Original article

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Short-term effects of night shift work on breast cancer risk: a cohort study of payroll data

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Objectives The objective was to examine if night shift work is a short-term risk factor for breast cancer, including combined estrogen receptor (ER) and human epidermal growth factor 2 (HER2) breast cancer subtypes.

Methods The cohort comprised 155 540 public sector female workers in Denmark who were followed from 2007–2012. Day-to-day work-hour information was available from payroll registers and 1245 incident cases of breast cancer were identified in national cancer registries together with receptor subtype information.

Results A rate ratio (RR) of 0.90 [95% confidence interval (95% CI) 0.80–1.01] was observed for workers ever working night shifts during the follow-up period compared with workers only working day shifts after adjustment for age, age at first child, parity, family history of breast or ovarian cancer, sex hormones, medications related to alcoholism, family educational level, mammography screening, and other potential confounders. Comparable results were seen for the inception population of employees with first recorded employment after 2007. Modestly increased RR were suggested for breast cancer subtypes characterized by a positive HER2 status irrespective of ER status.

Conclusions These findings do not support an overall short-term effect of night shift work on breast cancer risk. Future studies should explore further the impact of HER2 status.

Key terms circadian disruption; epidemiology; shift worker; working time.

In 2007, a working group convened by the International Agency for Research on Cancer (IARC) classified night shift work that involves circadian disruption as probably carcinogenic to humans based on sufficient evidence in animals, and limited evidence in humans (1). Since then several epidemiologic studies and systematic reviews have been published, but despite these efforts the epidemiological evidence is still limited (2–5).

Reduction of nocturnal pineal melatonin production is suggested as a pivotal element of the mechanisms linking night shift work and breast cancer (6–13). From animal studies it is known that melatonin reduces the growth of chemically induced mammary tumors (10, 14). It has also been shown that melatonin at physiological levels suppresses the proliferation of human breast cancer xenografts (15–17). Furthermore, melatonin may reduce the invasiveness of human breast cancer, and the suppression of melatonin during the biological night may act as a promoter of oncogenesis (10, 16). This experimental evidence suggests that suppression of melatonin from night shift work may exert its response downstream the complex casual pathways that lead to breast cancer. Hence, recent night shift work may be associated with short-term risk of breast cancer in humans.

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Of the several epidemiologic studies conducted, only three studies have examined possible short-term risk of recent night shift work (18–20). Davis et al observed an increased risk of breast cancer among women who ever worked the graveyard shift during the last ten years (19). However, Pesch et al (18) did not corroborate this finding. The well-established effects of prolonged exposure of breast tissue to estrogen vary according to breast cancer receptor subtypes and are most consistent for the hormone dependent tumors (21–23). This suggests distinct etiologic pathways for breast cancer subtypes and new risk factors may be overseen if this is not accounted for (24). Night shift work has been associated with estrogen receptor positive (ER+) (25–29), ER- (26, 30), progesterone receptor positive (PR+) (26–29), human epidermal growth factor 2 positive (HER2+) (29, 31) and HER2- breast cancer subtypes (29). The strongest association was reported for HER2+ in combination with ER+ or PR+ receptor status (29).

Previous studies of the association between night shift work and breast cancer have relied on crude and self-reported information on working time, and findings may have been influenced by non-differential as well as differential misclassification of exposure that perhaps only can be circumvented by continuously and objectively recorded information of working hours (2).

The present study combines day-to-day information on exact working time obtained from a large and recently established payroll register with cancer incidence and tumor receptor subtype information. The objective was to examine if night shift work is a short-term risk factor for overall breast cancer and combined ER and HER2 receptor breast cancer subtypes.

