Open access • Journal Article • DOI:10.1007/S10654-020-00610-X

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Published on: 06 Feb 2020 - European Journal of Epidemiology (Eur J Epidemiol)

Topics: Breast cancer and Population

Ritonja, J., McIsaac, M. A., Sanders, E., Kyba, C., Grundy, A., Cordina-Duverger, E., Spinelli, J. J., Aronson, K. J. (2020): Outdoor light at night at residences and breast cancer risk in Canada. - European Journal of Epidemiology, 35, 579-589.

https://doi.org/10.1007/s10654-020-00610-x

Outdoor light at night at residences and breast cancer risk in Canada

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Acknowledgments
We would like to thank all study participants, and Alejandro Sánchez de Miguel (Environment and Sustainability Institute, University Exeter). We would also like to acknowledge our funding sources (see Funding Sources section), and the DAAD German Faculty Research Exchange for funding travel during collaboration. DMSP and DNB Image and Data processing by NOAA's National Geophysical Data Center. This paper is dedicated to the late Richard Stevens who postulated the association between ambient light at night and breast cancer risk, and steadfastly encouraged research.

Word count: 4991 (excluding references, abstract, and tables).

Abstract
Experimental and epidemiologic studies suggest that light at night (LAN) exposure disrupts circadian rhythm, and this disruption may increase breast cancer risk. We investigated the potential association between residential outdoor LAN and breast cancer risk in Canada. A population-based case-control study was conducted in Vancouver, British Columbia and Kingston, Ontario, Canada with incident breast cancer cases, and controls frequency matched by age in the same region. This analysis was restricted to 844 cases and 905 controls who provided lifetime residential histories. Using time-weighted average duration at each home 5-20 years prior to study entry, two measures of cumulative average outdoor LAN were calculated using two satellite data sources. Logistic regression was used to estimate the relationship between outdoor LAN and breast cancer risk, considering interactions for menopausal status and night shift work. We found no association between residential outdoor LAN and breast cancer for either measure of LAN (OR comparing highest vs. lowest tertile [DNB] = 0.95, 95% CI: 0.70-1.27). We also found no association when considering interactions for menopausal status and past/current night work status. These findings were robust to changes to years of residential data considered, residential mobility, and longer exposure windows. Our findings are consistent with studies reporting that outdoor LAN has a small effect or no effect on breast cancer risk.

Key words: light-at-night; breast cancer; circadian disruption; case-control study; night work

INTRODUCTION

With the development of cities and a modern society that supports the availability of work and services 24/7, exposure to artificial light at night (LAN) is prevalent. Light emissions are growing worldwide at over 2% per year [1], and it is estimated that more than 80% of the world's population lives under light-polluted skies, with the population of the United States and Europe having the highest exposure (99%) [2]. International differences in breast cancer incidence across countries point to a link between environmental factors and breast cancer risk, particularly in high-income countries [3]. Due to the ability of LAN exposure to disrupt circadian rhythm, particularly melatonin production, it is hypothesized that exposure to LAN may promote carcinogenesis [4].

Recent experimental and epidemiologic evidence support the hypothesis that exposure to LAN is a carcinogen for breast cancer. In 2007, the International Agency for Research on Cancer (IARC) classified shift work that involves circadian disruption as a probable (Group 2A) carcinogen [5], and the IARC assessment of night shift work in 2019 resulted in the same classification [6]. In 2018, the U.S. National Toxicology Program (NTP) classified night shift work as a carcinogen for breast cancer [7]. Exposure to indoor LAN during night shifts is hypothesized as a mediator between night shift work and breast cancer development [8, 9]. Animal and epidemiologic studies support that LAN exposure modifies pineal gland function, with higher LAN exposure shown to suppress melatonin secretion [8, 10]. This suppression is thought to disrupt circadian rhythm and sleep patterns, which may be conducive to the development of breast cancer [11-13]. There is also evidence that increases in melatonin have direct oncostatic effects, particularly for breast cancer tumors [14].

Exposure to artificial light at night can occur from a variety of sources, including outdoor exposure from street lights and other buildings, as well as within buildings through electric lighting and appliances. A person's total exposure to artificial LAN reflects a cumulative combination of LAN exposure from multiple sources over time. For this study, we focus on one aspect of an individual's total LAN exposure: outdoor LAN exposure at homes. Outdoor LAN is used as a surrogate for evening and nighttime light exposure [15]. It is hypothesized that people living in communities with higher outdoor LAN exposure are likely to have higher overall exposure to LAN due to their immediate environment [14]. People living in these communities are theorized to experience higher levels of light intrusion into their houses at night, and are exposed to outdoor LAN during evening outdoor activities such as driving on roads lit by streetlights [15]. However, there is still debate on how measured outdoor LAN correlates with personal LAN exposure [15, 16].

Animal and experimental studies strongly support a link between exposure to LAN and breast cancer development [11, 12, 17], and epidemiologic studies show similar findings [18-26]. Studies that are ecologic in design show increased breast cancer incidence in geographic areas with relatively higher LAN than comparison areas [18-22]. Causal inference is, however, hampered in these studies because of challenges with ecologic bias and the lack of control for individual-level confounders [27]. These ecologic studies are also limited because they measure LAN at a single time point, rather than taking into account cumulative exposure, a more precise and biologically relevant measure. Case-control and cohort studies that have analyzed the association between objectively measured LAN and breast cancer suggest a link between greater outdoor LAN exposure and higher breast cancer risk [23-26]. These studies were stronger methodologically because of the use of LAN exposure geocoded to participants' residences, and the inclusion of individual-level confounders. Three of these studies, however, used LAN data from only one residence [23, 25, 26], which may not accurately reflect a person's exposure over time, whereas one study of U.S. nurses [24] estimated LAN exposure by averaging LAN levels over multiple residences.

