Night shift work and breast cancer incidence among women: a population-based cohort study

Doctoral Thesis in Medicine (MD)

Joy Sudan

University of Fribourg (Switzerland)
Faculty of Science and Medicine
Department of Public Health

UNI FR
#Pop Health Lab
UNIVERSITÉ DE FRIBOURG
UNIVERSITÄT FREIBURG

SSPH+
SWISS SCHOOL OF PUBLIC HEALTH

Night shift work and breast cancer incidence among women: a population-based cohort study

THESIS

presented to the Faculty of Science and Medicine of the University of Fribourg (Switzerland) in consideration for the award of the academic grade of Doctor of Medicine
by

Joy Sudan

From

Broc, Switzerland

Accepted by the Faculty of Science and Medicine of the University of Fribourg (Switzerland) upon the recommendation of Dr. Pauline Brindel and Dr. Bernadette van der Linden.

Fribourg, October 14th, 2025.

Co-director

Senior Lecturer at the Faculty of

Science and Medicine:

PD Stéphane Cullati

Co-director

Professor at the Faculty of

Science and Medicine:

Prof. Arnaud Chiolero

Dean of the Faculty of

Science and Medicine:

Prof. Michael Walch

Table of content

Summary / résumé

Abstract

Objective: Night shift work may increase breast cancer incidence, but evidence is inconclusive. We aimed to investigate the effect of night shift work on breast cancer incidence, considering night shift work characteristics across the life course and the influence of sleep and menopausal status.

Methods: We analyzed two UK Biobank cohorts, using Cox proportional hazards regression models. The first cohort included 20,860 participants and investigated the effect of night shift work on breast cancer incidence (688 cases) from baseline (2006–2010) to the end of follow-up in 2022, stratified by sleep patterns and menopausal status. The second cohort included 64,539 participants and investigated night shift work characteristics (duration, frequency, length, consecutive shifts, rest days) and breast cancer incidence (4,455 cases), using retrospective data spanning from participants' first job to the end of follow-up.

Results: No effect of night shift work on breast cancer incidence was observed in the first cohort (hazard ratio (HR) 0.95, 95% CI: 0.85-1.06) or in the second cohort (HR 1.05% CI: 0.96-1.13). Stratification by sleep patterns and menopausal status showed no modifying effect. In addition, no night shift work characteristics were linked to breast cancer incidence.

Discussion: Our findings suggest no effect of night shift work on breast cancer incidence, even when considering sleep patterns, menopausal status, and detailed life course characteristics.

Résumé

Objectif : Le travail de nuit pourrait augmenter l'incidence du cancer du sein, mais les données actuelles demeurent non concluantes. Nous avons examiné l'effet du travail de nuit sur l'incidence du cancer du sein, en considérant diverses caractéristiques de travail de nuit tout au long de la vie ainsi que de l'influence du sommeil et du statut ménopausique.

Méthodes : Nous avons analysé deux cohortes issues de la UK Biobank à l'aide de modèles de régression de Cox à risques proportionnels. La première cohorte comprenait 20'860 participantes et portait sur l'effet du travail de nuit sur l'incidence du cancer du sein (688 cas) entre la période de recrutement (2006–2010) et la fin du suivi en 2022, avec une stratification selon les caractéristiques de sommeil et le statut ménopausique. La seconde cohorte comprenait 64'539 participantes et analysait les caractéristiques du travail de nuit (durée d'exposition, fréquence, durée d'une nuit, nombre de nuits consécutives, jours de repos) en lien avec l'incidence du cancer du sein (4'455 cas), à partir de données rétrospectives couvrant la période allant du premier emploi à la fin du suivi.

Résultats : Aucun effet du travail de nuit sur l'incidence du cancer du sein n'a été observée pour la première cohorte (rapport de risques (HR) 0,95 ; IC à 95 % : 0,85–1,06), ni pour la seconde cohorte (HR 1,05 ; IC à 95 % : 0,96–1,13). La stratification selon les caractéristiques de sommeil et le statut ménopausique n'a révélé aucun effet modérateur. De plus, aucune caractéristique de travail de nuit n'a été associée à l'incidence du cancer du sein.

Discussion : Nos résultats suggèrent l'absence d'effet du travail de nuit sur l'incidence du cancer du sein, même en tenant compte des profils de sommeil, du statut ménopausique et des caractéristiques détaillées du travail de nuit au cours de la vie.

Text of the thesis

Night shift work and breast cancer incidence among women: a population-based cohort study

Joy Sudan[1], Drinbardha Elshani[1], Arnaud Chiolero[1,2], Stéphane Cullati[1,3,4], Bernadette W.A. van der Linden[1]

[1] Population Health Laboratory (#PopHealthLab), University of Fribourg, Switzerland

[2] School of Population and Global Health, McGill University, Canada

[3] Institute of Sociological Research, University of Geneva, Switzerland

[4] Swiss Centre LIVES Understanding Vulnerability and Resilience across the Life Course, Switzerland

Introduction

Breast cancer is the most common cancer among women, with a global lifetime risk of 12% (1). Established risk factors include reproductive factors such as nulliparity and late menopause (2,3), lifestyle factors including alcohol consumption and sedentary behavior (4,5), along with genetic mutations (6). Recent research has also identified disturbances in circadian rhythms, particularly those caused by night shift work, as an emerging risk factor for breast cancer (7–9). In many countries, night shift work has become increasingly prevalent due to the demands of a 24/7 economy, with 14% of women working night shifts in the European Union in 2020 (10).

Estrogen dysregulation due to melatonin desynchronization is a proposed mechanism linking night shift work to breast cancer. Melatonin not only regulates the sleep-wake cycle but also has well-documented anti-estrogenic and anti-tumor effects (11,12). When melatonin production is disrupted due to irregular sleep patterns (13), it may result in an imbalance of estrogen levels, a known risk factor for breast cancer (14,15). Factors such as sleep duration, sleep quality, and chronotype can influence how the body adapts to night shifts, thereby modulating the risk of estrogen-related breast cancer (16–19). Finally, the impact of night shift work on hormonal regulation may differ between premenopausal and postmenopausal women, as estrogen levels naturally vary between these groups, potentially influencing breast cancer incidence (7,20,21).

In 2019, the International Agency for Research on Cancer (IARC) classified night shift work, defined as work during the typical sleeping hours of the general population, as a probable human carcinogen. This classification was based on evidence from experimental animal studies and mechanistic insights, although direct human evidence remains limited (22). Indeed, the current evidence on the association between night shift work and breast cancer shows inconsistent results, even across meta-analyses (20,23–29). Case-control studies tend to report a positive association between night shift work and breast cancer incidence (16,21,30–32), while cohort studies do not support this link (33–36). The 2011 Canadian Burden of Occupational Cancer study estimated that between 2% and 5% of breast cancer cases in Canada can be attributable to night shift work (37).

A recurring limitation in the literature is the binary classification of night shift work, which typically compares breast cancer incidence between night shift workers and non-night shift workers at a single timepoint. This approach fails to consider the dynamic nature of night shift work characteristics throughout the working life course, such as monthly exposure frequency, number of consecutive night shifts, and rest periods (38). Few studies have examined those characteristics in detail, but those that have done so reported conflicting results regarding the effect of duration (24,25,39), frequency (20,21) and number of consecutive nights worked (40,41). Further research is required that takes into account the specific characteristics of night shift work over the course of an individual's entire career (42).

Our goal was to assess the effect of night shift work on breast cancer incidence in women, using data from a large population-based cohort study. Specifically, we examined (1) the effect of night shift work on breast cancer incidence, and whether this effect was moderated by (2) sleep patterns (duration, quality, and chronotype) and (3) menopausal status. Additionally, we investigated (4) whether night shift work characteristics across the life course (duration, frequency, number of consecutive night shifts worked, shift length and rest periods) were associated with breast cancer incidence.

Methods

Study design and population

We used data from the UK Biobank, a large-scale biomedical database and research resource in the United Kingdom (UK). All individuals aged 40-69 years, registered with the UK's National Health Service, and residing within 40 km of one of 22 assessment centers in England, Wales, and Scotland, were invited. Over 500,000 participants underwent baseline assessment (2006-2010), yielding a 5.5% participation rate. Individuals were repeatedly invited to complete touchscreen questionnaires, detailed interviews, and to provide physiological measurements, multimodal imaging, and biological samples.

The flow chart (Figure 1) describes exclusion of participants for the current analyses in detail. Men (n = 229,067) and women lost to follow-up (n = 691) were excluded from the full cohort.

To prospectively assess the effect of night shift work and breast cancer incidence (Aim 1) and the moderation effect of sleep patterns and menopausal status (Aims 2 and 3), we used data from a first cohort (Baseline Cohort). This Baseline Cohort consisted of women without a breast cancer diagnosis at baseline (according to cancer registries or based on self-reported diagnosis), who were in the labor force at baseline, with available data on their shift work pattern at baseline. Follow-up for the Baseline Cohort started at baseline and ended on May 13, 2022, the date of the last update of the UK Biobank via linkage with cancer registries, before data extraction.