Methods

Data sources

This study linked information from seven Danish registries on the individual level by use of the civil registration number given to all residents in Denmark since 1968: (i) *The Danish Working Hour Database* is a newly established database encompassing all employees of each of the five administrative regions, which operate in healthcare and other public sectors. The database covers individual payroll information on day, hour, and minute of the beginning and end of every work shift and information on occupation. Data have been available since 1 January 2007 for four of the regions and from 2008 for all regions; (ii) *The Civil Registration System* encompasses all residents in Denmark with information on sex, vital status, date of birth and links to first degree relatives since 1968 (32); (iii) *The clinical database of the Danish Breast Cancer Corporative Group* includes pathological and clinical information on all new diagnosed breast cancers diagnosed since 1977 as well as information on ER and HER2 status (33); (iv) *The Danish Cancer Registry keeps* records on all cancers diagnosed classified according to ICD-7 and ICD-10 codes (the International Classification of Diseases), and date of diagnosis since 1943 (34); (v) *The National Register of Medicinal Product Statistics* encompasses all purchases of prescription drugs at private pharmacies with information on the medication by ATC codes (the Anatomical Therapeutic Chemical Classification System), date of purchase, and purchaser (35). Data have been available since 1995; (vi) *The Family Income Register from Statistics Denmark* encompasses all individuals born or living in Denmark with information on the highest educational level in a family living at the same address (36). We included information as of 1 January 2007; (vii) *The Clinical Database of Mammography Screening* records women aged 50–69 years and invited to participate in the national mammography screening programme (37). The database includes information on dates of invitation and examination since the start of the program by the end of 2007.

Data were retrieved up to and including 31 December 2012 for all registers, though Danish Cancer Registry data were only available up to 31 December 2011.

The Danish Data Protection Agency approved the study (j.no. 2011-41-6850). In Denmark, register studies do not need the approval of the Danish Health Research Ethics Committee System.

Study population

The study population was women aged ≥18 years with ≥1 registration of work in the Danish Working Hour Database between 1 January 2007 and 31 December 2011 (N=156 927). We excluded 1357 women diagnosed with breast cancer prior to follow-up, one woman with missing date of breast cancer diagnosis, and 29 women who had <3 consecutive hours of work. The final study population included 155 540 women free of breast cancer at start of follow-up.

We had no information on the study participants' working hours prior to 2007. Therefore, to reduce possible bias and confounding from night shift work prior to 2007 we established a sub-population of subjects first employed by 1 January 2008 or later (the inception population). This included subjects with no recorded employment in any of the regions during 2007 (washout period) and was possible for employees in four of the five regions. In total 55 381 (35.6%) fulfilled the criterion.

Breast cancer

Breast cancer cases and date of diagnosis together with information on ER and HER2 status were identified in the clinical database of the Danish Breast Cancer Corporative Group for all available years and supplemented with breast cancer cases from the Danish Cancer Registry [ICD-10 code C50 (1978–2012) or ICD-7 code 170 (<1978)]. Cases were classified into four subtypes on the basis of their ER and HER2 status: (i) ER-/HER2-, (ii) ER+/HER2-, (iii) ER-/HER2+, and (iv) ER+/HER2+ tumors. Progesterone receptor status is strongly associated with ER status and has not been routinely analyzed in Denmark since 2007. Information on PR status was only available for a small subset of cases and was not included for the analyses.

ER status was defined using a cut-off at 10% positive estrogen cells. HER2 status was established using immunohistological markers from 0–3+, where 2+ is regarded as "equivocal", and 3+ as positive. In cases which were equivocal (2+), the immunohistological test was supplied with fluorescence or chromogenic in situ hybridization (FISH and CISH test, respectively), and the tumor was classified as positive (HER2+) if oncogenic amplification was found (38).

Definition of shifts

A night shift was defined according to a 2009 IARC working group as ≥3 hours of work between midnight and 05:00 hours (39). We defined a day shift as ≥3 hours of work between 06:00–20:00 hours and all other shifts of ≥3 hours as a non-day, non-night shift. In the analyses, we considered six different exposure time windows: Since entry, and the past 1, 1–2, 1–3, 1–4, and 1–5 years.