It is hypothesized that the relationship between LAN and breast cancer may differ by breast cancer subtype because of anti-estrogenic effects of melatonin [28]. Women exposed to higher LAN may be at a higher risk for developing hormone-receptor positive breast cancer (e.g. estrogen or progesterone receptor positive breast cancer) [17], a finding that is supported by pooled case-control studies of female night shift workers, particularly among pre-menopausal women [29]. Night workers, particularly those who are pre-menopausal, exposed to higher residential LAN may be at a greater risk for breast cancer [24].

Using participants' residential history in a population-based case-control study in Canada, we investigated if residential outdoor LAN is associated with breast cancer risk, considering interactions with menopausal status and night shift work. To our knowledge, no prior study has investigated the relationship between outdoor LAN and breast cancer risk in Canada, i.e. at higher latitude locations than previous studies. This is important because seasonal variation in sun exposure and outdoor behaviors at higher latitudes may impact the relationship.

METHODS

Study Population

A population-based case-control study was conducted in Vancouver, British Columbia (BC) and Kingston, Ontario (ON) from 2005 to 2010.

Vancouver, BC

Women aged 40–80 diagnosed with incident in situ or invasive breast cancer between 2005 and 2009 living in the greater Vancouver area (including New Westminster, Richmond, and Burnaby) at the time of enrollment were recruited from the BC Cancer Registry. Controls were women with either normal mammogram results or a diagnosis of benign breast disease, recruited from the Screening Mammography Program of BC from the same geographic area, frequency matched to cases in five-year age groups. Participants received a study package including a letter describing the study, a consent form, and study questionnaire including lifetime residential histories. Questionnaire responses were collected by phone or mail, with the option of phone interviews in English, Cantonese, Mandarin, or Punjabi, and all participants also submitted a blood sample as well as consenting to access to medical records concerning breast health. Response was 54% among cases and 57% among controls, with a total of 1003 cases and 1015 controls. Ethics approval for the data collection was provided by the University of British Columbia BC Cancer Agency Research Ethics Board, and informed consent was obtained from all individuals included in the study.

Kingston, ON

Cases and controls were recruited from the Hotel Dieu Breast Assessment Program in Kingston, ON. Women were eligible if they were 40-80 years of age, had no previous cancer history (with the exception of non-melanoma skin cancer), were not too ill to participate, or were not taking cancer-preventative drugs. Eligible women were contacted by the study coordinator and sent a package including study information, questionnaire, and consent form. Cases were defined as women with a diagnosis of in situ or invasive breast cancer, while controls were defined as women with either normal mammogram results or a diagnosis of benign breast disease, frequency matched in five-year age groups to cases. Response was 59% among cases and 49% among controls, with a total of 131 cases and 164 controls recruited. Data collection involved the same process as in Vancouver, although in Kingston all participants self-administered the questionnaire. Ethics approval was provided by the Queen's University Health Sciences Research Ethics Board, and informed consent was obtained from all individuals included in the study.

Outdoor LAN Measurement

Data on residential outdoor LAN exposure was derived from global satellite imagery from two space-based radiometers: the U.S. Defense Meteorological Satellite Program Operational Linescan System (DMSP) and the Visible Infrared Imaging Radiometer Suite Day-Night Band (DNB). Imagery data for both sources was retrieved from the National Oceanic and Atmospheric Administration (https://ngdc.noaa.gov/eog/download.html).

The aim is to measure risk relative to residence-level data for outdoor LAN. The DNB data are far superior to DMSP [30] because of the higher resolution (~750 m compared to ~5 km) of DNB, lack of saturation in urban areas, and the fact that DNB is radiometrically calibrated while DMSP is not. The DMSP overpass time was centered around 7:30pm, which restricts data to winter months at high latitudes, whereas DNB is acquired around 1:30 am. Monthly cloud-free VIIRS DNB mosaics for September-December 2012 were downloaded from the National Oceanic and Atmospheric Administration and combined by taking the mean at each study location (values were not interpolated within pixels). The DMSP data are from the annual "radiometrically calibrated" product for 2010. Both datasets are reported in units of $nW/cm^2/sr$, but the DMSP is not a calibrated radiometer. Both instruments are sensitive to light in the wavelength range 500-900nm, notably excluding wavelengths near the peak sensitivity for circadian disruption [31]. While DNB data are considered superior to DMSP data [32], DMSP data were also included since this source allows for comparison with other studies. For DNB data, 2012 was chosen because it was the earliest year for which these data are available. For DMSP data, 2010 was chosen because this is a similar time period as the DNB data, and these data were radiometrically calibrated. Since street lighting tended to be fairly stable during the period 1990-2012 [32, 33], the use of earlier data would produce presumably similar LAN values.

Addresses within Canada were geocoded to longitude-latitude coordinates using the Google Maps database and an app available through Google (Geocode by Awesome Table), and the coordinates were then used to extract DNB and DMSP measurements from the calibrated image data. Two cumulative average outdoor LAN exposures using DMSP and DNB data were calculated across participants' residential histories for the exposure time window from 5 to 20 years before study entry. Participants were eligible for inclusion if they had at least one useable address for a minimum of 5 years of residential history within the 5-20 year time window before study enrollment. If a participant lived in multiple residences over this 15-year period, weighted average LAN exposures were calculated based on the length of time the participant spent at each address.

Breast tumor biomarker assessment

Estrogen receptor (ER) and progesterone receptor (PR) tumor biomarker status was obtained from the BC Cancer Breast Cancer Outcomes Unit in Vancouver, and obtained from electronic medical records in Kingston for all breast cancer cases. ER and PR status was determined by immunohistochemistry and classified into one of six categories: 1) negative, 2) weakly positive, 3) moderately positive, 4) strongly positive, 5) not sufficient quantity for interpretation or borderline/equivocal and 6) not tested. ER and PR status were considered positive if immunohistochemistry results classified tumors as weakly, moderately, or strongly positive.

