Original Contribution

Shift Work, Light at Night, and Breast Cancer on Long Island, New York

Erin S. O’Leary¹, Elinor R. Schoenfeld¹, Richard G. Stevens², Geoffrey C. Kabat¹, Kevin Henderson¹, Roger Grimson¹, Marilie D. Gammon³, and M. Cristina Leske¹ for the Electromagnetic Fields and Breast Cancer on Long Island Study Group

¹ Department of Preventive Medicine, School of Medicine, Stony Brook University, Stony Brook, NY.  
² Department of Community Health, University of Connecticut Health Center, Farmington, CT.  
³ Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC.

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The hypothesized association between breast cancer and circadian disruption was evaluated in the Electromagnetic Fields and Breast Cancer on Long Island Study. Participants included 576 women with breast cancer diagnosed from August 1996 to June 1997 and 585 population-based controls (87% and 83% participation rates, respectively) aged <75 years and living in the same Long Island, New York, home for ≥15 years. An in-person interview ascertained light-at-night exposure histories through shift work (previous 15 years) and at home (previous 5 years). Odds ratios and 95% confidence intervals were estimated by unconditional multivariate logistic regression. Breast cancer was not associated with overall shift work (odds ratio (OR) = 1.04, 95% confidence interval (CI): 0.79, 1.38) or evening shift work (OR = 1.08, 95% CI: 0.81, 1.44). However, overnight shift workers were at lower risk than women never working shifts (OR = 0.55, 95% CI: 0.32, 0.94). Women who frequently turned on lights at home during sleep hours (≥twice/week and ≥twice/night) had increased risks (OR = 1.65, 95% CI: 1.02, 2.69). The latter results suggest positive associations with residential light-at-night exposure, or they could reflect response biases. Furthermore, overall and evening shift work were not significant factors, and analyses of overnight shift workers yielded reduced risk estimates. The study thus provides mixed evidence for the light-at-night hypothesis.

breast neoplasms; case-control studies; circadian rhythm; electromagnetic fields; light; melatonin; occupation; women

Abbreviations: CI, confidence interval; EBCLIS, Electromagnetic Fields and Breast Cancer on Long Island Study; LIBCSP, Long Island Breast Cancer Study Project; OR, odds ratio.

Breast cancer incidence varies widely among countries, incidence is increasing worldwide, and, in historically low-risk societies, mortality has also increased in recent decades (1). The causes of these increases remain unclear (2, 3). One potential hypothesis involves the hormone melatonin, which is secreted by the pineal gland and follows a circadian rhythm according to the light:dark cycle in most people; melatonin levels are low during the day and peak at night (usually between 2 a.m. and 4 a.m.) (4). Exposure to artificial lighting during the night could suppress the normal nocturnal rise in melatonin (5, 6), which could in turn increase circulating estrogen levels (7) or inhibit tumor anti-proliferative mechanisms and possibly increase breast cancer risk (5–7). Predictions concerning this “light-at-night” hypothesis are that women who work evening or overnight shifts would have a higher risk because they have constant light exposure at night (8) and that blind women would be at lower risk since their melatonin levels may not be affected by light (9). Limited epidemiologic evidence provides some support for the hypothesis, with several studies showing a
positive association between overnight shift work and breast cancer (10–13) and a tendency toward a negative association in blind women based on small numbers of cases (9, 14–16). Circadian disruption (17), especially during long-duration airline flights, is one hypothesized mechanism proposed for a potential increased breast cancer risk in flight attendants (18–20). Evidence is inconsistent, however (18–24).

This paper evaluates the hypothesized association between breast cancer and light-at-night exposures from both shift work and at home. It is based on data from the Electromagnetic Fields and Breast Cancer on Long Island Study (EBCLIS), a population-based case-control study of residually stable women. The main EBCLIS aim was to evaluate associations with residential magnetic fields; the secondary aim was to evaluate associations with light-at-night exposures.

