

Breast cancer and night work among Norwegian nurses

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Abstract

Objective Previous studies have suggested an association between breast cancer and night work. We evaluated the relationship among Norwegian nurses.

Methods A case–control study, nested within a cohort of 44,835 nurses educated between 1914 and 1980 was performed, based on a registry of all Norwegian nurses. Four controls were individually matched by year of birth to each of 537 breast cancer cases that occurred during the period 1960–1982. The reconstruction of work history and number of years with night work for each nurse was based on information from the nurse registry, and data from three censuses. We used conditional logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for total duration of work as a nurse and parity. All statistical tests were two-sided.

Results The adjusted OR of breast cancer among nurses who worked nights for 30 or more years was 2.21 (CI 1.10–4.45) compared with those who did not work nights after graduation from nursing school ($p_{\text{trend}} = 0.01$).

Conclusion Our results are in accordance with previous studies that find an association between night work and breast cancer risk among women.

Keywords Nurses · Occupation · Night work · Breast cancer · Melatonin

Introduction

Breast cancer is the most common cancer in women in Western societies, with incidence-rates increasing during the last decades [1]. Despite substantial research into its etiology, only about 20–40% of breast cancer incidence can be attributed to known risk factors, such as family history of breast cancer, early menarche, late age at first birth, low parity etc. [2, 3]. During the last decades a growing number of women in Western societies have entered the workforce, but so far few studies have evaluated the possible breast cancer risk associated with occupational exposures among women. Recently, the possible effect of night work has, however, been investigated. Exposure to light at night has been hypothesized to influence breast cancer risk among persons with night work, as a result of a decrease in the secretion of the hormone melatonin, and a subsequent increase in circulating estrogens [4]. Cohort studies from the Nordic countries have reported an elevated risk of breast cancer among such shift workers as flight attendants and radio and telegraph operators [5–7]. Three recent studies, two of case–control design and one prospective cohort study, have focused on a possible association between work at night and breast cancer risk [8–10]. The results of these studies were consistent, and showed a moderately increased risk of breast cancer in women who had worked nights. The participants in the prospective cohort study [10] were registered nurses, an occupational group in which night work is quite common. Descriptive studies among nurses in different countries, including Norway, have indicated that nurses have a higher risk of breast cancer, when compared with the general female population [11–14]. However, it is still unclear whether the increase was caused by occupational exposures or other factors. We examined the association between duration of night work and breast

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cancer risk in a nested case–control study among female Norwegian nurses, including all 537 first occurrence breast cancer cases diagnosed between 1960 and 1982.

Materials and methods

Cohort information

A cohort of 44,835 women who graduated from a three-year nursing school between 1914 and 1980, and were alive 01.01.1953 or born later, was established, based on information from the Norwegian Board of Health's registry of nurses. This registry was established in 1949, and included all nurses who graduated from a Norwegian nursing school and were alive in 1949, or born later. It also included nurses with graduation from other countries, who had obtained a Norwegian authorization. Cancer cases were identified by linkage to The Cancer Registry of Norway, which has virtually complete records of individual cases of cancer in the Norwegian population since 1 January 1953. The coding of cancers is based on a modified version of the 7th revision of the International Classification of Diseases (ICD-7).

Nested case–control study

A nested case–control study was carried out within the cohort. Since data on fertility was available only from 1960, it was decided to include cancer cases diagnosed from this year. Inclusion of new breast cancer cases ended in 1982, after which year data on individual work histories were no longer complete. A total of 537 first occurrence breast cancer cases were identified by linkage to the Cancer Registry. The linkage was based on the personal identification number introduced to all citizens alive in 1960, or born later. All dates of death and emigration were obtained from Statistics Norway by the same linkage procedure.

For each case four controls, alive and without breast cancer at the time of diagnosis of the case, were randomly drawn from the nurse registry according to the incidence density sampling method. The controls were matched by year of birth of the case (± 1 year) and were required to have graduated (or started in the first job) the year the case was diagnosed at the latest.