Covariates

Participants completed a questionnaire including sociodemographic characteristics (e.g. education, ethnicity), past and current health (e.g. medical and reproductive history, family history of cancer), lifestyle characteristics (e.g. lifetime tobacco and alcohol consumption), and occupational histories (e.g. shift work). Women were considered post-menopausal at the time of study entry if: 1) menstruation had stopped for more than one year, 2) menstruation had stopped naturally, they were over 50 years of age, and time since last menstruation was unavailable, 3) they had a bilateral oophorectomy; or 4) they were over age 55 years and menstruation stopped due to other reasons (e.g. chemotherapy) [34]. Night work was defined as a work schedule that included at least three hours of work between midnight and 5:00AM [35, 6]. Participants who reported working this schedule for a minimum of six months were classified as exposed to night work (i.e. ever exposed), while those who reported not working within these hours were classified as never exposed to night work; this included both day workers and non-workers. Median household income and population density (per km^2) were obtained by linking participants' addresses to the 2006 Canadian Census at the census tract for residences in cities, and census agglomeration for residences in rural areas. An average time-weighted measure of median household income and population density was estimated for residential histories of each participant 5-20 years prior to study entry. Census data from 2006 were used since it was the nearest data available chronologically, prior to study completion in 2010.

Exclusion criteria

Of the 2313 participants (1134 cases, 1179 controls) eligible for enrollment from both study centers, 1749 participants were included in this analysis. Participants were primarily excluded if no residential history was provided for the 15-year exposure window (n=59). For the remaining 2254 participants, 6049 addresses were provided in this 15-year period, and 1107 residential addresses without a street address were considered as missing, therefore 167 participants were excluded. Addresses outside of Canada (n=258), in the province of Newfoundland (not available in the 60-180W data tile used, n=5), and that did not exist according to the Google Maps database (n=73) were also excluded, further excluding 53 participants. Of the remaining 2034 participants, 185 were excluded since they did not have at least 5 years of residential data available during the 15-year exposure window period. Finally, 100 participants were excluded due to missing covariate data, with a total of 1749 participants and 3575 addresses included in this analysis (844 cases, 905 controls).

Statistical Analysis

Multivariable unconditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between outdoor LAN and breast cancer risk. Separate models were run for LAN using DMSP and DNB data, and outdoor LAN was analyzed as categorical variables using tertiles of LAN based on the distribution among controls. Confounders were determined *a priori*, and included: age (continuous), ethnicity (Caucasian/Asian/other), family history of breast cancer (yes/no), menopausal status (pre-/post-

menopausal), age at menarche (continuous), body mass index (BMI, continuous), household income (not-stated/≤$30,000/$30,000-$59,000/$60,000-$99,999/≥$100,000), education (completed high school/post-secondary/university or above), parity and age at first birth (nulliparous/1-2 births and <30 years old/1-2 births and ≥30 years old/3-4 births and <30 years old/3-4 births and ≥30 years old/≥5 births and any age), years of oral contraceptive use (none/>0-4.49/4.5-10/>10), age at first mammography screening (continuous), smoking status (current/past/never), average alcoholic drinks/week during adulthood (continuous), and night work status (ever/never). Area-level socioeconomic status was accounted for by adjusting for time-weighted median neighborhood income during the 5-20 year time period across residences (tertiles based on the distribution among controls) and time-weighted average neighborhood population density across residences (continuous). Differences between hormone receptor subtypes was evaluated in a case-only analysis, where hormone receptor status was classified either ER and/or PR-positive, or ER and PR-negative.

Possible effect modification by menopausal status on the relationship between outdoor LAN and breast cancer risk was assessed by including an interaction term. We also examined potential effect modification by night work status in the association between LAN and breast cancer using an interaction term, while stratifying by menopausal status. Sensitivity analyses were conducted that considered two other exposure time windows: 20-year exposure time window from 5-years to 25-years before study entry; and 25-year time window from 5-years to 30-years before study entry. The influence of years of residential history was tested by restricting analyses to participants who had 10 or more years of residential data available within the exposure window, and we tested whether lower residential mobility during the 15-year period may influence our findings in a sensitivity analysis: since most participants reported living at one or two residences during the 15-year period, we excluded those who reported three or more residences during the 15-year period for this analysis. It is also possible that differences may exist by the urbanicity of the residences included, since light levels are generally lower in more rural areas. We therefore tested for effect modification by population density (divided into tertiles) using an interaction term in a sensitivity analysis.

Results

Characteristics of the study population are described in Table 1. Cases and controls were similar in age, and had a similar proportion of pre-menopausal women. Both case and control groups were comprised predominately of Caucasian ethnicity, although cases had a lower proportion of Caucasians than controls (69% vs. 82%, respectively) and had a higher proportion of Asians (22% vs. 12%, respectively). Cases were also more likely to have a family history of breast cancer, less likely to have a university degree or higher, and less likely to have a household income ≥$100,000 in comparison to controls. There was no strong difference in the proportion of night workers, the proportion of current smokers, neighborhood income level, or mean BMI between cases and controls.

Most participants lived at one or two residences during the 5-20 year time period (median of two residences, maximum of 11 residences reported). Characteristics of light measures by city and case/control status are shown in Table 2. For LAN measures derived from DNB data, Vancouver participants had considerably higher cumulative average outdoor LAN levels, with a mean of 31 nW/cm^2/sr (SD: 15) than Kingston participants who had a mean of 18 nW/cm^2/sr (SD: 15). A greater difference was seen for LAN measures derived from DMSP data, where Vancouver participants had over two times higher cumulative average of outdoor LAN levels compared to Kingston participants [166 nW/cm^2/sr (SD: 74) vs. 73 nW/cm^2/sr (SD: 75), respectively]. For both DNB and DMSP measurements, cumulative average LAN values were similar between cases and controls. This large difference in radiance between DNB and DMSP is not surprising, given that DMSP is not calibrated and the data are only acquired at these high latitude locations during winter months.