At a given day in the follow-up and with a chosen exposure time windows, a woman was classified as working: (i) only day shifts if she only had day shifts throughout the time window; (ii) ever non-day/non-night shift, if she had ≥1 non-day shift but no night shift in the time window; and (iii) ever night shift if she had ≥1 night shift in the time window.

The cumulated number of night shifts since entry was divided into four categories defined by the person-year quartiles. The mean numbers of night shifts during the past 1, 1–2, 1–3, 1–4, and 1–5 years time windows were calculated and categorized into four groups: 0.1–0.9, 1.0–3.9, 4.0–9.9, and ≥10.0 night shifts per month.

Covariates

From the registries, information was retrieved on age, age at birth of first child, number of children, a family history of either breast cancer before the age of 50 or ovarian cancer at any age among female first degree relatives (mothers and sisters), use of oral contraception, hormone replacement therapy, other hormone medications in the G03 ATC group, use of medications related to alcohol over-consumption and addiction (ATC groups N03AA, N05AB and N07BB), highest educational level in the family, and attending mammography screening. These potential confounders were based on register availability, a review of the literature, and decided upon a priori (40, 41). Data were virtually complete within the time frame of available data for all variables except for female first degree relatives (5% missing). Missing values were evenly distributed across work hour categories.

Statistical analysis

Each woman was followed on a daily basis from start of follow-up, which was the first registration of work (earliest on 1 January 2007) until the date of first primary breast cancer diagnosis, death, disappearance, emigration, or end of follow-up at 31 December 2012. In the analyses of mean number of night shifts during the past exposure time windows, follow-up started subsequent to the end of a time window and the earliest one year after the first registration of work for the one-year time window.

Data were analyzed as incidence rate, ie, as the number of incident breast cancer cases per time units at risk. We computed rate ratios (RR) of overall breast cancer with Poisson regression and breast cancer subtypes by stacked Poisson regression by the different night shift metrics. The only day shift category was the reference. A separate RR estimate was provided for the ever non-day, non-night category (presented in the supplementary material www.sjweh.fi/index.php?page=data-repository). The stacked Poisson regression analysis was based on a table combining person years at risk and number of events for ER-/HER2-, ER+/HER2-, ER-/HER2+, ER+/HER2+, and unclassified tumors (no receptor status available). This allowed us to test whether the association between night shift work and the incidence of breast cancer differed between subtypes. Both crude and adjusted estimates were reported.

Age, age at birth of first child, number of children, a family history of breast cancer or ovarian cancer, and hormone replacement therapy may have distinct effects on breast cancer subtypes (42–44). Therefore, we divided the potential confounders into two sets of covariates: (A) age (<40, 40–44, 45–49, and every second year from age 50), age at birth of the first child (<20, 20–29, ≥30, no children), number of births (0, 1, 2, 3, ≥4), family history of breast cancer or ovarian cancer (0, ≥1, no information), hormone replacement therapy (no, yes); and (B) calendar year (each year 2007–2012), oral contraceptives (no, yes), other sex hormones (no, yes), medication related to alcoholism, (no, yes), mammography screening attendance (invited but not screened, invited and screened, not

invited), and highest family educational level at the first registration of work (unspecified, primary and secondary school, advanced level education, vocational education, undergraduate and bachelor degree, higher education, and no information on education). Analyses of overall breast cancer included all sets of A and B covariates. In the adjusted stacked Poisson regression models, the effects of the covariates in set A were allowed to differ between breast cancer subtypes while the covariates in set B were assumed to have the same effect on the rate independently of the subtype.

All variables were time dependent, ie, varied for each date from start until the end of follow-up. Estimates were reported with a 95% confidence interval. Two different trend analyses were conducted across the grouped cumulated and average number of night shifts; the one was restricted to ever night shifts, the other included only day shift as a null exposed category. All data management and analyses were done with Stata 14.1 (Stata Corp, College Station, TX, USA).