To assess the effect of various night shift work characteristics and breast cancer incidence (Aim 4), we used data from a second cohort (Lifecourse Cohort) consisting of women with an available job history questionnaire, which detailed the entire working life course, including information on the characteristics of night shift work. Women with a breast cancer diagnosis before starting their first job were excluded. Breast cancer cases were assessed from the reported year of start of the first job in the job history until May 13, 2022.
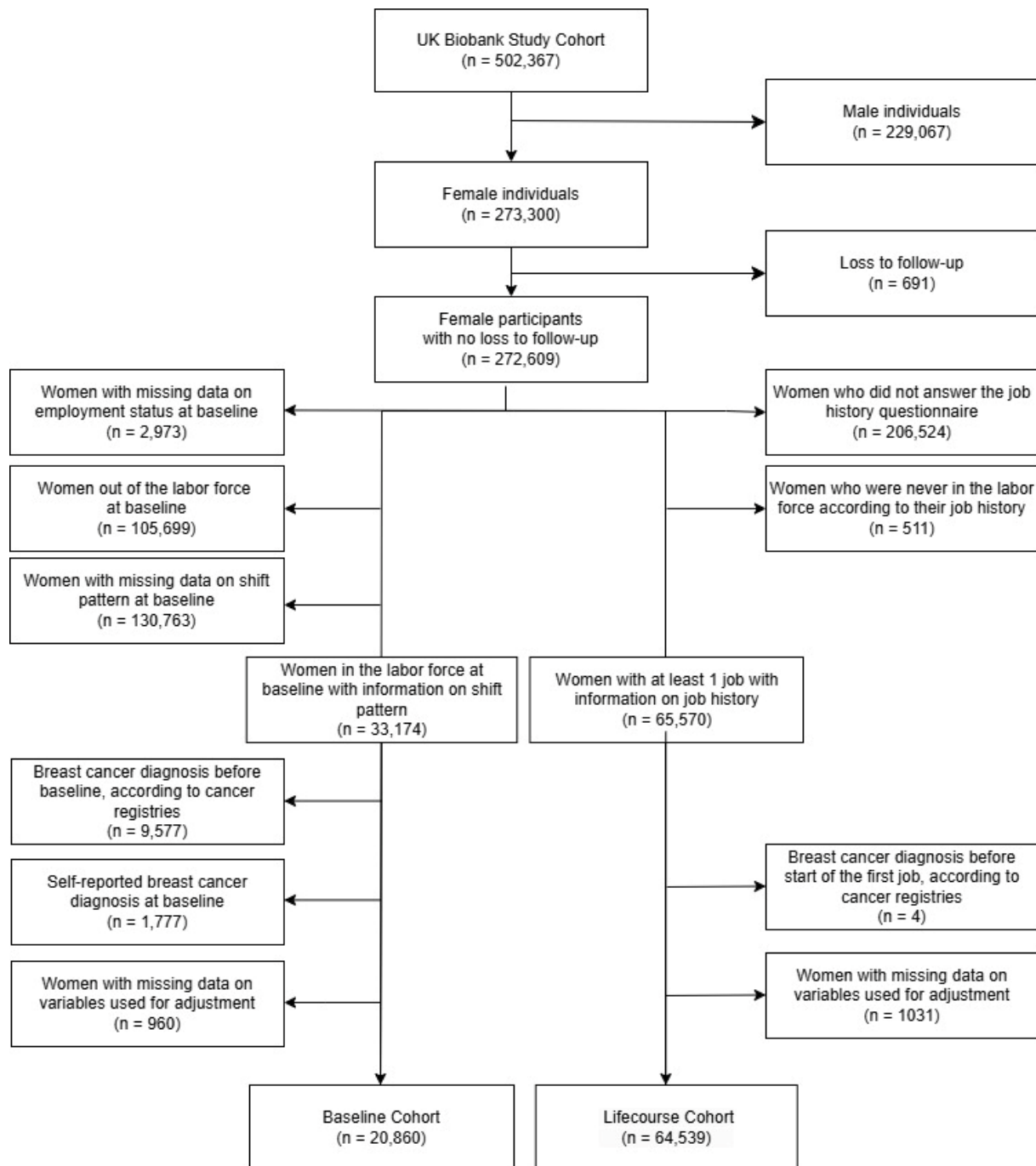
Figure 1: Selection of the participants who were included in the analyses

Boxes in flowchart:

- UK Biobank Study Cohort (n = 502,367)
  - Male individuals (n = 229,067)
- Female individuals (n = 273,300)
  - Loss to follow-up (n = 691)
- Female participants with no loss to follow-up (n = 272,609)
  - Women with missing data on employment status at baseline (n = 2,973)
  - Women who did not answer the job history questionnaire (n = 206,524)
  - Women out of the labor force at baseline (n = 105,699)
  - Women who were never in the labor force according to their job history (n = 511)
  - Women with missing data on shift pattern at baseline (n = 130,763)
- Women in the labor force at baseline with information on shift pattern (n = 33,174)
- Women with at least 1 job with information on job history (n = 65,570)
  - Breast cancer diagnosis before baseline, according to cancer registries (n = 9,577)
  - Breast cancer diagnosis before start of the first job, according to cancer registries (n = 4)
  - Self-reported breast cancer diagnosis at baseline (n = 1,777)
  - Women with missing data on variables used for adjustment (n = 960)
  - Women with missing data on variables used for adjustment (n = 1031)
- Baseline Cohort (n = 20,860)
- Lifecourse Cohort (n = 64,539)

Exposure assessment

Night shift work

Employment details were collected through a touchscreen questionnaire. For the Baseline Cohort, participants were grouped into day workers or night shift workers based on their response to the baseline question: "Does your main job involve night shifts?". Night shifts were defined as "a work schedule that involves working through the normal sleeping hours, for instance working through the hours from 12 am to 6 am". Participants who answered "Never" or "Rarely" were categorized as day workers, while those who answered "Always," "Usually," or "Sometimes" were classified as night shift workers.

For the Lifecourse Cohort, we used a job history questionnaire, which documented the entire working life course. For each position held, participants reported the start and end years of employment and specified whether the job involved night shift work (defined in this questionnaire as "at least 3 hours of work between midnight and 5 am"). In this cohort, we categorized participants as either "ever night shift workers" if they reported at least one job involving night shift work in their job history, or "never night shift workers" if they reported none. If night shifts were reported, participants provided additional details, including: the length of a night shift in hours, the number of night shifts worked in a month, the number of nights worked in a row before a rest day, and the number of rest days after a block of night shifts. Participants were instructed to answer based on the most common night shift patterns for each position held. As the questions for each night shift characteristic allowed participants to provide specific numbers or lengths, we recoded them into categories, based on the most common night shift work policies (43–45) and relevant studies on the subject (20,21). This was done to enable comparisons between our results and existing studies.

We computed five life course night shift characteristics: lifecourse duration, monthly frequency, number of consecutive night shifts, length of each night shift, and number of rest days after a block of night shifts. Using the recorded start and end years for night shift jobs, we calculated the total duration of night shift exposure over the participants' working life course. This lifecourse exposure duration was grouped into three categories: <5 years, 5-10 years and >10 years of exposure. If night shift work periods overlapped, the overlap time in years was calculated and divided by 2, then added to the non-overlapping duration of each period to avoid overestimating the exposure duration. We calculated the average frequency of night shifts per month over the participants' working life course, accounting for the duration of each job in years. Each job's duration was used as a weight to ensure an accurate estimation. Based on the calculated average, participants were then categorized into three groups: <10, 10-20 and >20 night shifts per month. The average frequency of night shifts per month was calculated using the following formula:

$$\text{Average frequency of night shift} = \frac{\sum (\text{Duration of each job involving night shifts in years} \times \text{Frequency of night shifts for that job})}{\text{Total duration of exposure to night shifts in years}}$$

We employed similar weighting methods to determine the length of individual night shifts, the number of consecutive night shifts and number of rest days after a block of night shifts. The length of individual night shifts was grouped into 0–7 hours, 8–12 hours, or >12 hours, reflecting common night shift patterns, particularly 8- and 12-hour shifts. The number of consecutive night shifts was grouped into 1–4 or >4 consecutive nights. To examine recovery time after night shifts, we categorized the number of rest days following a block of night shifts into 3 groups: 1 rest day, 1–3 rest days, and >3 rest days. These categories were based on findings from studies addressing recovery needs after night shifts (46,47).

Sleep
We used self-reported baseline information on sleep traits, including sleep duration and quality, along with information on chronotype.

Sleep duration was assessed with the question: "About how many hours of sleep do you get in every 24 hours? (please include naps)". We recoded participants' answers into 2 categories : 7-9 hours, which corresponds to the recommendations (48), and < 7 or > 9 hours, which both are linked to poor health outcomes, including breast cancer, although the evidence regarding the impact of sleeping more than 9 hours on breast cancer remains mixed (49–51).

Sleep quality was assessed based on participants' answers to four questions: "Do you have trouble falling asleep at night or do you wake up in the middle of the night?", "How likely are you to doze off or fall asleep during the daytime, when you don't mean to?", "How easy do you find getting up in the morning?", and "Do you have a nap during the day?". If participants answered yes to at least one of these questions, their sleep quality was considered poor. Otherwise, their sleep quality was considered good.

Chronotype was reported by participants, who selected their type from several options ranging from morning person to evening person. For our analyses, we categorized participants into two categories: 'morning chronotype', if participants considered themselves "Definitely a 'morning' person" or "More a 'morning' than an 'evening' person", and 'evening chronotype' if participants reported considering themself "Definitely an 'evening' person" or "More an 'evening' than a 'morning' person".

Menopausal status

Baseline data on menopausal status were obtained from participants in the Baseline Cohort through the question: "Have you had your menopause (periods stopped)?". Women who answered "Yes" were classified as postmenopausal, those who answered "No" as premenopausal, and women who selected "Prefer not to answer," "Not sure, had a hysterectomy," or "Not sure, other reason" were classified as missing.

Outcome assessment: breast cancer

Incident breast cancer cases were identified through linkage with cancer registries, using the International Classification of Diseases (ICD) codes: ICD-10 (code C50) and ICD-9 (code 174). If a participant received multiple breast cancer diagnoses during her life course, only the first diagnosis was retained for outcome assessment.