The Norwegian Nurses' Association approved the study. Permission was obtained from the Norwegian Data Inspectorate to do the computer linkage.

Exposure

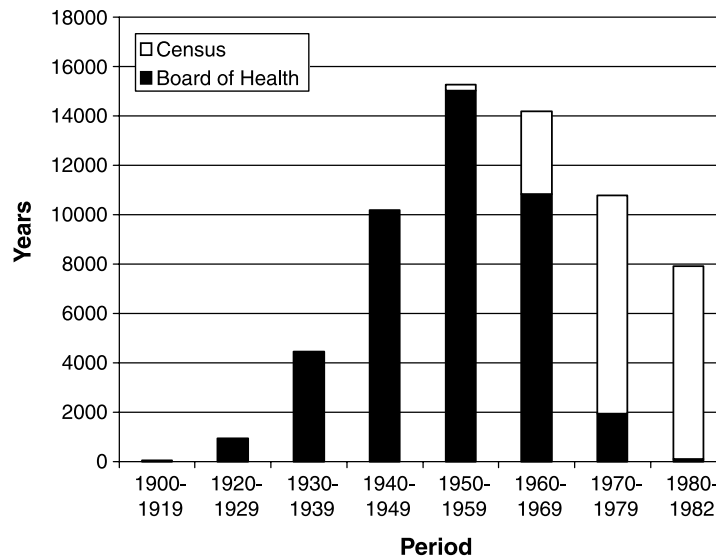
From the time a three-year nursing education was established in Norway (around 1900) and several decades

onwards, almost all nurses who were employed at infirmaries worked rotating night shifts. The burden of night work has varied between hospitals and departments during the years, as has the use of permanent night workers, which became more common from the middle of last century. Nurses with rotating night shifts have usually worked at least three nights per month.

The reconstruction of total work history as a nurse and number of years with night work was based on individual information from two sources, the Norwegian Board of Health's registry of nurses, from which the cohort was formed, and census data from 1960, 1970, and 1980. Number of working years was accumulated from first year of employment until termination of the last employment, date of diagnosis of the case, or the 67th birthday, whichever came first. Work history from the nurse registry was self-reported, and for each employment as a nurse included beginning and end dates, work place, and to some extent, department/ward. Until 1960 the registry was updated yearly. The last regular update was performed in 1968, and thereafter only sporadically. Data about occupation and industry at the time of the censuses in 1960, 1970, and 1980 was obtained by individual record linkage to the censuses at Statistics Norway. In the present study the median duration of employment in one job was four years. A period of maximum four years was therefore imputed to total work time around 1960, 1970, or 1980, if no other work history was available for these years, and the census' work code was 'nursing' or 'nursing and other care work' or the industry code was 'health work'.

In order to calculate number of years of night work out of total work time as a nurse, some assumptions had to be made. We assumed that work sites other than infirmaries only involved daytime work. All work at infirmaries however, was assumed to include night work, except for managerial jobs, teaching, and work at physiotherapy- or out-patients' departments. The five-digit industry codes of the 1980 census that were equivalent with nursing, covered work sites within and outside institutions, and were used to evaluate whether a job included night work or not. (Industry was classified according to The Standard Industrial Classification, based on the International Standard Classification of all Economic Activities.) Four years of night work was imputed for jobs assumed to include night work. Industry codes in the 1960 and 1970 censuses were less informative, and imputation of night work around these years was only performed if the nurse registry held information about night work within one and a half years from the years of the censuses. Since work history was updated yearly in the nurse registry until 1960, the need for imputation from the 1960 census was limited (Figure 1). Imputation around the 1970 census was mainly based on work history from the last update of the nurse register in 1968, one and a half years before the

Fig. 1 Number of years with night shifts in different periods, from two sources. (a) Work history from the Norwegian Board of Health's Registry of nurses, and (b) Imputed work history, based on the 1960, 1970 and 1980 censuses (Statistics Norway)



census. If a four-year imputation period overlapped in time with registered work history, or exceeded age of retirement (67 years), number of imputed years was reduced correspondingly. Night work during the three years of nursing school was disregarded, since this was assumed to be the same for all nurses.