Estimated associations between cumulative average outdoor LAN and breast cancer are shown in Table 3. There was no apparent association between LAN and breast cancer, and no difference by hormone receptor biomarker status for either DNB (p-value=0.25) or DMSP (p-value=0.32) models (results not shown). Estimated associations between cumulative average outdoor LAN, menopausal status, and breast cancer risk are shown in Table 4. There was no association between LAN and breast cancer risk when considering an interaction for menopausal status, and the interaction was not statistically significant.

Estimated associations between cumulative average outdoor LAN, night work status, and breast cancer risk stratified by menopausal status are shown in Table 5. We found no association between LAN and breast cancer among pre- or post-menopausal night workers or never night workers, for either DMSP and DNB. Among post-menopausal women, an interaction between LAN and night work status neared statistical significance (p=0.05),

although 95% confidence intervals for the effect of LAN included 1.0 among both night workers and those who never worked at night.

In sensitivity analyses, there was no apparent relationship between outdoor LAN and breast cancer when considering the 20-year exposure window 5-25 years before study entry, or the 25-year exposure window 5-30 years before study entry (see Supplementary Materials). Restricting our analysis to participants who had 10 years or more of residential data available for the 5-20 year period before study entry also did not change the original findings (see Supplementary Materials). Excluding participants who reported living at three or more residences during 5-20 years before study entry did not change findings, and there was no difference in the association between LAN and breast cancer by population density (divided into tertiles) for either DNB or DMSP measures (results not shown).

Discussion

We found no overall association between outdoor LAN and breast cancer in this study in Canada. We also found no association when considering menopausal status and night shift work status as effect modifiers in the relationship. Our findings did not change when considering the influence of population density (as a proxy for urban/rural status), residential mobility, or longer exposure windows.

Some previous studies have found small increases in breast cancer risk in relation to the measures used to estimate outdoor ambient LAN. A case-control study in Georgia, U.S., found that higher LAN exposure (>41 $nW/cm^2/sr$) as measured through DMSP was associated with a 12% higher risk of breast cancer compared with the lowest LAN exposure (<20 $nW/cm^2/r$) (95% CI: 1.04-1.20) [23]. Another study among a cohort of California school teachers with no night workers found that women living in the highest quintile of LAN (as measured using DMSP, range: 53–175 $nW/cm^2/sr$) compared with the lowest quintile (range: 0–14 $nW/cm^2/sr$) had a 12% higher risk of breast cancer (95% CI: 1.00-1.26) [25]. In both studies, LAN exposure was estimated at only one residence which may not accurately reflect exposure over time. Further, the study in Georgia used the residence at time of breast cancer diagnosis, which fails to capture LAN exposure during the hypothesized etiologic window.

A case-control study in Spain examining outdoor LAN and breast cancer risk used high resolution LAN exposure data from photographs taken by the International Space Station at the residence with the longest duration for each study participant, with no apparent relationship between outdoor LAN and breast cancer risk (third vs. first tertile OR: 0.81, 95% CI: 0.54-1.20) [26]. However, outdoor LAN in the blue light spectrum only was associated with 47% higher risk of breast cancer (95% CI: 1.00-2.17) comparing the highest to the lowest tertile. The Nurses' Health Study II improved on other studies by using time-varying cumulative average outdoor LAN from multiple residences: they found that LAN was associated with a 5% increase in breast cancer risk (95% CI: 1.00-1.11) for every one-interquartile range increase in LAN exposure.

We found no evidence that night shift work or menopausal status has a synergistic effect in the relationship between outdoor LAN and breast cancer, similar to the case-control study in Spain that found no evidence that menopausal status or hormone receptor status modifies the relationship [26]. Conversely, in the Nurses' Health Study II, the association between outdoor LAN and breast cancer risk was limited to pre-menopausal women (HR: 1.20; 95% CI: 1.07-1.41), comparing the highest vs. the lowest LAN quintile in mainly ER+ breast cancer cases, and this association was not seen for post-menopausal women (HR: 0.95; 95%: CI: 0.78-1.15) (p-value for interaction = 0.08) [24]. The California Teachers' Study also reported that the association may be limited to pre-menopausal women [25], and, similar to our study, they did not find differences by tumor hormone receptor status. However, this could be due to small numbers of ER/PR negative cases in the California Teachers' Study, similar to our study. The Nurses' Health Study II also found that night shift workers exposed to higher LAN levels may be at a higher risk of breast cancer: comparing the highest vs. the lowest LAN quintile, past and current night shift workers had a 29% higher risk of breast cancer (95% CI: 1.06-1.56), and this elevated risk was not seen in day workers (HR: 1.04, 95% CI: 0.90-1.20) (p-value for interaction = 0.10).

There are some differences in the study populations across the few studies that have investigated this relationship. Other studies have examined the association between outdoor LAN and breast cancer at latitudes closer to the equator where outdoor natural light allows extended outdoor activity later into the evening. As hypothesized by Boris Portnov, people living at higher latitudes may be less likely to be outdoors in the evening and nighttime because of earlier darkness compared to lower latitude locations [36]. In Canada, this would mean that we would expect a weaker association or no association, even if there is a relationship at locations closer to

the equator. Another difference in study population is the Nurses' Health Study II has a high prevalence (>42%) of night shift workers in their sample [24], compared to our study with a prevalence of 18%.

Regarding a possible interaction with menopausal status that was found in the Nurses' Health Study, although we found slightly higher effect estimates among pre-menopausal night shift workers (OR's ranging from 1.43-2.11), none was statistically significant. We cannot rule out that an association between outdoor LAN and breast cancer does exist, and that our analysis failed to these detect small effect sizes. Future studies with larger samples sizes are needed to investigate the relationship between LAN and breast cancer, particularly when considering interactions.