Covariates

Within a causal framework, we selected the set of covariates using a directed acyclic graph (DAG) for all aims (Figure 2 for a simplified DAG and Supplemental Figure 1 for the full DAG). The minimal sufficient adjustment set for estimating the effect of night shift work on breast cancer incidence comprised four variables assessed at baseline: age, ethnicity, education, and parity. Ethnicity was assessed using the question "What is your ethnic group?" and then categorized as White, Asian, Black and Mixed (52). Education was measured based on the question "Which of the following qualifications do you have? (You can select more than one)", and grouped into College, A levels, O levels/GCSEs, CSEs or equivalent, and Compulsory (53). Parity was assessed with the question "How many children have you given birth to? (Please include live births only)" and categorized as 0, 1, or ≥ 2 children (54). We excluded women with missing data on any of those variables from the analyses (see Figure 1).
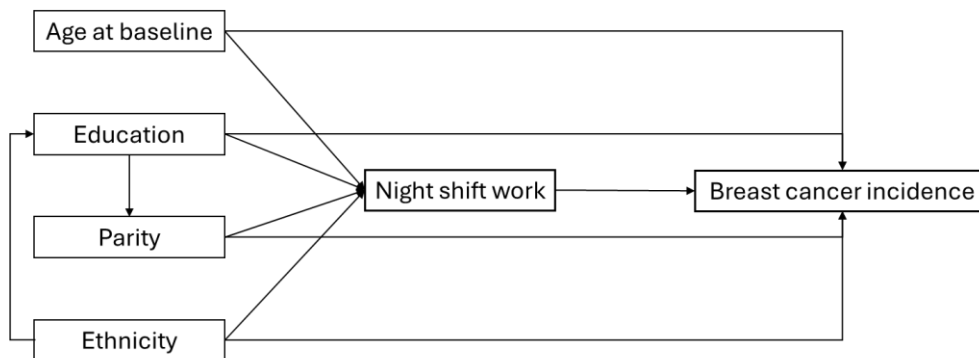
Figure 2: Simplified Directed Acyclic Graph for night shift work and breast cancer incidence.

Statistical analyses

Baseline characteristics were reported as means and standard deviations for continuous variables, or as counts and percentages for categorical variables.

In the Baseline Cohort, we used Cox proportional hazard regression to estimate multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (95% CIs) to assess the effect of night shift work at baseline on breast cancer incidence (Aim 1). Analyses were performed with adjustment for age at baseline only as well as with adjustment for the final set of covariates.

In the same cohort, stratified analyses explored whether sleep quality, quantity, or chronotype modified the night shift work-breast cancer relationship (Aim 2). We compared sleep duration, quality, and chronotype among night shift workers, allowing us to identify potential subgroups with differing risks of breast cancer related to night shift work. A further stratified analysis assessed whether menopausal status (premenopausal versus postmenopausal) at baseline modified the association between night shift work and breast cancer (Aim 3).

We used the Lifecourse Cohort, to assess the effect of night shift work on breast cancer incidence, and more specifically the effect of various night shift characteristics (durations, frequencies, consecutive nights worked, and rest periods) on breast cancer incidence (Aim 4).

We verified the assumptions for Cox models through visual inspection of residual and statistical tests and no violations were detected. We also performed a sensitivity analysis in the Baseline Cohort by reclassifying participants who answered "Sometimes" as day workers instead of night shift workers.

R version 4.3.1 (2023-06-16 ucrt) - 'Beagle Scouts', was used to conduct the analyses.

Results

Participant Characteristics

The Baseline Cohort included 20,680 breast cancer-free women who were in the labor force at baseline, with data on shift patterns and covariates. The Lifecourse Cohort comprised 64,539 women who were breast cancer-free before starting their first job, completed a detailed job history questionnaire with at least one period of employment in the labor force, and with data on all covariates.

Table 1 presents the descriptive characteristics of the cohorts at baseline. All detailed characteristics corresponding to the variables used for the creation of the full DAG, with their distribution across the two cohorts, are presented in Supplemental Table 1. For the Baseline Cohort, the mean age at baseline was 51.7 years old. For the Lifecourse Cohort, the mean age at

baseline was 55.6 years old. Most participants were of white ethnicity, had attended college, and had given birth to two or more children.

Table 1: Participant Characteristics at Baseline: Comparison by Baseline Shift Patterns (Baseline Cohort) and Night Shift Worker Status (Lifecourse Cohort)

	Baseline Cohort			Lifecourse Cohort		
	Shift work at baseline (2006-2010)			Night shift worker status based on job history		
	Day workers	Night shift workers	Full cohort	Never night shift worker	Ever night shift worker	Full cohort
	n = 11,996 (57.5%)	n = 8,864 (42.5%)	n = 20,860	n = 53,698 (83.2%)	n = 10,841 (16.8%)	n = 64,539
Age at baseline (mean (SD))	52.3 (6.8)	51.1 (6.6)	51.7 (6.8)	55.9 (7.6)	54.0 (7.6)	55.6 (7.6)
Education						
College	3,205 (27%)	2,212 (25%)	5,417 (26%)	24,778 (46%)	4,950 (46%)	29,728 (46%)
A levels	1,474 (12%)	1,111 (13%)	2,585 (12%)	7,835 (15%)	1,550 (14%)	9,385 (14%)
O levels/GCSEs	2,988 (25%)	2,166 (24%)	5,154 (25%)	11,531 (21%)	2,347 (22%)	13,878 (22%)
CSEs or equivalent	2,946 (25%)	2,662 (30%)	5,608 (27%)	6,364 (12%)	1,389 (13%)	7,753 (12%)
Compulsory	1,383 (11%)	713 (8%)	2,096 (10%)	3,190 (6%)	605 (6%)	3,795 (6%)
Ethnic background						
White	11,133 (93%)	7,844 (89%)	18,977 (91%)	52,829 (98%)	10,527 (97%)	63,356 (98%)
Mixed	113 (1%)	121 (1%)	234 (1%)	247 (1%)	89 (1%)	336 (0.5%)
Asian	393 (3%)	298 (3%)	691 (3%)	389 (1%)	109 (1%)	498 (1%)
Black	357 (3%)	601 (7%)	958 (5%)	233 (0,4%)	116 (1%)	349 (0.5%)
Parity						
0 child	2,424 (20%)	1,882 (21%)	4,306 (21%)	12,051 (22%)	2,570 (24%)	14,621 (23%)
1 child	1,656 (14%)	1,258 (14%)	2,914 (14%)	6,686 (13%)	1,402 (13%)	8,088 (12%)
2 children or more	7,916 (66%)	5,724 (65%)	13,640 (65%)	34,961 (65%)	6,869 (63%)	41,830 (65%)

Data are shown as n (%) unless otherwise indicated.

The participants of the Lifecourse Cohort had between 1 and 20 different work periods throughout their careers, with an average of 4 distinct jobs per participant over their working life course. These work periods began between 1949 and 2015. In the ever night shift worker subgroup, participants held between 1 and 11 jobs involving night shifts. The median duration of night shift work was 10 years (first quartile: 4 years; third quartile: 27 years). Additionally, 100 participants had overlapping night shift work periods during their careers.

Night shift work and breast cancer incidence

In the Baseline Cohort, the median follow-up duration was 14 years, during which 688 breast cancer cases were diagnosed, resulting in an incidence rate of 236 cases per 100,000 person-years. The adjusted HR for breast cancer incidence in relation to being a night shift worker at baseline was 0.95 (95% CI: 0.85-1.06) (Table 2). The sensitivity analysis, in which participants who answered 'Sometimes' were reclassified as day workers instead of night shift workers, did not alter the results.

Table 2: Cox regression hazard ratios for shift work pattern at baseline[a], with breast cancer incidence, Baseline Cohort

	Participants (n = 20,860)	Breast cancer diagnosis (n = 688)	Breast cancer incidence	
			Age-adjusted HR (95% CI)	Fully adjusted HR[b] (95% CI)
Work pattern at baseline[a]				
Day workers	11,996	391	1.00 (Ref)	1.00 (Ref)
Night shift workers	8,864	297	0.97 (0.87-1.08)	0.95 (0.85-1.06)

HR Hazard Ratio, *CI* Confidence Interval
[a]Participants were separated into Day workers or Night shift workers depending on the answer to the question "Does your main job involve night shifts" at baseline. Participants answering "Never/rarely" were defined as day workers, participants answering "Always", "Usually" or "Sometimes" were defined as night shift workers.
[b]HR adjusted for: Age at baseline, Ethnicity (White, Mixed, Asian, Black), Education (College, A levels, O levels/GCSEs, CSEs or equivalent, Compulsory), Parity (0, 1, 2 or more children)

In the Lifecourse Cohort, the median follow-up duration was 50 years, during which 4,455 cases of breast cancer were diagnosed, corresponding to an incidence rate of 138 cases per 100,000 person-years. The adjusted HR for breast cancer incidence in relation to being a night shift worker over the working life course was 1.04 (95% CI: 0.96-1.13) (Table 3).

The duration of exposure to night shift work (in years) over a woman's working life course was not associated with an increased incidence of breast cancer. Specifically, compared to women who never worked in jobs involving night shifts, the total duration of night shift work was not associated with breast cancer incidence for those with less than 5 years in jobs involving night shifts (HR 0.98; 95% CI: 0.84–1.14), 5 to 10 years (HR 1.10; 95% CI: 0.91–1.32), nor more than 10 years (HR 1.06; 95% CI: 0.95–1.18).

The mean monthly frequency of night shift work was not associated with breast cancer incidence, with fully adjusted HRs of 1.07 (95% CI: 0.97-1.19) for women working less than 10 nights a month, 1.01 (95% CI: 0.88-1.16) for women working between 10 and 20 nights a month, and 0.84 (95% CI: 0.55-1.29) for women working more than 20 nights a month.