MATERIALS AND METHODS

Source of cases and controls

The EBCLIS methods have been described in previous publications (25–28). Briefly, women eligible for EBCLIS were participants in the Long Island Breast Cancer Study Project (LIBCSP) (29). LIBCSP cases were residents of Nassau and Suffolk counties on Long Island, New York, newly diagnosed with a first primary in situ or invasive breast cancer between August 1, 1996, and July 31, 1997. LIBCSP controls were also Long Island residents, frequency matched to the expected age distribution of cases by 5-year age groups. Controls less than 65 years of age were identified by random digit dialing; controls 65 years of age or older were selected from Health Care Financing Administration rosters. Potential study participants were introduced to the study by mail, followed by a telephone call to answer questions and schedule an in-home visit. At this visit, women responded to a comprehensive questionnaire (1,508 cases and 1,556 controls) and provided blood and urine samples, after written informed consent; they also received a brochure informing them about EBCLIS.

LIBCSP participants eligible for EBCLIS were those women younger than 75 years of age (a group with LIBCSP participation rates of 86 percent for cases and 69 percent for controls (29)) who had lived in the same Long Island residence for 15 years or longer at the time of either diagnosis (cases) or identification (controls). We selected residually stable women so that our assessment of long-term residential exposure to electromagnetic fields would be as comprehensive as possible (25). On average, the EBCLIS interview was administered 239 days after the LIBCSP interview for cases and 202 days for controls. Eleven eligible breast cancer cases and three controls died between the two interviews. EBCLIS recruitment was based on 663 eligible cases diagnosed between August 1, 1996, and June 20, 1997, and a random sample of 702 controls frequency matched by age. Overall, 576 cases (87 percent) and 585 controls (83 percent) participated, with refusal as the main reason for nonparticipation (25). Since LIBCSP did not collect participation data according to length of residence, we could not estimate response rates for EBCLIS-eligible women based on the LIBCSP rates.

The EBCLIS staff administered a 30-minute in-home interview, after obtaining signed informed consent, and took comprehensive residential measurements of electromagnetic fields (25). The outside wiring around the home was mapped at a subsequent visit (26). Review boards from participating institutions approved the study protocols and informed consent procedures.

Exposure histories

Employment and shift work. The LIBCSP interview included an occupational history of all jobs held for 6 months or longer since the age of 16 years, part-time or full-time, paid or unpaid, including military assignments; no information was collected on shift work (29). The EBCLIS interview confirmed the job title, location, and start and end dates for each job held during the 15-year period prior to the reference date (i.e., date of diagnosis for cases or identification for controls). The frequency (days per week, months, or years), duration (number of months or years), and type of shift work were ascertained for each of these jobs, and the interview asked separately about evening shifts (an evening shift could start in the afternoon and end as late as 2:00 a.m.) and overnight shifts (an overnight shift could start as early as 7:00 p.m. and continue until the following morning) (30).

Light at night at home. To obtain more accurate answers, residential light-at-night exposures were ascertained for the 5-year period prior to the reference date compared with the distant past. Questions covered sleep hours, frequency of turning on lights during sleep hours, and length of time the light was on (30).

Statistical methods

Shift-work exposure history. All analyses were based on data for 487 (85 percent) of 576 cases and 509 (87 percent) of 585 controls who worked during the 15 years prior to the reference date.

Definitions of shift work were based on ever working in at least one job during the past 15 years that included 1) any shift work (i.e., any evening or overnight shift job); 2) any evening shift (i.e., including jobs with both evening and overnight shift work); 3) evening shifts only (i.e., excluding jobs with both evening and overnight shift work); 4) any overnight shift (i.e., including jobs with both overnight and evening shift work); and 5) overnight shifts only (i.e., excluding jobs with both overnight and evening shift work). The referent group for these analyses included women who had never held jobs involving shift work.