Possible confounding factors

Fertility factors may be associated with occupational history, and were thus considered as possible confounders. Information on age at birth of first child and number of children was obtained from Statistics Norway, for all cases and controls. To control for other possible occupational hazards than night work adjustments were made for total employment time, as no specific data on individual exposures were available.

Statistical methods

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using conditional logistic regression analyses. The duration of night work after graduation from nursing school was categorized into four groups: no night work, 1–14 years, 15–29 years or 30 or more years. The categories were chosen to facilitate comparison with previous studies. Total employment time as a nurse was categorized in 0–2, 3–14, 15–29, ≥ 30 years. The variables total employment time as a nurse and number of children (0, 1–2, ≥ 3 children) were both associated with increased risk of breast cancer at the $p = 0.05$ level of significance, and were included in the model as potential confounders. Age at first birth was not significantly associated with breast cancer risk, and was excluded from the final analyses.

Separate analyses stratified by age at diagnosis were performed (age < 50 and 50+), since risk factors for breast cancer may differ by menopausal status [15, 16].

In order to evaluate light at night as a possible cancer-promoter, analyses were performed with work history limited to the most recent years before diagnosis (five and ten years, respectively). However, no increase of risk was observed (not shown).

Furthermore lag-time analyses were performed, disregarding exposure the 20 most recent years before diagnosis, to evaluate a possible influence of occupational risk factors that are suspected to initiate development of breast cancer, such as radiation [17]. In these analyses categories were somewhat different, due to a lower number of cases, (for night work: 0 years, 0–4, 5–14, ≥ 15 years, and for total employment time: 0–2, 3–9, 10–14, ≥ 15 years).

It has been proposed that breast cancers may differ in their etiology according to their estrogen receptor (ER) status [18]. However, the proportion of nurses for whom ER-status was known (11%), was too low to conduct meaningful analyses.

Tests for trends were calculated using number of years as a continuous variable, and all statistical tests were two-sided. The analyses were carried out using the STATA software [19].

Results

Table 1 shows the distribution of cases and controls by exposure categories, year of birth of the nurses, age at graduation from nursing school or at first employment, age at diagnosis, and fertility characteristics. The nurses were born between 1893 and 1955 (not shown). Maximum

Table 1 Selected characteristics of 2680 female Norwegian nurses, (537 breast cancer cases diagnosed between 1960 and 1982, and 2143 controls)

Characteristic	Cases number (%)	Controls number (%)
Years with night work		
0 years	50 (9)	215 (10)
>0–14 years	362 (67)	1511 (70)
15–29 years	101 (19)	359 (17)
≥30 years	24 (5)	58 (3)
Total employment time as a nurse (years)		
0–2	48 (9)	246 (11)
3–14	283 (53)	1081 (51)
15–29	149 (28)	600 (28)
≥30	57 (11)	216 (10)
Year of birth of nurses		
Before 1910	113 (21)	459 (21)
1910–1919	141 (26)	564 (26)
1920–1929	148 (28)	592 (28)
1930–1939	97 (18)	373 (17)
1940 or later	38 (7)	155 (7)
Age at graduation/first job (years)		
20–23	132 (25)	529 (25)
24–26	210 (39)	856 (40)
27–29	120 (22)	451 (21)
≥30	75 (14)	307 (14)
Age at diagnosis of case (years)		
<40	70 (13)	284 (13)
40–49	149 (28)	591 (28)
50–59	141 (26)	558 (26)
60–69	116 (22)	464 (22)
≥70	61 (11)	246 (11)
Nulliparous		
	265 (49)	946 (44)
	Mean	Mean
Number of children	1.15	1.34
Age at first birth	30.54	30.72

number of years with night work was 42 years (not shown). Age at diagnosis varied from 27 to 85 years, 59% of the cases were diagnosed at 50 years or older. The proportion of nulliparous women was higher among cases than among controls (49% versus 44%). Among parous women no differences were observed between cases and controls for age at first birth.