In our study, LAN measures derived from DMSP and DNB data produced similar findings when investigating the link between outdoor LAN and breast cancer. This finding is different than that reported by an ecologic study in Israel where DNB measures were a better predictor of breast cancer incidence in geographic areas with higher LAN in comparison to DMSP measures [21]. However, due to the ecologic design in that study, they could not measure LAN exposure at a specific participant's residence, considered to be a better surrogate of outdoor nighttime light exposure [15], nor could they adjust for individual-level confounders. LAN measures derived from DMSP data have been criticized for the problem of saturation in the brightest parts of cities, and inability to capture individual-level exposure which leads to risk of conflation with other urban factors, such as noise and air pollution [33, 32]. While our findings indicate DMSP and DNB provide similar measures of LAN exposure, this may be a consequence of grouping the data into tertiles, rather than using a continuous scale.

In addition, it is unclear how outdoor nighttime light measures derived from DMSP and DNB data correlate to personal LAN exposure. Personal LAN exposure reflects the amount of light that falls onto a persons' retina at nighttime [15]. Higher resolution LAN data may be a better surrogate for individual-level LAN exposure (e.g. light intrusion into the home) [33], whereas lower resolution LAN data (including to some extent DNB but especially DMSP) measure degree of "urbanness." In addition, our study did not have information on factors such as bedroom placement in the home, curtain type, and use of sleep masks, so it is unclear how LAN protection behaviors such as black-out curtains and use of sleep masks may have influenced our findings. It is also unclear if outdoor LAN from either data source can be used as an accurate proxy for personal LAN exposure [16]. More work is needed assess the relationship between satellite-measured LAN levels and personal LAN levels [32].

Our study investigated the relationship between outdoor LAN and breast cancer risk using LAN measures that characterize brightness. Artificial LAN contains light with different spectra and intensities [37]. Experimental studies indicate that different spectrums and intensities of light, particularly blue light, differentially impact melatonin production and circadian rhythms, and may therefore differentially impact carcinogenesis [10]. Garcia-Saenz and colleagues found that exposure to outdoor LAN in the blue light spectrum was associated with a 47% higher risk of breast cancer (95% CI: 1.00-2.17) when comparing the highest to the lowest tertile of LAN exposure. Future studies should aim to better understand the relationship between spectral parameters of outdoor LAN and breast cancer risk, particularly in terms of light in the blue spectrum. This also highlights the need for future night light observing satellites to have measure radiance in multiple spectral bands.

This study has a number of strengths. This is the first study to our knowledge to examine the relationship between outdoor LAN and breast cancer in women living at a higher latitude than previous studies. Outdoor LAN at residences was measured objectively using satellite data over a 15-year period before study entry, accounting for time-varying residence data. This allowed us to capture a cumulative average LAN exposure at participants' residences over a 15-year period, more accurately reflecting exposure over time. Our study was also strengthened by the use of LAN data retrieved from DNB data which has higher spatial resolution and is radiance calibrated, and is therefore more likely to correlate with individual-level data. However, because the resolution is 750m, it is still likely to be correlated to some extent with other urban factors such as noise and air pollution [32, 33]. We were also able to adjust for individual-level confounders, including many established and suspected breast cancer risk factors, and neighborhood-level confounders. Finally, our study was also strengthened by examining how residential mobility, total years of residential history available, and population density (as a proxy for urban/rural status) may influence our findings.

Our study has some limitations including the potential for exposure misclassification. While residence information was captured in the hypothesized etiologic window, we used satellite images from 2010/2012 to estimate LAN exposure and extrapolated this to residential histories of participants. Since outdoor LAN was not measured during the hypothesized etiologic window, exposure misclassification is possible, although it is likely to be non-differential. Since street lighting tended to be fairly stable during the period 1990-2012, use of earlier

images would produce presumably similar results [33, 32]. In addition, there is potential for participants who were excluded due to missing exposure or residential data to differ from those included, although this is unlikely to be related to the outcome of breast cancer. When examining differences in characteristics of the study population, we found no strong difference between participants who were excluded vs. those included, with the exception that more participants were excluded from the Vancouver centre. A similar proportion of cases and controls were excluded. There is also potential for selection bias during recruitment, where people who lived in neighborhoods with higher LAN exposure may have been less likely to be included in the study. If this is also related to breast cancer, there is potential for selection bias, although we hypothesize it would attenuate our effect estimates to the null. It is also unclear how outdoor LAN captured in this study may correlate with personal LAN exposure [15], and how higher resolution data (i.e. DNB data) and lower resolution data (i.e. DMSP data) may differ as a surrogate for personal LAN exposure. Also, we were unable to control for or exclude controls diagnosed with benign breast disease, a risk factor for breast cancer. Due to our small sample size in sub-groups, we were underpowered to detect interactions with menopausal status, night work, and hormone receptor breast cancer. Finally, there is potential for uncontrolled and residual confounding. While we adjusted for neighborhood-level confounders, we may not have fully accounted for the effect of these confounders on the relationship, and we cannot rule out the possibility that other unmeasured confounders that are correlated with outdoor LAN (e.g. air pollution, noise pollution, etc.) may explain our findings.

Conclusions

Our findings are consistent that outdoor LAN has a small or no effect on the breast cancer risk. More research is needed to better understand the link between ambient LAN, including spectral parameters, and breast cancer while considering breast cancer subtype, menopausal status, and night work.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Funding: This study was funded by the Canadian Institutes of Health Research (CIHR) (grant number 69036), Breast Cancer Action Kingston (grant number 70125) , the European Union's Horizon 2020 research and innovation programme ERA-PLANET (grant number 689443), via the GEOEssential project, and the Helmholtz Association Initiative and Networking Fund (grant number ERC-RA-0031).

Conflict of Interest: The authors declare that they have no conflict of interest.