Duration of evening shift work was categorized into groups according to the median number of years working in jobs with at least one evening shift per week, based on the distribution among the controls: 1) less than one evening shift per week (referent group), 2) one or more evening shift per week for fewer years than the median, and 3) one or more evening shift per week for the same or more years than the median. A similar categorization was used for duration of overnight shift work.
**Light-at-night exposure history at home.** Turning on lights during sleep hours. First, we determined how often participants woke up and turned on lights in their bedroom or any other room: less than once a month or never (referent group), one to three times a month, once a week, two to four times a week, and five or more times a week. Second, we evaluated the association among women who frequently turned on lights (≥once/week) during sleep hours, also considering number of times per night. The referent group consisted of women who never or infrequently (one to three times/month) woke up and turned on lights, and the exposed group comprised women who woke up and turned on lights 1) once a week or more often (either once/night or ≥twice/night) or 2) twice a week or more often (either once/night or ≥twice/night).

Nonpeak sleep. Similar to Davis et al. (11), we defined nonpeak sleep as either habitually waking up on weekdays between 8:00 p.m. and 1:00 a.m. or habitually going to sleep on weekdays between 2:00 a.m. and 8:00 a.m.

**Analytical methods.** In univariate analyses, we examined associations between breast cancer status and potential risk factors by using the independent t test and the Pearson's chi-square test. Independent variables considered for inclusion in multivariate unconditional logistic regression analyses were selected from established breast cancer risk factors and other variables for which the univariate p value was ≤0.25 (31, 32). We calculated odds ratios and 95 percent confidence intervals in univariate and multivariate unconditional logistic regression analyses, for all women and for premenopausal and postmenopausal women separately, by using maximum likelihood estimation in SAS software (33).

Menopausal status was derived from information provided by participants on the date of the last menstrual period, prior surgical information on hysterectomy or oophorectomies, cigarette smoking status, and hormone replacement therapy use from the LIBCSP questionnaire (29). A participant was defined as postmenopausal if her last menstrual period was more than 6 months before the reference date or if she had had both ovaries removed prior to the reference date. Women who were using hormone replacement therapy or had had a hysterectomy without removal of both ovaries were assigned a menopausal status based on their reference age and smoking status. Smokers were considered postmenopausal if their age at reference was 54.8 years or older (90th percentile for natural menopause among control smokers), and nonsmokers were considered postmenopausal if their age at reference was 55.4 years or older (90th percentile for natural menopause among control nonsmokers) (29).

For the models based on all women, we included the following covariates from the LIBCSP main questionnaire (29): age at reference date (continuous), parity (number of livebirths), education (less than high school or high school graduate as the referent versus some college, college graduate, or postcollege), first-degree family history of breast cancer (mother, sister, or daughter), and history of benign breast disease (yes/no). The premenopausal models included the same variables, with the addition of body mass index (weight in kilograms/height in meters squared, continuous) at the reference date. Additionally, the postmenopausal models included body mass index at age 20 years (kg/m², continuous). We also stratified our analyses for the subgroup less than 65 years of age, for invasive and in-situ breast cancer cases, and estrogen receptor status for invasive cases (positive, negative, and not ascertained). Tests for interaction were performed. Interactions were further assessed by stratified analyses in which the relation between breast cancer and either shift-work or light-at-night variables were evaluated in the corresponding strata of other breast cancer covariates.

**RESULTS**

**Shift-work history**

Of women who worked during the 15 years up to the reference date, 36.3 percent (cases and controls combined) had at least one shift-work occupation, including 33.5 percent who worked at least one evening shift job and 7.6 percent who worked at least one overnight shift job. Table 1 compares the characteristics of shift workers and non-shift-workers among the controls. Evening shift workers tended to be younger than non-shift-workers, be premenopausal (34 percent vs. 21 percent), and have five or more children (15 percent vs. 8 percent); and they were less likely to be Jewish (12 percent vs. 23 percent). Overnight shift workers tended to be younger than non-shift-workers, be more likely to use oral contraceptives (70 percent vs. 49 percent), be more likely to have ever lactated (46 percent vs. 28 percent), be premenopausal (39 percent vs. 21 percent), and be Protestant (34 percent vs. 19 percent); they were less likely to have ever had a mammogram (86 percent vs. 94 percent) and be Jewish (0 percent vs. 23 percent). Among the women reporting their household income (88 percent of cases and 86 percent of controls), no significant differences were found between overnight shift workers and other women; adjustment for income in this subset did not materially change the effect estimates.