The length of a typical night shift showed no effect on breast cancer incidence, with fully adjusted HRs of 1.25 (95% CI: 0.96-1.63) for women working night shifts lasting <7 hours, 1.03 (95% CI: 0.95-1.13) for women working night shifts lasting between 7 and 12 hours, and 0.97 (95% CI: 0.75-1.27) for women working night shifts lasting more than 12 hours.

The mean number of consecutive night shifts worked also showed no effect on breast cancer incidence, with fully adjusted HRs of 1.03 (95% CI: 0.92-1.14) for women working between 1 to 4 nights in a row, and 1.07 (95% CI: 0.95-1.20) for women working more than 4 nights in a row.

The number of rest days following a block of night shifts was not related to the risk of developing breast cancer, with fully adjusted HRs of 1.03 (95% CI: 0.88-1.20) for women getting 1 rest day after a block of night shifts, 1.06 (95% CI: 0.94-1.18) for women getting 2 to 3 rest days after a block of night shifts, and 1.04 (95% CI: 0.90-1.20) for women getting more than 3 rest days after a block of night shifts.

Table 3: Cox regression hazard ratios for night shift worker status according to job history[a], by life course exposure duration, monthly frequency, length of each night shift, number of consecutive night shifts, and number of rest days after a block of night shifts, Lifecourse Cohort

	Participants (n = 64,539)	Breast cancer diagnosis (n = 4,455)	Breast cancer incidence Age-adjusted HR (95% CI)	Fully adjusted HR[b] (95% CI)
Night shift worker status according to job history[a]				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
Ever night shift worker	10,841 (17%)	675 (6%)	1.03 (0.95-1.12)	1.04 (0.96-1.13)
Night shift work characteristics according to job history				
Life course duration of night shift work in years				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
Less than 1 year to 5 years	3,072 (5%)	194 (6%)	1.00 (0.86-1.15)	0.98 (0.84-1.14)
5-10 years	1,910 (3%)	114 (6%)	1.09 (0.91-1.32)	1.10 (0.91-1.32)
>10 years	5,859 (9%)	367 (6%)	1.02 (0.92-1.14)	1.06 (0.95-1.18)
Mean monthly frequency of night shifts				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
< 10	7,744 (12%)	444 (6%)	1.06 (0.96-1.17)	1.07 (0.97-1.19)
10-20	2,868 (4%)	210 (7%)	0.99 (0.86-1.13)	1.01 (0.88-1.16)
>20	229 (0.4%)	21 (9%)	0.87 (0.57-1.34)	0.84 (0.55-1.29)
Mean length of each night shift in hours				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
0-7	833 (1%)	57 (7%)	1.16 (0.89-1.51)	1.25 (0.96-1.63)
8-12	9,205 (14%)	562 (6%)	1.02 (0.93-1.11)	1.03 (0.95-1.13)
>12	803 (1%)	56 (7%)	1.02 (0.78-1.33)	0.97 (0.75-1.27)
Mean number of consecutive night shifts				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
1-4	6,894 (11%)	395 (6%)	1.01 (0.91-1.12)	1.03 (0.92-1.14)
>4	3,947 (6%)	280 (7%)	1.06 (0.94-1.20)	1.07 (0.95-1.20)
Mean number of rest days after block of night shift				
Never night shift worker	53,698 (83%)	3,780 (7%)	1.00 (Ref)	1.00 (Ref)
1	2,825 (4%)	168 (6%)	1.04 (0.89-1.21)	1.03 (0.88-1.20)
1-3	4,959 (8%)	321 (7%)	1.03 (0.92-1.15)	1.06 (0.94-1.18)
>3	3,057 (5%)	186 (6%)	1.02 (0.88-1.18)	1.04 (0.90-1.20)

HR Hazard Ratio, *CI* Confidence Interval
Data are n (%) unless indicated.
[a]Night shift worker status: Participants were considered "ever night shift worker" if they reported at least 1 job involving night shift in their employment history
[b]HR adjusted for: Age at baseline, Ethnicity (White, Mixed, Asian, Black), Education (College, A levels, O levels/GCSEs, CSEs or equivalent, Compulsory), Parity (0, 1, 2 or more children)

Moderation of sleep, chronotype and menopausal status

Using the Baseline Cohort, we stratified the risk of breast cancer in relation to night shift worker status at baseline by sleep duration, sleep quality, and chronotype. In this cohort, 18,977 women had available data on sleep duration, sleep quality and chronotype. No associations or interactions were found for any of these factors (Table 4).

Further analysis by menopausal status at baseline also revealed no associations or interactions on the relationship between night shift work and breast cancer incidence (Table 5).

Table 4. Incidence of breast cancer associated with shift work pattern at baseline[a], stratified by sleep duration, sleep quality and chronotype, Baseline Cohort (participants with available data on sleep duration, sleep quality and chronotype only)

	Participants (n = 18,977)	Breast cancer diagnosis (n = 628)	Breast cancer incidence	
			Age-adjusted HR (95% CI)	Fully adjusted HR[b] (95% CI)
Work pattern at baseline[a]				
Day workers	10,968 (58%)	360 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	8,009 (42%)	268 (3%)	0.95 (0.85-1.06)	0.95 (0.85-1.06)
Sleep duration at baseline[c]				
Sleep 7-9 hours /24 hours				
Day workers	7,804 (41%)	258 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	5,260 (28%)	178 (3%)	0.90 (0.79-1.04)	0.91 (0.79-1.04)
Total	13,064 (69%)	436 (3%)		
Sleep <7 or >9 hours/24 hours				
Day workers	3,164 (17%)	102 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	2,749 (15%)	90 (3%)	1.07 (0.87-1.32)	1.06 (0.86-1.32)
Total	5,913 (31%)	192 (3%)		
p for interaction				0.20
Sleep quality at baseline[d]				
Good sleep quality				
Day workers	1,096 (6%)	30 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	715 (4%)	27 (4%)	1.28 (0.88-1.90)	1.35 (0.87-2.09)
Total	1,811(10%)	57 (3%)		
Poor sleep quality				
Day workers	9,872 (52%)	330 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	7,294 (38%)	241 (3%)	0.92 (0.82-1.04)	0.92 (0.82-1.04)
Total	17,166 (90%)	571 (3%)		
p for interaction				0.07
Chronotype at baseline[e]				
Morning chronotype				
Day workers	6,768 (36%)	221 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	4,380 (23%)	123 (3%)	0.96 (0.82-1.12)	0.93 (0.79-1.10)
Total	11,148 (59%)	344 (3%)		
Evening chronotype				
Day workers	4,200 (22%)	139 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	3,629 (19%)	145 (4%)	0.90 (0.76-1.06)	0.88 (0.74-1.04)
Total	7,829 (41%)	284 (4%)		
p for interaction				0.54

HR Hazard Ratio, *CI* Confidence Interval
Data are n (%) unless indicated.
[a]Participants were separated into Day workers or Night shift workers depending on the answer to the question "Does your main job involve night shifts" at baseline. Participants answering "Never/rarely" were defined as day workers, participants answering "Always", "Usually" or "Sometimes" were defined as night shift workers.
[b]HR adjusted for: Age at baseline, Ethnicity (White, Mixed, Asian, Black), Education (College, A levels, O levels/GCSEs, CSEs or equivalent, Compulsory), Number of live births (0, 1, 2 or more)
[c]Sleep duration: "About how many hours sleep do you get in every 24 hours? (please include naps)"
[d]Assessment of sleep quality was based on the questions: "Do you have trouble falling asleep at night or do you wake up in the middle of the night?", "How likely are you to doze off or fall asleep during the daytime, when you don't mean to?", "How easy do you find getting up in the morning?", and "Do you have a nap during the day?" If participants reported having trouble falling asleep, staying awake during the day, getting up, or needing to nap, their sleep quality was considered poor.
[e]Chronotype: morning chronotype if the participant reported considering themself "Definitely a 'morning' person" or "More a 'morning' than an 'evening' person", and evening type if the participant reported considering themself "Definitely a 'evening' person" or "More a 'evening' than an 'morning' person".

Table 5. Incidence of breast cancer associated with shift work pattern at baseline[a], stratified by menopausal status at baseline, Baseline Cohort (participants with available data on menopausal status at baseline only)

	Participants (n = 17,233)	Breast cancer diagnosis (n = 563)	Breast cancer incidence	
			Age-adjusted HR (95% CI)	Fully adjusted HR[b] (95% CI)
Work pattern at baseline[a]				
Day workers	9,912 (58%)	321 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	7,321 (42%)	242 (3%)	0.98 (0.87-1.10)	0.98 (0.87-1.10)
Menopausal status at baseline[c]				
Premenopausal				
Day workers	4,267 (25%)	131 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	3,565 (21%)	109 (3%)	0.96 (0.80-1.15)	0.98 (0.81-1.18)
Total	7,832 (45%)	240 (3%)		
Postmenopausal				
Day workers	5,645 (33%)	190 (3%)	1.00 (Ref)	1.00 (Ref)
Night shift workers	3,756 (22%)	133 (4%)	0.99 (0.85-1.16)	0.95 (0.81-1.11)
Total	9,401 (55%)	323 (3%)		
p for interaction				0.74

_HR_ Hazard Ratio, _CI_ Confidence Interval

[a]Participants were separated into Day workers or Night shift workers depending on the answer to the question "Does your main job involve night shifts" at baseline. Participants answering "Never/rarely" were defined as day workers, participants answering "Always", "Usually" or "Sometimes" were defined as night shift workers.