Results

The 155 540 women contributed a total of 771 062 person years and 1245 breast cancer cases during follow-up. ER status was available for 1177 (95%) cases, HER2 status for 1123 (90%) cases, and both ER and HER2 status for 1118 (90%) cases. In total 136 ER-/HER2-, 797 ER+/HER2-, 77 ER-/HER2+, 108 ER+/HER2+, and 127 not classifiable (because of missing receptor status) breast cancer cases were included. The inception population included 55 381 women and contributed a total of 199 617 person years and 230 breast cancer cases, 14 ER-/HER2-, 151 ER+/HER2-, 28 ER-/HER2+, 18 ER+/HER2+, and 19 not classifiable receptor subtypes.

Table 1 presents the distribution of age and age-standardized participant characteristics of person years by exposure status (only day shifts and ever night shifts) since study entry for the total population. Supplementary table A (www.sjweh.fi/index.php?page=data-repository) provides this information also for the ever non-day, non-night shift category and for quartiles of night shifts. Women who worked night shifts had a higher family educational level and were overall younger than women working only day shifts. Except from this, age-standardized person years were evenly distributed by participant characteristics and work hours. Healthcare professionals constituted 40%, personal care workers 23%, technicians 15%, elementary occupations 10%, and clerical support workers 5% of the employees.

In the inception population, more non-night shift workers did not have children, and this group was also less educated than the night shift workers (data not shown). The mean age of the inception population was 35.5 years compared to 39.4 years in the total population.

Table 2 presents rate ratios for all breast cancer and the four breast cancer subtypes defined by the cross classification of ER and HER2 status by night shifts since entry in the total study population. Overall decreased RR for all breast cancer was observed

Table 1. Age and age-standardized participant characteristics of person years (%) among female employees of the Danish public sector working only day or ever night shifts 2007–2012. [a]

Participant characteristics	Only day shifts (412 920 person years)	Ever night shifts (318 210 person years)
Age (years)		
<40	40	49
40–49	25	25
50–59	23	20
≥60	12	6
Calendar year of follow-up		
2007	13	9
2008	16	14
2009	17	17
2010	18	19
2011	18	20
2012	18	21
Age at first child's birth		
<20 years	5	4
20–29 years	53	57
≥30 years	16	16
No children	26	23
Number of children		
0	26	23
1	17	17
2	40	39
3	14	18
≥4	3	4
Family history of breast or ovarian cancer		
No	90	91
Yes	2	3
No information	8	7
Oral contraception		
No	39	38
Yes	61	62
Hormone replacement therapy		
No	75	75
Yes	25	25
Other sex hormones		
No	88	87
Yes	12	13
Medications for alcoholism		
No	98	99
Yes	2	1
Mammography screening		
No	4	4
Yes	16	18
Not invited	80	78
Highest family education		
Unspecified	1	1
Primary and secondary school	8	2
Advanced level education	36	25
Vocational education	6	2
Undergraduate and bachelor degree	31	54
Higher education	18	16
Missing	0	0

[a] A total of 39 932 person years of employees ever working non-day, non-night shifts were not included.

(adjusted RR 0.90, 95% CI 0.80–1.01). The ER+/HER2- subtype showed a RR of 0.80 (95% CI 0.68–0.95) and a decreasing trend by increasing number of night shifts when day worker were included as a null-exposed category in the trend test (P=0.05), but not when tested within the night shift workers only. A decreased RR was also seen for ER-/HER2- but not of statistical significance.

Non-significantly increased RR were observed for the ER-/HER2+ and ER+/HER2+ subtypes (RR 1.49, 95% CI 0.93–2.39 and RR 1.26, 95% CI 0.84–1.89, respectively). For the former subtype, an increasing trend by increasing number of night shifts was seen (P<0.05), but not when tested within the night shift workers only.