REFERENCES

1. Kyba CCM, Kuester T, Sánchez de Miguel A, Baugh K, Jechow A, Hölker F et al. Artificially lit surface of Earth at night increasing in radiance and extent. Sci Adv. 2017;3(11):e1701528.
2. Falchi F, Cinzano P, Duriscoe D, Kyba CCM, Elvidge CD, Baugh K et al. The new world atlas of artificial night sky brightness. Sci Adv. 2016;2(6):e1600377.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893-917.
4. Stevens RG. Electric power use and breast cancer: a hypothesis. Am J Epidemiol. 1987;125(4):556-61.
5. International Agency for Research on Cancer (IARC). Painting, firefighting, and shiftwork. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol 98. Lyon, France: International Agency for Research on Cancer; 2010.
6. Ward EM, Germolec D, Kogevinas M, McCormick D, Vermeulen R, V.N. A et al. Carcinogenicity of night shift work. Lancet Oncol. 2019;20(8):1058-9.
7. U.S. National Toxicology Program (NTP). Draft report on carcinogens monograph on night shift work and light at night. National Toxicology Program, U.S. Department of Health and Human Services. 2018.
8. Haim A, Zubidat AE. Artificial light at night: melatonin as a mediator between the environment and epigenome. Philos Trans R Soc Lond B Biol Sci. 2015;370(1667):pii: 20140121.
9. Schernhammer ES, Schulmeister K. Melatonin and cancer risk: does light at night compromise physiologic cancer protection by lowering serum melatonin levels? Br J Cancer. 2004;90(5):941-3.
10. Zubidat AE, Fares B, Fares F, Haim A. Artificial light at night of different spectral compositions differentially affects tumor growth in mice: interaction with melatonin and epigenetic pathways. Cancer Control. 2018;25(1):1073274818812908.
11. Blask DE, Dauchy RT, Dauchy EM, Mao L, Hill SM, Greene MW et al. Light exposure at night disrupts host/cancer circadian regulatory dynamics: impact on the Warburg effect, lipid signaling and tumor growth prevention. PLoS One. 2014;9(8):e102776.
12. Ouyang JQ, Davies S, Dominoni D. Hormonally mediated effects of artificial light at night on behavior and fitness: linking endocrine mechanisms with function. J Exp Biol. 2018;221(Pt 6):pii: jeb156893.
13. Stevens RG. Light-at-night, circadian disruption and breast cancer: assessment of existing evidence. Int J Epidemiol. 2009;38(4):963-70.
14. Cos S, Gonzalez A, Martinez-Campa C, Mediavilla MD, Alonso-Gonzalez C, Sanchez-Barcelo EJ. Estrogen-signaling pathway: a link between breast cancer and melatonin oncostatic actions. Cancer Detect Prev. 2006;30(2):118-28.
15. Stevens RG. Testing the light-at-night (LAN) theory for breast cancer causation. Chronobiol Int. 2011;28(8):653-6.
16. Huss A, van Wel L, Bogaards L, Vrijkotte T, Wolf L, Hoek G et al. Shedding some light in the dark-a comparison of personal measurements with satellite-based estimates of exposure to light at night among children in the Netherlands. Environ Health Perspect. 2019;127(6):67001.
17. Blask DE, Brainard GC, Dauchy RT, Hanifin JP, Davidson LK, Krause JA et al. Melatonin-depleted blood from premenopausal women exposed to light at night stimulates growth of human breast cancer xenografts in nude rats. Cancer Res. 2005;65(23):11174-84.
18. Keshet-Sitton A, Or-Chen K, Huber E, Haim A. Illuminating a risk for breast cancer: a preliminary ecological study on the association between streetlight and breast cancer. Integr Cancer Ther. 2017;16(4):451-63.
19. Kloog I, Stevens RG, Haim A, Portnov BA. Nighttime light level co-distributes with breast cancer incidence worldwide. Cancer Causes Control. 2010;21(12):2059-68.
20. Kloog I, Haim A, Stevens RG, Barchana M, Portnov BA. Light at night co-distributes with incident breast but not lung cancer in the female population of Israel. Chronobiol Int. 2008;25(1):65-81.

21. Rybnikova NA, Portnov BA. Outdoor light and breast cancer incidence: a comparative analysis of DMSP and VIIRS-DNB satellite data. Int J Remote Sens. 2017;38(21):5952-61.
22. Kim YJ, Lee E, Lee HS, Kim M, Park MS. High prevalence of breast cancer in light polluted areas in urban and rural regions of South Korea: an ecologic study on the treatment prevalence of female cancers based on National Health Insurance data. Chronobiol Int. 2015;32(5):657-67.
23. Bauer SE, Wagner SE, Burch J, Bayakly R, Vena JE. A case-referent study: Light at night and breast cancer risk in Georgia. Int J Health Geogr. 2013;12::23.
24. James P, Bertrand KA, Hart JE, Schernhammer ES, Tamimi RM, Laden F. Outdoor light at night and breast cancer incidence in the Nurses' Health Study II. Environ Health Perspect. 2017;125(8):087010.
25. Hurley S, Goldberg D, Nelson D, Hertz A, Horn-Ross PL, Bernstein L et al. Light at night and breast cancer risk among California teachers. Epidemiology. 2014;25(5):697-706.
26. 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;126(4):047011.
27. Lunn RM, Blask DE, Coogan AN, Figueiro MG, Gorman MR, Hall JE et al. Health consequences of electric lighting practices in the modern world: A report on the National Toxicology Program's workshop on shift work at night, artificial light at night, and circadian disruption. Sci Total Environ. 2017;607-608:1073-84.
28. Kubatka P, Zubor P, Busselberg D, Kwon TK, Adamek M, Petrovic D et al. Melatonin and breast cancer: Evidences from preclinical and human studies. Crit Rev Oncol Hematol. 2018;122:133-43.
29. 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;33(4):369-79.
30. Miller SD, Straka W, Mills SP, Elvidge CD, Lee TF, Solbrig J et al. Illuminating the capabilities of the Suomi National Polar-Orbiting Partnership (NPP) Visible Infrared Imaging Radiometer Suite (VIIRS) Day/Night Band. Remote Sensing. 2013;5(12):6717-66.
31. Lucas RJ, Peirson SN, Berson DM, Brown TM, Cooper HM, Czeisler CA et al. Measuring and using light in the melanopsin age. Trends in neurosciences. 2014;37(1):1-9.
32. Kyba CCM, Aronson KJ. Assessing exposure to outdoor lighting and health risks. Epidemiology. 2015;26(4):e50.
33. Kyba CCM. Defense Meteorological Satellite Program data should no longer be used for epidemiological studies. Chronobiology Int. 2016;33(8):943-5.
34. Friedenreich CM, Courneya KS, Bryant HE. Influence of physical activity in different age and life periods on the risk of breast cancer. Epidemiology. 2001;12(6):604-12.
35. 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;68(2):154-62.
36. Portnov BA, Stevens RG, Samociuk H, Wakefield D, Gregorio DI. Light at night and breast cancer incidence in Connecticut: An ecological study of age group effects. Sci Total Environ. 2016;572:1020-4.
37. Aubé M, Roby J, Kocifaj M. Evaluating Potential Spectral Impacts of Various Artificial Lights on Melatonin Suppression, Photosynthesis, and Star Visibility. PLoS One. 2013;8(7):e67798.