Table 2 shows the type and duration of shift work for cases and controls and their association with breast cancer. Compared with findings for non-shift-workers, there was no association between breast cancer and any shift work (whether in the evenings or overnight) or any evening shift work, with adjusted odds ratios of 1.04 and 1.08, respectively. Results were similar for pre- and postmenopausal women, for women less than 65 years of age, for invasive cases, and by estrogen receptor status (data not shown).

In contrast, any overnight shift work showed a negative association with breast cancer, with a decrease in the odds ratio to about one half (adjusted odds ratio (OR) = 0.55, 95 percent confidence interval (CI): 0.32, 0.94) that for the referent group. Similar results were obtained when restricting the analyses to women who worked only overnight shifts but not evening shifts, with an odds ratio of 0.64 (95 percent CI: 0.28, 1.45). Separate analyses for women who were health professionals, nurses, or not health professionals (business, law enforcement, communications, etc.), although based on small numbers, yielded odds ratios similar to the overall results. Findings were similar for pre- and postmenopausal women, for women less than 65 years of age, for invasive cases, and by estrogen receptor status; but results were...
significant for only postmenopausal women and women less than 65 years of age (data not shown). The significantly decreased association for overnight shift workers persisted after additional analyses that adjusted for all of the characteristics for which overnight shift workers differed from non-shift-workers (table 1). In addition, there was no interaction between established breast cancer risk factors and overnight shift work (data not shown).

Table 2 shows results of analyses by duration of evening shift work and overnight shift work. We found no association between breast cancer and increasing number of years working one or more evening shift per week. Women who worked one or more overnight shift per week for more than 8 years (the median number of years that controls worked) had about one third the risk (OR = 0.32, 95 percent CI: 0.12, 0.83) of the referent group. All of these results were similar for pre- and postmenopausal women, women less than 65 years of age, and invasive cases (data not shown), but they were not statistically significant in the pre- and postmenopausal strata. Numbers of cases who reported overnight shift work were too small to further evaluate these findings stratified by estrogen receptor status.