We observed a decreased association between ever working night shift during the past one year time window and all breast cancer (RR 0.80, 95% CI 0.69–0.93) and a decreasing trend (P=0.01) by the mean number of night shifts when day workers were included in the test (table 3). Such trends were also seen for the other time windows, except for the past 1–5 years window, but not when tested among the night shift workers only.

Table 4 presents associations between all breast cancer and night shifts since entry and during the past 1 to 1–4 years time windows in the inception population. In the crude analyses, we observed a decreased RR for all breast cancer following night shift work the past 1 year (RR 0.69, 95% CI 0.48–0.98). This association was attenuated in the adjusted analyses and none of the adjusted RR estimates differed statistically from unity.

We observed age, age at birth of first child, family history of breast cancer or ovarian cancer, mammography screening attendance, family educational level to be associated with increased breast cancer risk, all as expected. Supplementary tables A–D (www.sjweh.fi/index.php?page=data-repository) correspond with tables 1–4 but include comprehensive and more detailed data. No increased risk of breast cancer was seen for the ever non-day, non-night shifts category in neither the total nor the inception population.

Table 2. Rate ratios (RR) and 95% confidence intervals (95% CI) of all breast cancer and combined estrogen receptor (ER) and human epidermal growth factor 2 (HER2) breast cancer subtypes by night shifts since start of follow-up. Results from female employees of the Danish public sector 2007–2012.

Breast cancer	Only day shifts (reference) [a]	Ever night shifts [a]					Test for trend P-value I [b]	Test for trend P-value II [c]
	Cases	Cases	Crude RR	95% CI	Adjusted RR [d]	95% CI		
All breast cancer	751	425	0.73	0.65–0.83	0.90	0.80–1.01	0.56	0.10
ER-/HER2-	80	49	0.79	0.56–1.13	0.85	0.59–1.23	0.66	0.46
ER+/HER2-	503	250	0.64	0.55–0.75	0.80	0.68–0.95	0.33	0.05
ER-/HER2+	37	37	1.30	0.82–2.05	1.49	0.93–2.39	0.67	<0.05
ER+/HER2+	55	48	1.13	0.77–1.67	1.26	0.84–1.89	0.18	0.51

[a] The distribution of person years by exposure is shown in supplementary table B (www.sjweh.fi/index.php?page=data-repository).
[b] Test for trend by number of night shifts among night shift workers, adjusted P-value. See supplementary table B for definition of night shift categories.
[c] Test for trend by number of night shifts among night and day shift workers.
[d] Poisson regression model adjusted for calendar year, age, age at birth of first child, number of births, family history of breast cancer or ovarian cancer, oral contraception, hormone replacement therapy, other sex hormones, medication related to alcoholism, mammography screening attendance, and highest family educational level. For details, refer to the text.

Table 3. Rate ratios (RR) and 95% confidence intervals (95% CI) of all breast cancer by night shifts during the past 1 to 1–5 years time windows. Results from female employees of the Danish public sector 2008–2012.

Time window	Only day shifts (reference)		Ever night shifts						Test for trend P-value I [a]	Test for trend P-value II [b]
	Person years	Cases	Person years	Cases	Crude RR	95% CI	Adjusted RR [c]	95% CI		
Past 1 year	399 092	748	181 375	220	0.64	0.55–0.74	0.80	0.89–0.93	0.39	0.01
Past 1–2 years	465 255	822	160 800	218	0.84	0.54–1.30	0.89	0.72–1.10	0.64	0.04
Past 1–3 years	192 055	397	123 451	170	0.67	0.56–0.80	0.83	0.69–1.00	0.87	0.04
Past 1–4 years	110 486	240	80 153	110–114 [d]	0.64	0.51–0.80	0.80	0.64–1.01	0.87	0.05
Past 1–5 years	43 611	113	35 783	69	0.75	0.56–1.01	0.97	0.71–1.32	0.62	0.70