Tables

Table 1: Characteristics of study population (mean (SD) or count (%)).

Characteristic	Cases (n=844)	Controls (n=905)
City		
Vancouver, BC	736 (87.2)	781 (86.3)
Kingston, ON	108 (12.8)	124 (13.7)
Age (years)	58.3 (10.0)	57.5 (9.8)
Menopausal status		
Pre-menopausal	263 (31.2)	326 (36.0)
Post-menopausal	581 (68.8)	579 (64.0)
Ethnicity		
Caucasian	581 (68.8)	742 (82.0)
Asian	186 (22.0)	112 (12.4)
Other	77 (9.1)	51 (5.6)
Household income (in Canadian $)		
Not stated	100 (11.9)	125 (13.8)
<$30,000	118 (14.0)	80 (8.8)
$30,000-$59,999	209 (24.8)	196 (21.7)
$60,000-$99,999	208 (24.6)	219 (24.2)
≥$100,000	209 (24.8)	285 (31.5)
Education		
High school diploma or less	294 (34.8)	240 (26.5)
College/trade certificate	265 (31.4)	268 (29.6)
University degree or higher	285 (33.8)	397 (43.9)
Family history of breast cancer		
Yes	179 (21.2)	126 (13.9)
No	665 (78.8)	779 (86.1)
BMI (kg/m^2)	25.9 (5.6)	25.3 (5.8)
Parity & age at first birth		
Nulliparous	146 (17.3)	187 (20.7)
1-2 births and <30 years old	214 (25.4)	224 (24.8)
1-2 births and ≥30 years old	139 (16.5)	115 (12.7)
3-4 births and <30 years old	198 (23.5)	225 (24.9)
3-4 births and ≥30 years old	85 (10.1)	83 (9.2)
≥5 births and any age	62 (7.4)	71 (7.9)
Number of years of oral contraceptive use		

None	377 (44.7)	316 (34.9)
<4.5	157 (18.6)	194 (21.4)
4.5-10.0	173 (20.5)	211 (23.3)
≥10.0	137 (16.2)	184 (20.3)
Age at first mammography (years)	44.6 (8.5)	43.1 (7.2)
Age at menarche (years)	12.9 (1.6)	12.8 (1.5)
Night work status		
Never	693 (82.1)	740 (81.8)
Ever	151 (17.9)	165 (18.2)
Smoking status		
Never	491 (58.2)	526 (58.1)
Past	302 (35.8)	332 (36.7)
Current	51 (6.0)	47 (5.2)
Average alcoholic drinks/week during adulthood	3.1 (4.5)	3.9 (5.5)
Average population density (per KM^2)	4558.9 (3860.4)	5099.2 (4423.9)
Average neighborhood income (in Canadian $)		
Tertile 1	287 (34.0)	302 (33.4)
Tertile 2	275 (32.6)	301 (33.3)
Tertile 3	282 (33.4)	302 (33.4)

BC, British Columbia; BMI, body mass index; KM, kilometer; ON, Ontario.

Table 2: Characteristics of light measures, by recruitment city and case/control status.

Characteristic	n (n_{cases})	DNB (nW/cm^2/sr)	n (n_{cases})	DMSP (nW/cm^2/sr)
Total study population				
Mean (SD)	1749 (844)	29.15 (16.04)	1749 (844)	153.78 (80.79)
Range of Tertile 1	597 (296)	0.00 – 22.07	598 (296)	0.00 – 123.05
Range of Tertile 2	590 (288)	22.08 – 32.79	625 (325)	123.10 – 194.62
Range of Tertile 3	562 (260)	32.83 – 149.47	526 (223)	194.75 – 628.56
Vancouver – Mean (SD)				
Total	1517 (736)	30.91 (15.45)	1517 (736)	166.14 (74.27)
Cases only	736	30.46 (14.44)	736	161.63 (71.55)
Controls only	781	31.32 (16.35)	781	170.38 (76.56)
Kingston – Mean (SD)				
Total	232 (108)	17.67 (15.05)	232 (108)	72.95 (75.00)
Cases only	108	16.48 (12.63)	108	67.58 (63.40)
Controls only	124	18.71 (16.85)	124	77.63 (83.79)

DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; SD, standard deviation.

Table 3. Fully-adjusted logistic regression models examining the relationship between LAN exposure and risk of breast cancer.

Measure	Exposure	n (n_{cases})	OR (95% CI)[a]
DNB	Tertile 1	597 (296)	Ref.
	Tertile 2	590 (288)	0.97 (0.75, 1.26)
	Tertile 3	562 (260)	0.95 (0.70, 1.27)
DMSP	Tertile 1	598 (296)	Ref.
	Tertile 2	625 (325)	1.05 (0.82, 1.34)
	Tertile 3	526 (223)	0.83 (0.63, 1.09)

[a]All models adjusted for age, ethnicity, menopausal status, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio.