The OR of breast cancer among nurses who worked nights for 30 years or more, adjusted for parity and total employment time as a nurse, was 2.21 (CI = 1.10–4.45, $p_{\text{trend}} = 0.01$), compared with those who had not worked at night after graduation from nursing school (Table 2). Other possible occupational risk factors, for which total employment time could be a proxy variable, did not influence the risk of breast cancer substantially. A 29% non-significant increase of risk was observed among those who had 15–29 years of night work (CI = 0.82–2.02). For nurses aged 50 years and older, we found a 2-fold non-significant increase of risk among those who worked nights

for 30 or more years, when adjusted for total employment time as a nurse and parity. A statistically significant trend was observed ($p_{\text{trend}} = 0.02$). An elevated risk estimate after 15 or more years of night work, but no significant trend was seen for nurses younger than 50 years.

When applying 20 years lag-time (Table 3), maximum number of years with night work was 24.5 years. The observed OR in the highest (≥15 years) exposure group was 1.55, (CI = 0.87–2.78, $p_{\text{trend}} = 0.06$). A non-significant elevation of risk was also observed among postmenopausal women who worked nights for 15 or more years (OR = 1.68; CI = 0.90–3.12; $p_{\text{trend}} = 0.05$). In the lowest age group, no increase of risk was seen.

Discussion

The present study was designed to evaluate the role of night work as a potential occupational risk factor for breast cancer among nurses. For all ages combined, and for nurses aged 50 years or older, an increase of risk was observed in those who worked at night for 30 or more years, compared with those with no night work after graduation from nursing school. The increase was statistically significant for all ages, and borderline significant for women 50 years or older. For nurses younger than 50 years, a non-significant increase in risk was seen after 15 years of night work.

Our finding of an association between night work and breast cancer, and a positive trend between cancer risk and duration of night work, are consistent with results from other recent studies. In a large, prospective cohort study including 78,562 women from the Nurses' Health Study, Schernhammer et al. [10] found an increased incidence of breast cancer among postmenopausal women who had worked for 30 or more years on rotating night shifts (RR = 1.36; 95% CI = 1.04–1.78). In a case control study by Davis et al. [8] night work was associated with a 60% increase in breast cancer risk (95% CI = 1.0–2.5). A positive trend was observed with increasing number of years or increasing hours per week of night work. A population-based case–control study by Hansen [9] showed increased risk for breast cancer in women who had worked for at least half a year in trades with predominantly night work (OR = 1.5; 95% CI = 1.3–1.7). All the three studies, and the present one, have controlled for reproductive history.

Exposure to light at night has been suggested to influence breast cancer risk through an effect on melatonin [4], a pineal hormone produced at night, shown to inhibit the growth of breast cancer in experimental studies on animals [20]. Light at night has been reported to suppress melatonin levels in humans [21], and the decreased level of melatonin might lead to an increased level of estrogens and consequently to the increased risk of breast cancer [4].

Table 2 Odds ratios (ORs) of breast cancer and 95% confidence intervals (CIs) among nurses diagnosed in the period 1960–1982, by years with night work in different age groups

Years with night work in different age groups	Number of cases	OR	95% CI	Test for trend	Adj. OR*	95% CI	Test for trend
All ages (years)							
0	50	1.00	Reference		1.00	Reference	
>0–14	362	1.02	0.73–1.41		0.95	0.67–1.33	
15–29	101	1.26	0.85–1.85		1.29	0.82–2.02	
30+	24	1.95	1.08–3.51	$p = 0.01$	2.21	1.10–4.45	$p = 0.01$
Age <50 (years)							
0	21	1.00	Reference		1.00	Reference	
>0–14	185	1.17	0.71–1.91		1.02	0.60–1.71	
15+	13	1.50	0.68–3.26	$p = 0.16$	1.72	0.56–5.26	$p = 0.52$
Age 50+ (years)							
0	29	1.00	Reference		1.00	Reference	
>0–14	177	0.87	0.56–1.36		0.86	0.54–1.37	
15–29	88	1.12	0.70–1.80		1.17	0.68–2.00	
30+	24	1.72	0.90–3.26	$p = 0.02$	2.01	0.95–4.26	$p = 0.02$