[a] Test for trend by mean number of night shifts during the specified time interval among night shift workers, adjusted p value. See supplementary table C (www.sjweh.fi/index.php?page=data-repository) for definition of night shift categories.
[b] Test for trend by mean number of night shifts during the specified time interval among night shift and day shift workers, adjusted P-value.
[c] Poisson regression model adjusted for calendar year, age, age at birth of first child, number of births, family history of breast cancer or ovarian cancer, oral contraception, hormone replacement therapy, other sex hormones, medication related to alcoholism, mammography screening attendance, and highest family educational level. For details, refer to the text.
[d] According to the data confidentiality policy of Statistics Denmark no less than 4 cases per cell must be reported. Providing the exact total here would allow the calculation of cases in cells with less than 4 cases in supplementary table C (www.sjweh.fi/index.php?page=data-repository).

Table 4. Rate ratios (RR) and 95% confidence intervals (95% CI) of all breast cancer by night shift work since entry and during the past 1 to 1–4 years time windows. Results from female employees from the inception population with first recorded employment in the Danish public sector 2008–2012.

Time window	Only day shifts (reference)		Ever night shifts					
	Person years	Cases	Person years	Cases	Crude RR	95% CI	Adjusted RR [a]	95% CI
Since entry	116 823	144	71 113	69	0.77	0.58–1.03	0.88	0.66–1.17
Past 1 year	98 747	128	40 208	37	0.69	0.48–0.98	0.82	0.56–1.18
Past 1–2 years	60 066	78	31 217	36	0.89	0.60–1.33	1.14	0.76–1.71
Past 1–3 years	30 965	43	18 828	29	1.13	0.71–1.81	1.33	0.82–2.17
Past 1–4 years	10 547	15	7390	10	0.96	0.43–2.14	1.01	0.44–2.32

[a] Poisson regression model adjusted for calendar year, age, age at birth of first child, number of births, family history of breast cancer or ovarian cancer, oral contraception, hormone replacement therapy, other sex hormones, medication related to alcoholism, mammography screening attendance, and highest family educational level. For details, refer to the text.

Discussion

In this large population of women with a high prevalence of night shift work, we observed no elevated risk of all breast cancer following recent night shift work. Modestly increased risks were suggested for HER2+ but not for HER2- breast cancer subtypes irrespective of ER status, but these findings were based on relatively few observations.

We could not corroborate a short-term effect of night shift work on the risk of breast cancer as suggested by experimental data (10, 16). This finding is consistent with that of Fritschi et al (20) and Pesch et al (18) who observed no elevated risk among women working night shifts within the recent ten years [odds ratios (OR) 1.02, 95% CI 0.73–1.43 and 1.04, 95% CI 0.31–3.53, respectively]. However, our findings are not consistent with the findings of Davis et al who observed a slightly elevated risk during the recent ten years of night shift work (OR 1.6, 95% CI 1.0–2.5) (19). As opposed to our study, these studies relied on self-reported information on night shift work and had limited statistical power.

The association between night shift work and HER2+ breast cancer has been examined in three previous studies. Wang et al (28), Papantoniou et al (31), and Cordina-Duverger et al (29) all suggested increased associations between HER2+ tumors and night shift work (OR 1.35, 95% CI 0.94–1.94; OR 1.31, 95% CI 0.93–1.85; and OR 1.91, 95% CI 1.09–3.33, respectively). Cordina-Duverger et al cross classified HER2 and hormone receptor status as we did and observed an OR of 2.52 (95% CI 1.36–4.68) for HER2+ in combination with ER+ or PR+ but no association for HER2+ in combination with ER- or PR- receptor status (OR 0.75, 95% CI 0.16–3.38) and were thus only partly in agreement with our findings (29). ER+/HER2- tumors constituted 88% of the ER+ tumors in this material and the decreased risk we observed for this subtype is not supportive of earlier studies showing associations between night shift work and ER+ tumors (without information on HER2 receptor status) (25–28). Experimental studies implicate melatonin suppression in HER2+ carcinogenesis (45, 46).