**TABLE 1. Characteristics of controls, according to shift-work status, who worked during the past 15 years up to the date of identification, Electromagnetic Fields and Breast Cancer on Long Island Study, New York, 1996–1997**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No shift work†</th>
<th>Any evening shift work‡</th>
<th>Any overnight shift work§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)¶</td>
<td>59.0 (8.2)*</td>
<td>55.0 (8.7)*</td>
<td>53.0 (8.0)*</td>
</tr>
<tr>
<td>Ever used alcohol</td>
<td>217 67.6</td>
<td>104 61.2</td>
<td>35 70.0</td>
</tr>
<tr>
<td>History of benign breast disease</td>
<td>43 13.4</td>
<td>24 14.1</td>
<td>11 22.0</td>
</tr>
<tr>
<td>Education beyond high school</td>
<td>196 61.1</td>
<td>113 66.5</td>
<td>31 62.0</td>
</tr>
<tr>
<td>Ever used hormone replacement therapy</td>
<td>110 34.3</td>
<td>56 32.9</td>
<td>12 24.0</td>
</tr>
<tr>
<td>Ever used oral contraceptives</td>
<td>156* 48.6*</td>
<td>94 55.6</td>
<td>35* 70.0*</td>
</tr>
<tr>
<td>Family history of breast cancer</td>
<td>37 11.8</td>
<td>18 10.8</td>
<td>4 8.0</td>
</tr>
<tr>
<td>History of fertility problems</td>
<td>65 20.3</td>
<td>26 15.5</td>
<td>12 24.0</td>
</tr>
<tr>
<td>Ever lactated</td>
<td>89* 27.7*</td>
<td>58 34.1</td>
<td>23* 46.0*</td>
</tr>
<tr>
<td>Latina</td>
<td>8 2.5</td>
<td>7 4.1</td>
<td>3 6.0</td>
</tr>
<tr>
<td>Ever had a mammogram</td>
<td>301* 93.8*</td>
<td>156 91.8</td>
<td>43* 86.0*</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>65* 21.0*</td>
<td>53* 34.2*</td>
<td>18* 39.1*</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>22 6.9</td>
<td>13 7.7</td>
<td>2 4.0</td>
</tr>
<tr>
<td>Parity# (≥5 children)</td>
<td>24* 8.0*</td>
<td>24* 15.3*</td>
<td>5 10.4</td>
</tr>
<tr>
<td>African American</td>
<td>9 2.8</td>
<td>5 2.9</td>
<td>4 8.0</td>
</tr>
<tr>
<td>Jewish</td>
<td>75* 23.4*</td>
<td>21* 12.4*</td>
<td>0* 0.0*</td>
</tr>
<tr>
<td>Protestant</td>
<td>62* 19.3*</td>
<td>44 25.9</td>
<td>17* 34.0*</td>
</tr>
<tr>
<td>Catholic</td>
<td>182 56.7</td>
<td>102 60.0</td>
<td>33 66.0</td>
</tr>
<tr>
<td>Total household income before taxes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in the last year ($)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20,000</td>
<td>12 4.5</td>
<td>11 7.2</td>
<td>2 4.1</td>
</tr>
<tr>
<td>20,000–49,999</td>
<td>90 33.8</td>
<td>54 35.3</td>
<td>21 42.9</td>
</tr>
<tr>
<td>50,000–89,999</td>
<td>102 38.4</td>
<td>59 38.6</td>
<td>16 32.6</td>
</tr>
<tr>
<td>≥$90,000</td>
<td>62 23.3</td>
<td>29 18.9</td>
<td>10 20.4</td>
</tr>
</tbody>
</table>

* p < 0.05 in independent t tests (mean age) or Pearson’s chi-square tests (all other characteristics) for the comparison between any evening shift work and no shift work or the comparison between any overnight shift work and no shift work.
† n = 321 for all characteristics except the following: family history of breast cancer (n = 313), menopausal status (n = 309), and household income (n = 266).
‡ n = 170 for all characteristics except the following: ever used oral contraceptives (n = 169), family history of breast cancer (n = 167), history of fertility problems (n = 168), menopausal status (n = 155), and household income (n = 153).
§ n = 50 for all characteristics except the following: menopausal status (n = 46) and household income (n = 49).
¶ Values are expressed as number of years (standard deviation).
# For parous women only: no shift work (n = 299), any evening shift work (n = 157), any overnight shift work (n = 48).
The first seven rows of table 3 show that we found no association between breast cancer and higher frequency, compared with lower frequencies, of turning on lights during sleep hours; all odds ratios were close to 1.0. When nightly frequency was considered, women who turned on lights once a week or more often, and twice a night or more often, had a nonsignificantly increased breast cancer risk (adjusted OR = 1.46, 95 percent CI: 0.92, 2.32) compared with the referent group. Women with the highest exposure, that is, those who woke up and turned on lights twice a week or more often, had an increased breast cancer risk (adjusted OR = 1.65, 95 percent CI: 1.02, 2.69). Compared with the referent group, the highest exposure group was more likely to be postmenopausal (86 percent vs. 76 percent) and tended to have less education (education beyond high school: 41 percent versus 58 percent) (data not shown). Results were similar for pre- and postmenopausal women, for women less than 65 years of age, for invasive cases, and by estrogen receptor status; but they were not statistically significant for premenopausal women ($n = 11$), women less than 65 years of age, and invasive cases whose estrogen receptor status was positive or not ascertained (data not shown). Finally, no significant associations were found between breast cancer and nonpeak weekday sleep (adjusted OR = 0.83, 95 percent CI: 0.44, 1.57).