* OR adjusted for total employment time as a nurse (0–2, 3–14, 15–29, ≥ 30 years) and parity (0, 1–2, 3 or more children)

The strength of the present study is that it is based on a large cohort, consisting of nurses educated during a period of more than 60 years. Compulsory reporting of all cancer cases to the national Cancer Registry made it possible to identify all breast cancer cases in the cohort for the period 1960–1982. Information about work history and reproductive history came from independent sources, and before the cancer diagnosis. Thus, information bias and recall bias has been avoided. By analyzing only one occupational group, we diminished the likelihood of possible influence of other confounding factors.

Some limitations should be pointed out. Although individual work history was available from the nurse registry, it did not include information about night work.

Assignment of night work was made specifically, by evaluating every registered job for each individual nurse as including night work or not, based on information on work place. Imputation of total work time and of years with night work was also performed at an individual level, around 1960, 1970 and 1980, if the only work history available for that year was that from a census. The assumptions we used when night work was assigned to an employment period may have introduced some non-differential misclassification of exposure. In the present study the average duration of one employment period was four years. Four years were therefore imputed around each census, when no other work history was available, and the census data indicated work as a nurse. This may be a conservative estimate. Jobs at

Table 3 Odds ratios (ORs) of breast cancer and 95% confidence intervals (CIs) among nurses diagnosed in the period 1960–1982, by years with night work in different age groups, when disregarding the 20 most recent years of exposure

Years with night work in different age groups	Number of cases	OR	95% CI	Test for trend	Adj. OR*	95% CI	Test for trend
All ages (years)							
0	201	1.00	Reference		1.00	Reference	
>0–4	186	1.00	0.76–1.32		1.03	0.77–1.37	
5–14	107	0.90	0.64–1.27		0.89	0.60–1.31	
15+	43	1.54	0.97–2.45	$p = 0.04$	1.55	0.87–2.78	$p = 0.06$
Age <50 (years)							
0	155	1.00	Reference		1.00	Reference	
>0–4	61	0.88	0.58–1.33		0.95	0.62–1.47	
5–14	3	0.95	0.25–3.68	$p = 0.93$	0.87	0.21–3.69	$p = 0.93$
15+	–	–	–	–	–	–	–
Age 50+ (years)							
0	46	1.00	Reference		1.00	Reference	
>0–4	125	1.13	0.78–1.64		1.13	0.76–1.68	
5–14	104	0.98	0.66–1.46		0.98	0.62–1.54	
15+	43	1.67	1.01–2.75	$p = 0.04$	1.68	0.90–3.12	$p = 0.05$

* OR adjusted for total employment time as a nurse (0–2, 3–9, 10–14, ≥ 15 years) and parity (0, 1–2, 3 or more children)

infirmaries were assumed to involve night work for nurses in most clinical departments. This is less the case if the working place had many permanent night workers.

The fact that all Norwegian nurses were working nights during the three years of education made it impossible to form a reference group of never exposed women, which might have led to a bias towards the null in the other exposure groups. Nurses not exposed to night work after graduation from the nursing school comprised the reference group.

Factors connected with hormones and reproductive behavior are known as the most important risk factors for breast cancer [1]. Among both cases and controls in our study age at first birth was high and mean number of children was low. This can partly be explained by the fact that until 1948 married women were not admitted to nursing schools, and nurses who married had to terminate their work as registered nurses [22]. We addressed fertility factors by adjusting for number of children in the analyses, however the results did not change essentially by this.

The nursing profession may involve other occupational risk factors for breast cancer, such as radiation. However, the data of this study does not hold such information. To control for other possible occupational hazards, adjustments were made for total employment time, however without substantial influence on risk estimates.

In conclusion, the results of our study support an association between night work and breast cancer risk among women. Future studies should include interviews of cases and controls for a refinement of the information on work history and exposures. The influence of other potential hazards related to the nursing profession, such as radiation should be evaluated.

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