The increasing and decreasing trends observed by cumulative and average number of night shifts were only seen when day workers were included as a null-exposed category in the trend tests and not when tested among night shift workers only. This points more towards a night shift worker effect than an effect of night shift work per se.

Strengths and limitations

A major strength of this study was the objective and detailed day-to-day information on working hours from a payroll register that is presumed to be complete for the years 2007–2012. Since the salary varies by working hours during the day and week, these recordings are expected to be precise and valid given that employers and employees have a common interest in correct recordings. We did not have access to information that made validation of the payroll data possible but a recent evaluation of comparable Finnish payroll data showed that the retrieved register data matched originally published shift plans (47).

The detailed work hour data allowed us to define a reference category of only day shifts that included no early morning or late evening shifts that could have affected circadian regulation and thus diluted a possible effect of night shifts. We observed no association between ever non-day, non-night shifts, and breast cancer.

Cases of breast cancer were identified in national registers encompassing all breast cancers diagnosed in Denmark since 1943 and information on HER2 and ER receptor status was recorded for a high proportion of cases (33, 34). Thus, because we relied only on registers with high coverage and completeness and no self-reports, information bias is unlikely.

Based on the extensive register data, we were able to account for major reproductive factors, hormonal treatment, and family history of breast cancer, which are all well-established risk factors for breast cancer.

During recent years, the possible risk of breast cancer following night shift work has attracted public interest in Denmark (48). For that reason, night shift workers may have been more willing to participate in breast cancer screening programs and thus more likely to be diagnosed with breast cancer than day workers. We had access to national mammography screening data and could therefore also adjust for this possible confounder.

We used prescription of medications related to alcoholism as a surrogate measure for alcohol consumption (involving about 1–2% of the population). This will to some extent account for severe alcohol consumption.

Income was not expected to vary substantially in this rather homogenous study population, and therefore we adjusted for the highest education in the family as a surrogate measure for socioeconomic status.

There were also limitations. Several epidemiological studies have observed an increased risk of breast cancer following long-term night shift work that we were not able to assess due to lack of work schedule data prior to 2007 (18, 25, 27, 49–52). An unknown part of the cohort subjects employed during 2007–2012 were hired prior to 2007 where we have no information on working time. They may represent a subset less susceptible to the effects of night shift work. Such left truncation bias is expected to provide underestimates of risk and could explain our decreased risks in several of the analyses (53). We therefore defined an inception population with no recorded employment during a one-year washout period in 2007 that included one third of the total population. Results from this population should not be affected to the same extent by left truncation bias by previous night shift work. However, the results were in line with those from the total study population, but based on small numbers. It should, however, be stressed that the mean age of the inception population was 35.5 years which implies that many have had employment prior to 2007, with and without night shift work.

Long-term night shift work beginning prior to 2007 could have confounded our findings for recent night shift work, if causally related with breast cancer. But this should only be the case if recent night shift work is inversely associated with long-term night shift work. In our opinion, this is perhaps an unlikely explanation.

We were not able to account for chronotype or diurnal preference, alcohol habits in the lower and average end, age at menarche and menopause, obesity, and physical activity, all well-documented risk factors for breast cancer and potential confounders. Previous studies on night shift work and breast cancer have only reported minor confounding effects from these exposures, if any (54).

Although the study population is large, the amount of exposed person time was small in several of the subanalyses and the statistical power thus limited.

Concluding remarks

We observed no increased risk of all breast cancer following recent night shift work. A modestly increased risk was suggested for breast cancer subtypes characterized by positive HER2 status. These findings do not support an overall short-term effect of night shift work. Future studies should explore further the impact of HER2 status.

From a policy perspective, these results are reassuring for the many women working night shifts, but only in the short run. It is still unclear if night shift work effects long-term breast cancer risk or the risk of breast cancer subtypes.

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