**DISCUSSION**

When considering overall shift work (evening or overnight shifts), we found no association with breast cancer risk. However, when we considered evening and overnight shift work separately, there was a negative association with overnight shift work, with no significant results for evening shift work. In addition, we found a positive association for women who reported rising frequently during the week and turning on lights multiple times per night. To our knowledge, ours is the first study to report such results.

**Shift-work history**

Our shift-work results are different from those reported in other studies. For example, Hansen (10) found a significant elevation in breast cancer risk with night-work occupations...
in a case-control study in Denmark, which included women aged 30–54 years (OR = 1.5, 95 percent CI: 1.3, 1.7). This study was based on a large number of breast cancer cases (>7,000) and a similar number of controls identified through a population registry. Women in occupations in which 60 percent of the workers had night-shift employment (based on a Danish occupational survey) were considered "night workers." This group included occupations in catering (the largest category), beverage manufacturing, and transport services. Our study would have classified caterers as evening shift workers since overnight shift work in this group was infrequent. Hansen separately reported an increased risk for hospital workers (OR = 1.2, 95 percent CI: 1.1, 1.5) and nurses (OR = 1.3, 95 percent CI: 1.1, 1.4), although only 41 percent of women in these occupations met the study criteria for "night workers" (34, 35).

A study in Seattle, Washington, by Davis et al. (11) reported an association with overnight shift work, defined as the shift in which the work period included midnight (OR = 1.6, 95 percent CI: 1.0, 2.5; p = 0.04). A trend was found for increased risk with increasing duration (more years and hours per week) of overnight shift work, with no information on the specific occupations involved. The reason for the inconsistent findings between that study and ours is unclear, but it could be due to our 15-year residency requirement, differences in study definitions, or the type and duration of shift work. Davis et al. (11) considered occupational histories 10 years prior to diagnosis versus 15 years in our study. The median number of years working overnight shifts was 3 in that study versus 8 in ours. When we analyzed our data by using 3 years as the cutpoint, our findings were unchanged.

Compared with non-shift-workers, overnight shift workers

<table>
<thead>
<tr>
<th>Light-at-night exposure</th>
<th>Cases</th>
<th>Controls</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>Adjusted odds ratio*</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of turning on lights during sleep hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 time/month or never (referent)</td>
<td>311</td>
<td>313</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1–3 times/month</td>
<td>66</td>
<td>69</td>
<td>0.96</td>
<td>0.66, 1.40</td>
<td>0.98</td>
<td>0.66, 1.44</td>
</tr>
<tr>
<td>1 time/week</td>
<td>31</td>
<td>50</td>
<td>0.62</td>
<td>0.39, 1.00</td>
<td>0.71</td>
<td>0.43, 1.16</td>
</tr>
<tr>
<td>2–4 times/week</td>
<td>63</td>
<td>63</td>
<td>1.01</td>
<td>0.69, 1.48</td>
<td>0.99</td>
<td>0.67, 1.48</td>
</tr>
<tr>
<td>≥5 times/week</td>
<td>105</td>
<td>88</td>
<td>1.20</td>
<td>0.87, 1.66</td>
<td>1.12</td>
<td>0.80, 1.57</td>
</tr>
<tr>
<td>Missing</td>
<td>2</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of waking up and turning on lights</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1–3 times/month or never (referent)</td>
<td>377</td>
<td>382</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≥1 time/week</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1 time/night</td>
<td>145</td>
<td>165</td>
<td>0.89</td>
<td>0.68, 1.16</td>
<td>0.88</td>
<td>0.67, 1.16</td>
</tr>
<tr>
<td>≥2 times/night</td>
<td>53</td>
<td>35</td>
<td>1.53</td>
<td>0.98, 2.41</td>
<td>1.46</td>
<td>0.92, 2.32</td>
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<tr>
<td>Missing†</td>
<td>1</td>
<td>3</td>
<td></td>
<td></td>
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<tr>
<td>≤1–3 times/month or never (referent)</td>
<td>377</td>
<td>382</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≥2 times/week‡</td>
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<td></td>
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</tr>
<tr>
<td>1 time/night</td>
<td>116</td>
<td>121</td>
<td>0.97</td>
<td>0.73, 1.30</td>
<td>0.91</td>
<td>0.67, 1.24</td>
</tr>
<tr>
<td>≥2 times/night</td>
<td>51</td>
<td>30</td>
<td>5.6</td>
<td>1.72§</td>
<td>1.07, 2.76</td>
<td>1.65§</td>
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<tr>
<td>Missing¶</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Nonpeak sleep</td>
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<tr>
<td>No</td>
<td>556</td>
<td>559</td>
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<td></td>
<td>1.00</td>
<td></td>
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<tr>
<td>Yes</td>
<td>19</td>
<td>24</td>
<td>4.1</td>
<td>0.80</td>
<td>0.43, 1.47</td>
<td>0.83</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>2</td>
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* Adjusted for age at reference date, parity (no. of livebirths), family history (defined as a mother, sister, or daughter with breast cancer), education (defined as less than high school or high school graduate as the referent vs. some college, college graduate, and postcollege education), and history of benign breast disease.
† For one case, a response regarding the number of times that a light was turned on per night was missing; two controls answered that they did not know the frequency of waking up and turning on a light; and one control responded "0" to the number of times she turned on a light per night.
‡ Excludes 31 cases and 50 controls who woke up and turned on lights 1 time/week.
§ The 95% confidence interval does not include 1.0.
¶ For one case, a response regarding the number of times that a light was turned on per night was missing; two controls answered that they did not know the frequency of waking up and turning on a light during sleep hours.