[b]HR adjusted for: Age at baseline, Ethnicity (White, Mixed, Asian, Black), Education (College, A levels, O levels/GCSEs, CSEs or equivalent, Compulsory), Parity (0, 1, 2 or more children)

[c]Menopausal status: "Have you had your menopause (periods stopped)?" (yes/no)

Discussion

Our large prospective study provides robust evidence on the effect of night shift work on breast cancer incidence, exploring lifecourse characteristics of night shift work while accounting for sleep habits, chronotype, and menopausal status. Specifically, we examined (1) whether night shift work was associated with breast cancer incidence, whether this association was modified by (2) sleep characteristics and (3) menopausal status, and (4) whether detailed working life course characteristics of night shift work (such as duration, frequency, number of consecutive night shifts worked, shift length, and rest periods) were linked to breast cancer incidence.

Night shift work and breast cancer

We found no effect of night shift work on breast cancer incidence. Our findings align with previous cohort studies (34,35), including the 2016 UK Biobank study by Travis et al., which also reported no association (33). However, our study improves on prior UK Biobank analyses by using updated follow-up data (through 2022) and on our use of a DAG to identify confounders for minimal adjustment.

In contrast, the positive association observed in case–control studies (16,21,30–32) may be misleading due to a higher risk of bias inherent in their design. Several meta-analyses (9,39,55–57) have reinforced the null findings from cohort studies. Taken together, the consistency of null findings across multiple well-designed cohort studies, including ours with relatively long follow-up time, strongly suggests that night shift work does not have an effect on breast cancer incidence.

Sleep and chronotype

We found no evidence that sleep duration, sleep quality and chronotype modifies the association between night shift work and breast cancer. This aligns with the 2016 UK Biobank study by Travis et al., which reported no impact of the number of hours of sleep and the diurnal preference on breast cancer incidence (33). Similarly, the IARC's 2019 evaluation concluded that there is no

evidence regarding the interaction of diurnal preference with the association between night shift work and breast cancer (22).

The classification of participants into good or poor sleep quality merits caution. Indeed, in our study, nap-taking was used as a proxy for poor sleep quality, but it may also reflect sleep fragmentation – a common occurrence after night shifts – rather than restorative naps, which could be part of the natural adaptation to disrupted sleep cycles following night shifts.

Menopause

Some studies suggested that postmenopausal women could have a lower incidence of breast cancer compared with premenopausal women when working night shifts (7,20,21). This could be explained considering that premenopausal women could experience more estrogen dysregulation due to circadian rhythm disruption (7,20,21). In our study, we did not find a modifying effect of menopausal status and a null association was observed both in premenopausal and postmenopausal women.

Night shift work across the entire working life course and breast cancer

Although we found no association between night shift work and breast cancer incidence, current evidence remains limited due to a lack of detailed assessments of night shift work characteristics across the entire working life course. Addressing this gap, our study used a bi-directional design – which combines a prospective approach (Baseline Cohort) with retrospective data collection (Lifecourse Cohort) – to provide a more comprehensive assessment of night shift work across the entire working life course. Our results showed that key characteristics of night shift work over the working life course – including exposure duration, monthly frequency, shift length, number of consecutive night shifts, and rest days after night shift blocks – were not associated with an increased incidence of breast cancer.

To our knowledge, this is the first study to evaluate such a comprehensive range of night shift work characteristics, particularly rest days and consecutive night shifts, while accounting for exposure across the entire working life course. Unlike traditional carcinogens, where risk is typically linked to cumulative exposure duration and dose-response relationships, night shift work over the life course does not appear to follow this type of cumulative risk mechanism.

Several studies have suggested an increased risk of breast cancer among women with long-term exposure to night shift work. For example, two meta-analyses based on both cohort and case-control studies found a positive association between long-term night shift work and breast cancer incidence (with statistically significant increases observed after 10, 20, and 30 years of exposure) (20,28). Some studies and meta-analyses even reported a dose–response relationship, with breast cancer incidence increasing with the number of years of night shift work (27,28,58,59). Our results contradict these findings and are more consistent with those of the meta-analysis by Travis et al. (2016), which included the first UK Biobank study on this topic and reported no association between long-term night shift work (>20 years) and breast cancer incidence (33), and those of a recent dose-response meta-analysis (23). One possible explanation lies in differences in exposure assessment. In our study, night shift work was quantified as a cumulative duration based on the participant's entire job history, whereas many other studies have focused on night shift work during the follow-up period only. Our approach provides a more realistic estimate of lifetime exposure. However, it assumes a linear dose–response relationship and may overlook the existence of sensitive periods or threshold effects, such as heightened vulnerability to circadian disruption during specific life stages.

Regarding frequency of night shift work, a meta-analysis conducted by Hong et al. found that high-frequency night shift work (>5 shifts/week) is a risk factor to develop breast cancer (20), which aligns with the results of the 2018 pooled case-control study of Cordina-Duverger et al. finding a positive association for premenopausal women working at least 3 night shifts per week (21). Notably, these studies assessed night shift work on a weekly basis, whereas our study used a weighted monthly average frequency, calculated from the entire job history of each participant. This offers a more accurate measure of long-term exposure and its potential cumulative impact. Since cancer is a disease with a long latency period, it is essential to capture prolonged and repeated exposures over time.

Finally, the analysis of consecutive night shifts and rest periods between shifts revealed no association with breast cancer incidence. These findings do not support the hypothesis that insufficient recovery time exacerbates breast cancer incidence. It is important to note that in recent years, especially during the follow-up of the Lifecourse Cohort, work schedule policies has evolved to limit consecutive night shifts, allowing for more rest days between shifts, for example due to the 1998 Working Time Regulations or the 2003 European Parliament Directive (45,60,61). However, our study was not designed to evaluate the impact of these policies. Further studies considering contemporary policies about night shift work are needed to evaluate their impact and if further adjustments are necessary.

Strengths and limitations

A key strength lies in the complementary design of the two cohorts. The Baseline Cohort provided data on night shift work that minimized recall bias, while the Lifecourse Cohort enabled analyses of detailed night shift work characteristics across the entire working life course. Combining these approaches enhanced the reliability of our findings. Both cohorts had a relatively long follow-up and had large sample sizes, with sufficient cases for analyzing the main effects of night shift work. In both cohorts, the exposure chronologically preceded the outcome, and the outcome was based on registry data. Additionally, detailed data on other potential risk factors and the use of a DAG strengthened our methodology by clarifying the minimal sufficient adjustment set of confounding factors.

Despite these strengths, our study has several limitations. First, it relies on self-reported data for exposure assessment and covariates, which may introduce biases. Night shift work definition differed between our two analytical cohorts, potentially contributing to heterogeneity in findings, a known issue in prior studies (13). In the Lifecourse Cohort, job histories were based on retrospective self-reports, requiring participants to recall detailed work characteristics over their entire working life course, potentially leading to recall bias. Self-reported data on sleep patterns and chronotype may have introduced measurement errors, and we did not account for changes in sleep patterns and menopausal status during follow-up, potentially leading to misclassification.

Second, it has been shown that the UK Biobank population is not representative of the general UK population (62). Therefore, selection bias may affect our results and compromise their external validity (63). Furthermore, we applied strict exclusion criteria due to the lack of data on night shift work, which led to a reduced sample size in our analytical cohorts compared to the original dataset. This may have introduced an additional selection bias and limited the generalizability of our results.

Third, survivor bias is inherent to the UK biobank's design, which recruited participants aged 40-69 years. This may limit the generalizability of our findings to populations who survived to the

study period. However, the survivor bias may likely be limited, as the probability of dying from cancer before the age of 40 is low (64). On the other hand, the average follow-up of 14 years may have been insufficient to capture the development of all breast cancers in the sample.

Fourth, in the UK Biobank, information on whether participants emigrated or withdrew from the study was only available until 2017. We estimated that censoring may not have been accurately recorded beyond this date for approximately 470 individuals in our study. Given the small number of affected participants, any resulting bias is likely minimal.

Fifth, complete cancer incidence data for participants were not available until the end of follow-up: complete data from Wales were available only up to 2017, from England up to 2021, and from Scotland up to 2022 (65). This incomplete follow-up may have led to some underestimation of breast cancer cases in this subgroup, potentially affecting the accuracy of our findings.

Finally, our study also did not distinguish between consistent and intermittent night shift workers, nor did it address factors like workplace light exposure or other environmental exposures. Future research should incorporate these variables for a more comprehensive understanding.

Future perspectives

Our findings alleviate concerns about the overall risks of night shift work for breast cancer incidence. However, night shift work is associated with poor health behaviors and chronic stress, both recognized as carcinogenic risk factors (66). Additionally, night shift workers often face socio-economic disparities and limited access to healthcare (67). Therefore, it is crucial to maintain working time regulations, optimize shift schedules, and provide resources to help workers manage the health risks linked to disrupted circadian rhythms. In addition, future research should integrate genetic, hormonal, and lifestyle factors, along with objective and long-term measures of light exposure and circadian markers, to clarify the biological mechanisms linking night shift work and breast cancer as suggested by the IARC (22) and the US National Toxicology Program (68).

Conclusion

In conclusion, this study indicates that there is no effect of night shift work on breast cancer in the examined population. This adds to the current knowledge base on night shift work and breast cancer, suggesting the relationship may be more nuanced than previously thought. The lack of a direct association highlights the importance of exploring individual variability in response to night shift work. Future research should continue to address these complexities to provide clearer guidance for public health interventions and workplace policies.

Bibliography

1. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. Breast Edinb Scotl. 2022 Dec;66:15–23.

2. Dall GV, Britt KL. Estrogen Effects on the Mammary Gland in Early and Late Life and Breast Cancer Risk. Front Oncol. 2017;7:110.

3. David PS, Sobel T, Sahni S, Mehta J, Kling JM. Menopausal Hormone Therapy in Older Women: Examining the Current Balance of Evidence. Drugs Aging. 2023 Jun 21;

4. Kyu HH, Bachman VF, Alexander LT, Mumford JE, Afshin A, Estep K, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ. 2016 Aug 9;354:i3857.

5. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose–response meta-analysis. Br J Cancer. 2015 Feb;112(3):580–93.

6. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes Dis. 2018 Jun;5(2):77–106.

7. Wegrzyn LR, Tamimi RM, Rosner BA, Brown SB, Stevens RG, Eliassen AH, et al. Rotating Night-Shift Work and the Risk of Breast Cancer in the Nurses' Health Studies. Am J Epidemiol. 2017 Sep 1;186(5):532–40.

8. Fagundo-Rivera J, Gómez-Salgado J, García-Iglesias JJ, Gómez-Salgado C, Camacho-Martín S, Ruiz-Frutos C. Relationship between Night Shifts and Risk of Breast Cancer among Nurses: A Systematic Review. Med Kaunas Lith. 2020 Dec 10;56(12):680.

9. Pahwa M, Labrèche F, Demers PA. Night shift work and breast cancer risk: what do the meta-analyses tell us? Scand J Work Environ Health. 2018 Jul 1;44(4):432–5.

10. European Working Conditions Telephone Survey 2021 | European Foundation for the Improvement of Living and Working Conditions [Internet]. [cited 2025 Feb 11]. Available from: https://www.eurofound.europa.eu/en/data-catalogue/european-working-conditions-telephone-survey-2021-0

11. Garcia-Saenz A, Sánchez de Miguel A, Espinosa A, Valentin A, Aragonés N, Llorca J, et al. Evaluating the Association between Artificial Light-at-Night Exposure and Breast and Prostate Cancer Risk in Spain (MCC-Spain Study). Environ Health Perspect. 2018 Apr 23;126(4):047011.

12. Vasey C, McBride J, Penta K. Circadian Rhythm Dysregulation and Restoration: The Role of Melatonin. Nutrients. 2021 Sep 30;13(10):3480.

13. Stevens RG, Hansen J, Costa G, Haus E, Kauppinen T, Aronson KJ, et al. Considerations of circadian impact for defining 'shift work' in cancer studies: IARC Working Group Report. Occup Environ Med. 2011 Feb 1;68(2):154–62.

14. Xu J, Huang L, Sun GP. Urinary 6-sulfatoxymelatonin level and breast cancer risk: systematic review and meta-analysis. Sci Rep. 2017 Jul 13;7(1):5353.

15. Cos S, Alvarez-García V, González A, Alonso-González C, Martínez-Campa C. Melatonin modulation of crosstalk among malignant epithelial, endothelial and adipose cells in breast cancer (Review). Oncol Lett. 2014 Aug;8(2):487–92.

16. Szkiela M, Kusideł E, Makowiec-Dąbrowska T, Kaleta D. How the Intensity of Night Shift Work Affects Breast Cancer Risk. Int J Environ Res Public Health. 2021 Jan;18(9):4570.

17. Song S, Lei L, Zhang R, Liu H, Du J, Li N, et al. Circadian Disruption and Breast Cancer Risk: Evidence from a Case-Control Study in China. Cancers. 2023 Jan 8;15(2):419.

18. Vaughn CB, Freudenheim JL, Nie J, Sucheston-Campbell L, Wactawski-Wende J, Marian C, et al. Sleep and Breast Cancer in the Western New York Exposures and Breast Cancer (WEB) Study. J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med. 2018 Jan 15;14(1):81–6.

19. Von Behren J, Goldberg D, Hurley S, Clague DeHart J, Wang SS, Reynolds P. Prospective analysis of sleep characteristics, chronotype, and risk of breast cancer in the california teachers study. Cancer Causes Control CCC. 2024 Apr;35(4):597–604.

20. Hong J, He Y, Fu R, Si Y, Xu B, Xu J, et al. The relationship between night shift work and breast cancer incidence: A systematic review and meta-analysis of observational studies. Open Med Wars Pol. 2022;17(1):712–31.

21. Cordina-Duverger E, Menegaux F, Popa A, Rabstein S, Harth V, Pesch B, et al. Night shift work and breast cancer: a pooled analysis of population-based case–control studies with complete work history. Eur J Epidemiol. 2018 Apr 1;33(4):369–79.

22. IARC Working Group on the Identification of Carcinogenic Hazards to Humans. Night Shift Work [Internet]. Lyon (FR): International Agency for Research on Cancer; 2020 [cited 2023 Sep 8]. (IARC Monographs on the Identification of Carcinogenic Hazards to Humans). Available from: http://www.ncbi.nlm.nih.gov/books/NBK568195/

23. Van NTH, Hoang T, Myung SK. Night shift work and breast cancer risk: a meta-analysis of observational epidemiological studies. Carcinogenesis. 2021 Oct 26;42(10):1260–9.

24. Wei F, Chen W, Lin X. Night-shift work, breast cancer incidence, and all-cause mortality: an updated meta-analysis of prospective cohort studies. Sleep Breath Schlaf Atm. 2022 Dec;26(4):1509–26.

25. Manouchehri E, Taghipour A, Ghavami V, Ebadi A, Homaei F, Latifnejad Roudsari R. Night-shift work duration and breast cancer risk: an updated systematic review and meta-analysis. BMC Womens Health. 2021 Mar 2;21:89.

26. Lin X, Chen W, Wei F, Ying M, Wei W, Xie X. Night-shift work increases morbidity of breast cancer and all-cause mortality: a meta-analysis of 16 prospective cohort studies. Sleep Med. 2015 Nov 1;16(11):1381–7.

27. Wang F, Yeung KL, Chan WC, Kwok CCH, Leung SL, Wu C, et al. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. Ann Oncol Off J Eur Soc Med Oncol. 2013 Nov;24(11):2724–32.

28. Moon J, Ikeda-Araki A, Mun Y. Night shift work and female breast cancer: a two-stage dose-response meta-analysis for the correct risk definition. BMC Public Health. 2024 Jul 31;24(1):2065.

29. Schwarz C, Pedraza-Flechas AM, Pastor-Barriuso R, Lope V, de Larrea NF, Jiménez-Moleón JJ, et al. Long-Term Nightshift Work and Breast Cancer Risk: An Updated Systematic Review and Meta-Analysis with Special Attention to Menopausal Status and to Recent Nightshift Work. Cancers. 2021 Nov 26;13(23):5952.

30. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. J Natl Cancer Inst. 2001 Oct 17;93(20):1557–62.

31.   Hansen J, Stevens RG. Case–control study of shift-work and breast cancer risk in Danish nurses: Impact of shift systems. Eur J Cancer. 2012 Jul 1;48(11):1722–9.

32.   Hansen J, Lassen CF. Nested case-control study of night shift work and breast cancer risk among women in the Danish military. Occup Environ Med. 2012 Aug;69(8):551–6.

33.   Travis RC, Balkwill A, Fensom GK, Appleby PN, Reeves GK, Wang XS, et al. Night Shift Work and Breast Cancer Incidence: Three Prospective Studies and Meta-analysis of Published Studies. J Natl Cancer Inst. 2016 Dec;108(12):djw169.

34.   Pronk A, Ji BT, Shu XO, Xue S, Yang G, Li HL, et al. Night-shift work and breast cancer risk in a cohort of Chinese women. Am J Epidemiol. 2010 May 1;171(9):953–9.

35.   Koppes LLJ, Geuskens GA, Pronk A, Vermeulen RCH, de Vroome EMM. Night work and breast cancer risk in a general population prospective cohort study in The Netherlands. Eur J Epidemiol. 2014 Aug 1;29(8):577–84.

36.   Jones ME, Schoemaker MJ, McFadden EC, Wright LB, Johns LE, Swerdlow AJ. Night shift work and risk of breast cancer in women: the Generations Study cohort. Br J Cancer. 2019 Jul;121(2):172–9.

37.   Labrèche F, Kim J, Song C, Pahwa M, Ge CB, Arrandale VH, et al. The current burden of cancer attributable to occupational exposures in Canada. Prev Med. 2019 May;122:128–39.

38.   Hansen J, Pedersen JE. Night shift work and breast cancer risk – 2023 update of epidemiologic evidence. J Natl Cancer Cent [Internet]. 2024 Sep 25 [cited 2024 Nov 16]; Available from: https://www.sciencedirect.com/science/article/pii/S2667005424000838

39.   Ijaz S, Verbeek J, Seidler A, Lindbohm ML, Ojajärvi A, Orsini N, et al. Night-shift work and breast cancer--a systematic review and meta-analysis. Scand J Work Environ Health. 2013 Sep 1;39(5):431–47.

40.   Lie JAS, Kjuus H, Zienolddiny S, Haugen A, Stevens RG, Kjærheim K. Night Work and Breast Cancer Risk Among Norwegian Nurses: Assessment by Different Exposure Metrics. Am J Epidemiol. 2011 Jun 1;173(11):1272–9.

41.   Li W, Ray RM, Thomas DB, Davis S, Yost M, Breslow N, et al. Shift work and breast cancer among women textile workers in Shanghai, China. Cancer Causes Control. 2015 Jan 1;26(1):143–50.

42.   Papantoniou K, Hansen J. Cohort Studies Versus Case-Control Studies on Night-Shift Work and Cancer Risk: The Importance of Exposure Assessment. Am J Epidemiol. 2024 Apr 8;193(4):577–9.

43.   BAuA - Working Time - Organisation of Night and Shift Work - Federal Institute for Occupational Safety and Health [Internet]. [cited 2024 Dec 31]. Available from: https://www.baua.de/EN/Topics/Work-design/Working-time/Night-and-shift-work

44.   KVK NC of C. business.gov.nl. [cited 2024 Dec 31]. Your employee works night shifts. Available from: https://business.gov.nl/running-your-business/staff/terms-of-employment/your-employee-works-night-shifts/

45.   GOV.UK [Internet]. [cited 2023 Jul 4]. Night working hours. Available from: https://www.gov.uk/night-working-hours

46.   Khan WAA, Jackson ML, Kennedy GA, Conduit R. A field investigation of the relationship between rotating shifts, sleep, mental health and physical activity of Australian paramedics. Sci Rep. 2021 Jan 13;11(1):866.

