1.09)	1.01 (0.95 to 1.08)	0.97 (0.90 to 1.05)	1.05 (0.97 to 1.15)
Model 2‡‡	Ref	1.02 (0.96 to 1.08)	0.99 (0.93 to 1.05)	0.97 (0.89 to 1.04)	1.00 (0.92 to 1.09)
Current smoker	–	–	–	–	–
N (cases/non-cases)†	764/14 627	599/7248	573/6342	468/4974	395/3514
Model 1‡	Ref	1.19 (1.07 to 1.31)	1.22 (1.09 to 1.36)	1.08 (0.94 to 1.23)	1.47 (1.28 to 1.69)
Model 2§§	Ref	1.19 (1.07 to 1.32)	1.22 (1.09 to 1.36)	1.03 (0.90 to 1.18)	1.25 (1.08 to 1.44)
Average sleep (≤7 h)¶¶	–	–	–	–	–
N (cases/non-cases)†	9233/5595	5019/2557	4471/2211	3573/1682	2671/1095
Model 1‡	Ref	1.05 (1.00 to 1.11)	1.03 (0.97 to 1.09)	1.00 (0.93 to 1.08)	1.32 (1.21 to 1.44)
Model 2***	Ref	1.06 (1.00 to 1.12)	1.03 (0.97 to 1.09)	1.00 (0.93 to 1.08)	1.33 (1.22 to 1.45)

*The number of women in ever night only shifts by age range does not include rotating night shifts and women can be in multiple age ranges when night shift work was performed.
†N's vary due to missing data among modifiable risk factors.
‡Model 1 is adjusted for age (5 years), education level of the nurse's spouse/partner (≤high school, 2-year or 4-year college, graduate school, or not married/missing), primary rotating with night shift work at age 20–25, 26–35, 36–45, 46+ (yes, no at each age-range).
§Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week) and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
¶Adjusted for model 2 covariates plus body mass index at age 18 (<18.5, 18.5 to <20, 20 to <22.5, 22.5 to <25, 25 to <27.5, ≤27.5 kg/m^2).
**Assessed in 2007 and median value based on never night shift workers.
††Adjusted for model 1 covariates plus total calories (quintiles, kcal/day) and smoking status (never, past, current smoker).
‡‡Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (quintiles, mg), smoking status (never, past, current smoker), chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
§§Adjusted for model 1 covariates plus physical activity (quintiles, met-hour/week), body mass index (18.5 to <25, 25 to <30, ≤30 kg/m^2), caffeine intake (quintiles, mg), alternative healthy eating index (quintiles), and chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).
¶¶Average hours of sleep over a 24-hour period.
***Adjusted for model 1 covariates plus chronotype (definitely a morning type, more of a morning than evening type, more of an evening than morning type, definitely an evening type and neither).

The observed differences we found in chronotype among shift workers (ie, a lower proportion of morning chronotypes among night shift workers) were consistent with previous publications.[8 36 37] Recent studies[36 37] have provided evidence that evening or 'neither' (ie, neither morning nor evening) chronotype may be associated with an increased risk of breast cancer compared to morning chronotype. While further research is warranted to validate these findings, it is nevertheless interesting that we observed a lower prevalence of morning types and less favourable health characteristics among night shift workers.

Strengths of this study include its size, wide variety of health and lifestyle characteristics, and detailed shift work information specific to the ages when work was performed. There are also several limitations of this study. First, these analyses are cross-sectional and do not necessarily have a causal interpretation. However, our results are intended to inform future prospective studies in exploring associations between night shift work and chronic disease risk. Second, our analyses utilise information on women's risk factor profiles from later in life, and therefore shorter term versus Longer term effects of shift work are not differentiated. Third, assessment of shift work was self-reported and ascertained retrospectively; hence, this exposure is susceptible to random misclassification. To alleviate some of this concern, we excluded women with inconsistent shift work histories in our analysis. If any misclassification is present, it is likely non-differential; however, given the nature of shift work, others have also reported the possibility of differential misclassification.[38 39] Finally, the study population consists primarily of white female nurses and may not be generalisable to other populations, such as men and different racial groups. Future studies should explore associations between shift work and chronic disease risk factors in diverse populations.

Taken together, our findings suggest that night shift work may be correlated with an adverse risk profile for chronic disease and that differences in risk profiles may exist, depending on the age range at which night shift work occurs. Differences in obesity risk suggested the most clinical relevance. Future prospective research is needed to confirm if timing of night shift work may impact adverse health effects. If confirmed, these findings may indicate that targeted lifestyle interventions for night shift workers should take into account the age at which night shift work starts and/or occurs, as risk factors may vary over the course of a woman's shift work career.

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Night shift work at specific age ranges and chronic disease risk factors

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Notes