TABLE 3. Frequencies, percentages, and odds ratios for breast cancer and residential light-at-night exposures during the past 5 years up to the date of breast cancer diagnosis (cases) or date of identification (controls) for participants in the Electromagnetic Fields and Breast Cancer on Long Island Study, New York, 1996–1997*
in both studies were more likely to use oral contraceptives and less likely to have a family history of breast cancer.

The Nurses’ Health Study, consisting of mostly older women (12), and the Nurses’ Health Study II, consisting of premenopausal women (13), reported on the relation between breast cancer and working rotating night shifts at least three times per month (in addition to days and evenings during that month). Nurses in the Nurses’ Health Study who worked rotating night shifts for 30 years or more showed a significantly elevated risk (relative risk = 1.36, 95 percent CI: 1.04, 1.78) (12), as did those in the Nurses’ Health Study II who worked rotating night shifts for 20 or more years (relative risk = 1.79, 95 percent CI: 1.06, 3.01) (13). Among a subset of nurses in the Nurses’ Health Study and Nurses’ Health Study II, a separate substudy showed increased levels of estradiol in premenopausal women working rotating night shifts for 15 years or more and a significant decrease in urinary melatonin with increasing number of nights worked in the previous 2 weeks (36). Results for nurses in our study were similar to our overall findings. The difference in definitions and criteria makes it difficult to compare our results with those of both Nurses’ Health Study cohorts; for example, we did not collect data on rotating night shifts. Their definition could exclude nurses on permanent night shifts, who would have been considered overnight shift workers in our study. Permanent night-shift workers may be more likely to adapt by changing their circadian rhythm, whereas women working rotating night shifts would be more likely to experience circadian disruptions (37). While rotating night-shift workers in the Nurses’ Health Study tended to be older and more frequently postmenopausal than other nurses, overnight shift workers in our study were younger and more frequently premenopausal than non-overnight-shift-workers. In addition, nurses may not be representative of all night-shift workers, since nurses have additional exposures.

**Light-at-night exposure history at home**

When the questionnaire for our study was being constructed, we included questions on frequency of turning on lights at night since several small studies have shown that intermittent nocturnal light exposure of sufficient intensity decreases melatonin levels (4, 38, 39). To date, only the study by Davis et al. (11) also evaluated residential light-at-night exposure as a possible breast cancer risk factor. The frequency of turning on lights (at each of the women’s residences over the preceding 10 years) was not related to risk in that study (11). The average number of awakenings per night with lights on was ascertained only if the participant responded that she “usually” awoke during the night at that residence. As such, our results are not strictly comparable. Nonpeak sleep (habitually being awake at 1:00 a.m.) showed a significant association (OR = 1.14, 95 percent CI: 1.01, 1.28) in the Davis et al. study (11). We did not find an association with nonpeak sleep in our study. We asked about the usual time that women went to sleep and woke up on weekdays and weekend days, while the Davis et al. study (11) asked this question for each day of the week.