47. Leung M, Tranmer J, Hung E, Korsiak J, Day AG, Aronson KJ. Shift Work, Chronotype, and Melatonin Patterns among Female Hospital Employees on Day and Night Shifts. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2016 May;25(5):830–8.

48. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health. 2015 Mar;1(1):40–3.

49. Itani O, Jike M, Watanabe N, Kaneita Y. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. Sleep Med. 2017 Apr 1;32:246–56.

50. Cao J, Eshak ES, Liu K, Muraki I, Cui R, Iso H, et al. Sleep duration and risk of breast cancer: The JACC Study. Breast Cancer Res Treat. 2019 Feb;174(1):219–25.

51. Shen J, Chrisman M, Wu X, Chow WH, Zhao H. Sleep duration and risk of cancer in the Mexican American Mano-a-Mano Cohort. Sleep Health. 2019 Feb;5(1):78–83.

52. Iqbal J, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in Breast Cancer Stage at Diagnosis and Cancer-Specific Survival by Race and Ethnicity in the United States. JAMA. 2015 Jan 13;313(2):165–73.

53. Dong JY, Qin LQ. Education level and breast cancer incidence: a meta-analysis of cohort studies. Menopause. 2020 Jan;27(1):113.

54. Park S, Moon BI, Oh SJ, Lee HB, Seong MK, Lee S, et al. Clinical subtypes and prognosis in breast cancer according to parity: a nationwide study in Korean Breast Cancer Society. Breast Cancer Res Treat. 2019 Feb;173(3):679–91.

55. Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Feb;138(1):291–301.

56. Dun A, Zhao X, Jin X, Wei T, Gao X, Wang Y, et al. Association Between Night-Shift Work and Cancer Risk: Updated Systematic Review and Meta-Analysis. Front Oncol. 2020;10:1006.

57. Salamanca-Fernández E, Rodríguez-Barranco M, Guevara M, Ardanaz E, Olry de Labry Lima A, Sánchez MJ. Night-shift work and breast and prostate cancer risk: updating the evidence from epidemiological studies. An Sist Sanit Navar. 2018 Aug 29;41(2):211–26.

58. Jia Y, Lu Y, Wu K, Lin Q, Shen W, Zhu M, et al. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. Cancer Epidemiol. 2013 Jun;37(3):197–206.

59. Yuan X, Zhu C, Wang M, Mo F, Du W, Ma X. Night Shift Work Increases the Risks of Multiple Primary Cancers in Women: A Systematic Review and Meta-analysis of 61 Articles. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2018 Jan;27(1):25–40.

60. Participation E. The Working Time Regulations 1998 [Internet]. Statute Law Database; [cited 2025 Jan 2]. Available from: https://www.legislation.gov.uk/uksi/1998/1833/contents

61. Directive 2003/88/EC of the European Parliament and of the Council of 4 November 2003 concerning certain aspects of the organisation of working time - EU monitor [Internet]. [cited 2025 Jan 2]. Available from: https://www.eumonitor.eu/9353000/1/j9vvik7m1c3gyxp/vhckn6xfgtzb

62. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of Sociodemographic and Health-Related Characteristics of UK Biobank Participants With Those of the General Population. Am J Epidemiol. 2017 Nov 1;186(9):1026–34.

63. Alten S van, Domingue BW, Galama T, Marees AT. Reweighting the UK Biobank to reflect its underlying sampling population substantially reduces pervasive selection bias due to volunteering [Internet]. medRxiv; 2022 [cited 2024 Jan 26]. p. 2022.05.16.22275048. Available from: https://www.medrxiv.org/content/10.1101/2022.05.16.22275048v1

64. Cancer Research UK [Internet]. 2015 [cited 2025 Jan 14]. Breast cancer statistics. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer

65.: External Info : Data_providers_and_dates [Internet]. [cited 2025 Apr 7]. Available from: https://biobank.ndph.ox.ac.uk/ukb/exinfo.cgi?src=Data_providers_and_dates

66. Schneider D, Harknett K. Consequences of Routine Work-Schedule Instability for Worker Health and Well-Being. Am Sociol Rev. 2019 Feb 1;84(1):82–114.

67. PRB [Internet]. [cited 2024 Dec 2]. A Demographic Profile of U.S. Workers Around the Clock. Available from: https://www.prb.org/resources/a-demographic-profile-of-u-s-workers-around-the-clock/

68. National Toxicology Program. NTP Cancer Hazard Assessment Report on Night Shift Work and Light at Night [Internet]. Research Triangle Park (NC): National Toxicology Program; 2021 [cited 2024 Dec 9]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK571598/

Supplementary material

Supplemental figures

Supplemental figure 1: Full Directed Acyclic Graph for night shift work and breast cancer incidence
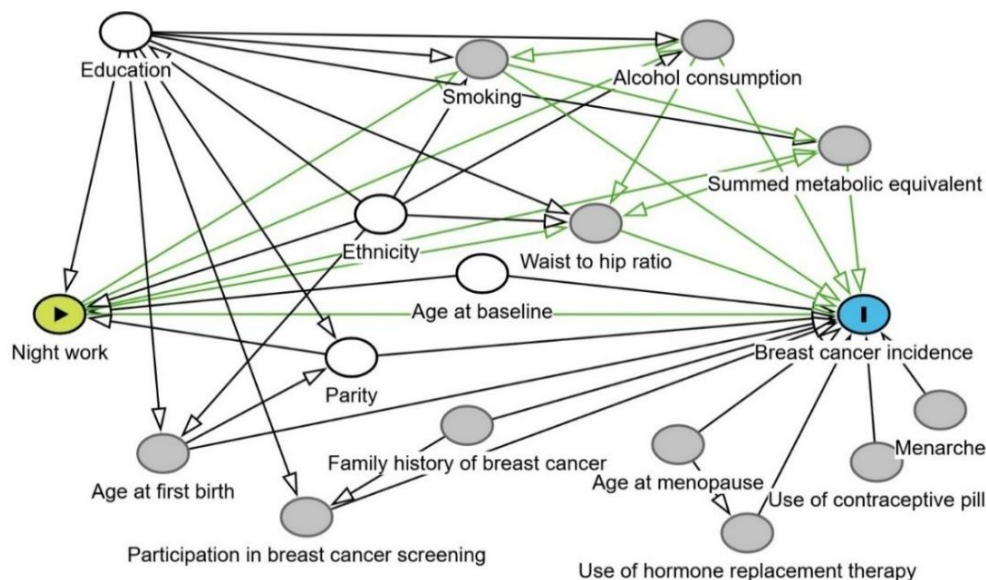
Supplemental tables

Supplemental table 1: Participant Characteristics at Baseline: Comparison by Baseline Shift Patterns (Baseline Cohort) and Night Worker Status (Lifetime Cohort)

	Baseline Cohort				Lifetime Cohort				
	Shift work at baseline (2006-2010)				Night shift worker status based on job history				
	Day workers	Night shift workers		Full cohort	Never night shift worker	Ever night shift worker		Full cohort	
	N = 11,996 (57.5%)	N = 8,864 (42.5%)	P value	N = 20,860	N = 53,698 (83.2%)	N = 10,841 (16.8%)	P value	N = 64,539	P value
Age at baseline (mean (SD))	52.3 (6.8)	51.1 (6.6)	< 0.01	51.7 (6.8)	55.9 (7.6)	54.0 (7.6)	< 0.01	55.6 (7.6)	< 0.01
Weight in kg in 2014 (mean (SD))	72.6 (15.0)	74.0 (15.6)	< 0.01	73.2 (15.3)	70.1 (13.2)	72.1 (14.6)	< 0.01	70.5 (13.5)	< 0.01
Missing	50 (1%)	40 (0.4%)		90 (0.4%)	88 (0.2%)	19 (0.2%)		107 (0.2%)	
Height in cm in 2014 (mean (SD))	162.8 (6.3)	162.8 (6.4)	0.31	162.8 (6.3)	163.4 (6.1)	163.9 (6.2)	< 0.01	163.5 (6.1)	< 0.01
Missing	40 (0.3%)	34 (0.4%)		74 (0.4%)	62 (0.1%)	9 (0.1)		71 (0.1%)	
BMI at recruitment (mean (SD))	27.4 (5.4)	27.9 (5.7)	< 0.01	27.6 (5.5)	26.3 (4.8)	26.8 (5.3)	< 0.01	26.4 (4.9)	< 0.01
Missing	50 (0.4%)	44 (0.5%)		94 (0.5%)	98 (0.2%)	20 (0.2%)		118 (0.1%)	
Waist to hip ratio at recruitment (mean (SD))	0.82 (0.07)	0.82 (0.07)	0.28	0.82 (0.07)	0.81 (0.07)	0.81 (0.07)	< 0.01	0.81 (0.07)	< 0.01
Missing	43 (0.4%)	30 (0.3%)		73 (0.3%)	65 (0.1%)	12 (0.1%)		77 (0.1%)	
MET at recruitment									
< 500	1,177 (10%)	737 (8%)	< 0.01	1,914 (9%)	6,643 (12%)	1,211 (11%)	< 0.01	7,854 (12%)	< 0.01
500-5000	6,023 (50%)	4,183 (47%)	< 0.01	10,206 (49%)	33,202 (62%)	6,584 (61%)	0.03	39,786 (62%)	< 0.01
> 5000	1,950 (16%)	1,643 (19%)	< 0.01	3,593 (17%)	4,684 (9%)	1,299 (12%)	< 0.01	5,983 (9%)	< 0.01
Unknown* or missing	2,846 (24%)	2,301 (26%)	< 0.01	5,147 (25%)	9,169 (17%)	1,747 (16%)	0.02	10,916 (17%)	< 0.01
Education									
College	3,205 (27%)	2,212 (25%)	< 0.01	5,417 (26%)	24,778 (46%)	4,950 (46%)	0.36	29,728 (46%)	< 0.01
A levels	1,474 (12%)	1,111 (13%)	0.61	2,585 (12%)	7,835 (15%)	1,550 (14%)	0.43	9,385 (14%)	< 0.01
O levels/GCSEs	2,988 (25%)	2,166 (24%)	0.44	5,154 (25%)	11,531 (21%)	2,347 (22%)	0.64	13,878 (22%)	< 0.01
CSEs or equivalent	2,946 (25%)	2,662 (30%)	< 0.01	5,608 (27%)	6,364 (12%)	1,389 (13%)	< 0.01	7,753 (12%)	< 0.01
Compulsory	1,383 (11%)	713 (8%)	< 0.01	2,096 (10%)	3,190 (6%)	605 (6%)	0.15	3,795 (6%)	< 0.01
Ethnic background									
White	11,133 (93%)	7,844 (89%)	< 0.01	18,977 (91%)	52,829 (98%)	10,527 (97%)	< 0.01	63,356 (98%)	< 0.01
Mixed	113 (1%)	121 (1%)	< 0.01	234 (1%)	247 (1%)	89 (1%)	< 0.01	336 (0.5%)	< 0.01
Asian	393 (3%)	298 (3%)	0.76	691 (3%)	389 (1%)	109 (1%)	< 0.01	498 (1%)	< 0.01
Black	357 (3%)	601 (7%)	< 0.01	958 (5%)	233 (0,4%)	116 (1%)	< 0.01	349 (0.5%)	< 0.01

Alcohol consumption at recruitment									
Never	656 (5%)	630 (7%)	< 0.01	1,286 (6%)	1,880 (4%)	363 (3%)	0.45	2243 (3%)	< 0.01
Previous	426 (4%)	320 (4%)	0.85	746 (4%)	1,392 (3%)	374 (3%)	< 0.01	1,766 (3%)	< 0.01
Current	10,907 (91%)	7,905 (89%)	< 0.01	18,812 (90%)	50,408 (93%)	10,099 (93%)	< 0.01	60,507 (94%)	< 0.01
Unknown or missing	7 (0.1%)	9 (0.1%)	1.00	16 (0.1%)	18 (0.1%)	5 (<0.1%)	0.72	23 (0.1%)	0.02
Smoking status at recruitment									
Never	6,804 (57%)	5,019 (57%)	0.90	11,823 (57%)	34,120 (64%)	6,244 (58%)	< 0.01	40,364 (62%)	< 0.01
Previous	3,615 (30%)	2,413 (27%)	< 0.01	6,028 (29%)	16,736 (31%)	3,763 (35%)	< 0.01	20,499 (32%)	< 0.01
Current	1,542 (13%)	1,407 (16%)	< 0.01	2,949 (14%)	2,764 (5%)	817 (7%)	< 0.01	3,581 (6%)	< 0.01
Unknown or missing	35 (0.3%)	25 (0.3%)	1	60 (0.3%)	78 (0.1%)	17 (0.2%)	0.88	95 (0.1%)	< 0.01
Parity									
0 child	2,424 (20%)	1,882 (21%)	0.07	4,306 (21%)	12,051 (22%)	2,570 (24%)	< 0.01	14,621 (23%)	< 0.01
1 child	1,656 (14%)	1,258 (14%)	0.43	2,914 (14%)	6,686 (13%)	1,402 (13%)	0.17	8,088 (12%)	< 0.01
2 children or more	7,916 (66%)	5,724 (65%)	0.04	13,640 (65%)	34,961 (65%)	6,869 (63%)	< 0.01	41,830 (65%)	0.13
Age at first live birth									
< 35 or = 35	7,763 (65%)	5,576 (63%)	< 0.01	13,339 (64%)	33,899 (63%)	6,629 (61%)	< 0.01	40,528 (63%)	< 0.01
> 35	136 (1%)	135 (1%)	< 0.01	271 (1%)	1,051 (2%)	237 (2%)	0.13	1,288 (2%)	< 0.01
Nullipara	2,424 (20%)	1,882 (21%)	0.07	4,306 (21%)	12,051 (22%)	2,570 (24%)	< 0.01	14,621 (23%)	< 0.01
Unknown or missing	1,673 (14%)	1,271 (14%)	0.43	2,944 (14%)	6,697 (13%)	1,405 (13%)	0.16	8,102 (12%)	< 0.01
Age at menarche									
<12 or = 12 years	4,485 (37%)	3,186 (36%)	0.03	7,671 (38%)	20,755 (39%)	4,216 (39%)	0.65	24,971 (39%)	< 0.01
>14 years	7,164 (60%)	5,433 (61%)	0.02	12,597 (60%)	31,665 (59%)	6,437 (59%)	0.41	38,102 (59%)	< 0.01
Unknown or missing	347 (3%)	245 (3%)	0.61	592 (3%)	1,278 (2%)	188 (2%)	< 0.01	1,466 (2%)	< 0.01
Menopause at recruitment									
Yes	4,267 (36%)	3,565 (40%)	< 0.01	9,401 (38%)	13,717 (26%)	2,762 (26%)	0.90	16,479 (26%)	< 0.01
No	5,645 (47%)	3,756 (42%)	< 0.01	7,832 (45%)	31,904 (59%)	6,430 (59%)	0.85	38,334 (59%)	< 0.01
Unknown or missing	2,084 (17%)	1,543 (17%)	0.96	3,627 (17%)	8,077 (15%)	1,649 (15%)	0.66	9,726 (15%)	< 0.01
Age at menopause (n (%))									
< 51 or = 51 years	3,549 (30%)	2,508 (28%)	0.04	6,057 (29%)	18,003 (33%)	3,643 (34%)	0.88	21,646 (36%)	< 0.01
> 51	1,867 (16%)	1,106 (12%)	< 0.01	2,973 (14%)	12,327 (23%)	2,496 (23%)	0.89	14,823 (26%)	< 0.01
Premenopausal or unknown	5,645 (47%)	3,756 (42%)	< 0.01	7,832 (45%)	13,717 (26%)	2,762 (25%)	0.89	16,479 (26%)	< 0.01
Unknown or missing	935 (8%)	1,494 (17%)	< 0.01	3,998 (12%)	9,651 (18%)	1,940 (18%)	0.85	11,591 (18%)	< 0.01
Use of contraception pill at recruitment									
Ever	1,675 (14%)	1,249 (14%)	0.81	2,904 (14%)	7,852 (15%)	1,356 (13%)	< 0.01	9,208 (14%)	0.21
Never	10,293 (86%)	7,592 (86%)	0.77	17,885 (86%)	45,781 (85%)	9,473 (87%)	< 0.01	55,254 (86%)	0.66
Unknown or missing	28 (0.2%)	23 (0.3%)	0.81	51 (0.2%)	65 (0.1%)	12 (0.1%)	0.90	77 (0.1%)	< 0.01
Use of HRT at recruitment									
Ever	8,391 (70%)	6,434 (73%)	< 0.01	14,825 (71%)	34,608 (64%)	7,055 (65%)	0.23	41,663 (65%)	< 0.01
Never	3,550 (29%)	2,392 (27%)	< 0.01	5,942 (29%)	19,001 (35%)	3,769 (35%)	0.22	22,770 (35%)	< 0.01
Unknown or missing	55 (1%)	38 (0.4%)	0.83	93 (0.4%)	89 (0.2%)	17 (0.2%)	0.94	106 (0.2%)	< 0.01
Family history of breast cancer (mother, siblings) at recruitment									
Breast cancer in family history	1254 (10%)	856 (10%)	0.06	2,110 (11%)	6,067 (11%)	1,272 (12%)	0.20	7,339 (11%)	< 0.01
Other cancer than breast cancer in family history	10,557 (88%)	7,846 (88%)	0.27	18,403 (88%)	46,948 (87%)	9,441 (87%)	0.33	56,389 (87%)	< 0.01
Missing or no cancer reported in family history	185 (2%)	162 (2%)	0.12	347 (0.2%)	683 (1%)	128 (1%)	0.47	811 (1%)	< 0.01
History of benign breast lesion at recruitment									
Yes	874 (7%)	589 (7%)	0.08	1,463 (7%)	5,255 (10%)	1,185 (11%)	< 0.01	58,099 (90%)	< 0.01
Not reported	11,122 (93%)	8,275 (93%)	0.08	19,397 (93%)	48,443 (90%)	9,656 (89%)	< 0.01	6,440 (10%)	< 0.01
Participation in mammography screening at recruitment)									
Yes, in the last 6 years	7,567 (63%)	5,088 (57%)	< 0.01	12,655 (61%)	41,065 (76%)	7,487 (69%)	< 0.01	1275 (2%)	< 0.01
Yes, but not since >6 years	338 (3%)	258 (3%)	0.72	596 (3%)	981 (2%)	294 (3%)	< 0.01	48,552 (75%)	< 0.01
No or not regularly	4,091 (34%)	3,518 (40%)	< 0.01	7,609 (36%)	11,652 (22%)	3,060 (28%)	< 0.01	14,712 (23%)	< 0.01

Data are n (%) unless indicated.

BMI Body Mass Index, *MET* Metabolic Equivalent Task, *HRT* hormone replacement therapy

"Unknown" means that the answer given by the participant was either "Do not know", "Do not remember" or "Prefer not to answer"

Acknowledgements