**Strengths and limitations**

We benefited from the experiences of two other studies that were in the data collection phase before the EBCLIS forms were completed (40, 41). Therefore, several questions on shift work and light at night in EBCLIS were comparable to those in the previous studies, and some aimed to more precisely assess those exposures. However, an unavoidable limitation is the retrospective estimation of exposures based on self-reported histories, which are inherently imprecise and may be subject to differential recall between cases and controls. Although we asked for shift-work and residential light-at-night exposures for the time period prior to the date of diagnosis, it is possible that cases’ recall was affected by changes in work or sleeping habits after breast cancer was diagnosed, although this possibility is unlikely for shift-work exposures. In particular, reports of waking and turning on lights at night could be influenced by morbidity or increased anxiety in cases, thus leading to a spurious association with breast cancer risk. We cannot rule out such an explanation for our findings.

By focusing on the previous 15-year period for shift work and the 5-year period for light-at-night exposures, our goal was to obtain more accurate answers than if we had asked about events and exposures in the distant past. However, if the more etiologically relevant time period was prior to these time periods, measurement of exposures would have been underestimated or possibly misclassified.

We limited our study population to LIBCS participants who lived in the same home for 15 years or more (long-term residents). Compared with non-long-term residents, our sample was more likely to be older, postmenopausal, White, parous, heavier, ever users of alcohol, and ever users of hormone replacement therapy and to be less likely to have more than a high school education and to have ever lactated (29). No other published study had this residential restriction (10–13). However, this limitation merely restricts the generalizability of the study and does not affect the validity. Inadequate control for confounding factors could result in biased estimation of risk. Cases and controls in EBCLIS were of comparable age, and multivariate analyses adjusted for this and many other variables. The large sample size and analytic control for potential confounders are strengths of the study, which lend support to the results presented.

**Concluding comments**

The light-at-night hypothesis (5) has some support from animal models (e.g., Blask et al. (42, 43)) and indirect evidence from human studies (6). Since the late 1970s, several clinical case series or case-control studies have examined differences in melatonin profiles and peak levels between breast cancer cases and controls or earlier- and later-stage breast cancer (44–51). These studies are difficult to compare because they differ in methodology, number, and age-distribution of participants; most have small sample sizes. While the overall findings of these studies are inconsistent, several provide support for the hypothesis that a shift in melatonin profile or a reduction in peak levels may be associated with breast cancer (44–47), whereas others did not.
(48–51). One recent nested case-control study within a cohort in which 24-hour urinary concentration of the primary melatonin metabolite (6-sulphatoxy melatonin) was measured 12 years on average before breast cancer diagnosis found no association among 127 breast cancer cases and 353 matched controls (52, 53). A second such study of 147 breast cancer cases and 291 matched controls in the Nurses’ Health Study II cohort, in which the first morning urinary concentration of 6-sulphatoxy melatonin was measured 4 years on average before breast cancer diagnosis, found that higher 6-sulphatoxy melatonin levels were associated with decreased breast cancer risk (54).

Our study does not support shift work as a factor that increases breast cancer risk. Our results on light-at-night exposure at home are consistent with the hypothesized relation, suggesting that women experiencing high levels of circadian disruption are at increased risk. However, this finding may be due to differential recall of these exposures or to other factors related to waking up multiple times during the night. To clarify these inconsistent findings, future studies should focus on a more robust estimation of shift work, innovative ways to evaluate nighttime light exposure in the home, accurate and appropriate melatonin measurements, and genetic polymorphisms that might interact with environmental lighting to affect risk of breast cancer (55–57).

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