Table 4. Fully-adjusted models examining the impact of menopausal status on the relationship between LAN exposure and risk of breast cancer.

		Pre-menopausal		Post-menopausal		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	165 (73)	Ref.	432 (223)	Ref.	0.61
	Tertile 2	189 (89)	1.17 (0.75, 1.84)	401 (199)	0.90 (0.67, 1.22)	
	Tertile 3	235 (101)	1.06 (0.68, 1.67)	327 (159)	0.90 (0.64, 1.27)	
DMSP	Tertile 1	172 (77)	Ref.	426 (219)	Ref.	0.90
	Tertile 2	223 (116)	1.13 (0.74, 1.73)	392 (209)	1.01 (0.76, 1.36)	
	Tertile 3	184 (70)	0.85 (0.53, 1.34)	342 (153)	0.82 (0.60, 1.14)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio

Table 5. Fully-adjusted models examining the impact of night work status on the relationship between LAN exposure and risk of breast cancer, stratified by menopausal status.

		Pre-menopausal night worker		Pre-menopausal never night worker[b]			Post-menopausal night worker		Post-menopausal never night worker[b]		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	28 (12)	Ref.	137 (61)	Ref.	0.81	80 (38)	Ref.	352 (185)	Ref.	0.05
	Tertile 2	32 (18)	1.43 (0.47, 4.31)	157 (71)	1.13 (0.66, 1.94)		55 (21)	0.70 (0.33, 1.47)	346 (178)	0.93 (0.66, 1.29)	
	Tertile 3	67 (31)	1.52 (0.55, 4.16)	168 (70)	1.06 (0.59, 1.92)		54 (31)	1.65 (0.75, 3.62)	273 (128)	0.76 (0.52, 1.12)	
DMSP	Tertile 1	33 (12)	Ref.	139 (65)	Ref.	0.24	83 (40)	Ref.	343 (179)	Ref.	0.61
	Tertile 2	46 (28)	2.11 (0.77, 5.74)	187 (88)	0.89 (0.53, 1.47)		58 (32)	1.38 (0.67, 2.84)	334 (177)	0.98 (0.71, 1.35)	
	Tertile 3	48 (21)	1.57 (0.58, 4.28)	136 (49)	0.70 (0.39, 1.27)		48 (18)	0.78 (0.35, 1.71)	294 (135)	0.82 (0.57, 1.17)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, average alcoholic drinks/week, average population density, and average neighborhood income.

[b]Includes both day workers and non-workers

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio

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Supplementary Tables

Table S1: Characteristics of light measures for exposure time window 5-25 years before study entry.

Characteristic	n (n_{cases})	DNB ($nW/cm^2/sr$)	n (n_{cases})	DMSP ($nW/cm^2/sr$)
Total study population				
Mean (SD)	1770 (853)	29.47 (15.59)	1770 (853)	155.58 (81.37)
Range of Tertile 1	597 (291)	0.00 – 22.61	596 (290)	0.00 – 122.84
Range of Tertile 2	600 (294)	22.61 – 32.78	633 (327)	122.90 – 193.77
Range of Tertile 3	573 (268)	32.79 – 161.95	541 (236)	193.84 – 654.07

DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; SD, standard deviation.

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Table S2. Fully-adjusted logistic regression models examining the relationship between LAN exposure and risk of breast cancer, for exposure time window 5-25 years before study entry.

Measure	Exposure	n (n_{cases})	OR (95% CI)[a]
DNB	Tertile 1	597 (291)	Ref.
	Tertile 2	600 (294)	0.99 (0.77, 1.28)
	Tertile 3	573 (268)	0.96 (0.72, 1.29)
DMSP	Tertile 1	596 (290)	Ref.
	Tertile 2	633 (327)	1.10 (0.86, 1.40)
	Tertile 3	541 (236)	0.89 (0.67, 1.17)

[a]All models adjusted for age, ethnicity, menopausal status, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

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Table S3. Fully-adjusted models examining the impact of menopausal status on the relationship between LAN exposure and risk of breast cancer, for exposure time window 5-25 years before study entry.

		Pre-menopausal		Post-menopausal		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	160 (67)	Ref.	437 (224)	Ref.	0.34
	Tertile 2	202 (96)	1.30 (0.83, 2.04)	398 (198)	0.88 (0.66, 1.19)	
	Tertile 3	236 (102)	1.13 (0.72, 1.78)	337 (166)	0.90 (0.64, 1.27)	
DMSP	Tertile 1	182 (78)	Ref.	414 (212)	Ref.	0.83
	Tertile 2	232 (115)	1.22 (0.80, 1.85)	401 (212)	1.04 (0.78, 1.40)	
	Tertile 3	184 (72)	0.93 (0.59, 1.46)	357 (164)	0.87 (0.63, 1.21)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

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Table S4. Fully-adjusted models comparing LAN exposure to risk of breast cancer by night work status, stratified by menopausal status, for exposure time window 5-25 years before study entry.

		Pre-menopausal night worker		Pre-menopausal never night worker[b]			Post-menopausal night worker		Post-menopausal never night worker[b]		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	28 (12)	Ref.	132 (55)	Ref.	0.83	82 (37)	Ref.	355 (187)	Ref.	0.16
	Tertile 2	36 (21)	1.68 (0.58, 4.89)	166 (75)	1.19 (0.69, 2.05)		55 (24)	0.92 (0.44, 1.95)	343 (174)	0.85 (0.61, 1.18)	
	Tertile 3	63 (28)	1.29 (0.47, 3.53)	173 (74)	1.17 (0.64, 2.11)		53 (30)	1.64 (0.75, 3.57)	284 (136)	0.76 (0.52, 1.12)	
DMSP	Tertile 1	37 (14)	Ref.	145 (64)	Ref.	0.30	82 (39)	Ref.	332 (173)	Ref.	0.33
	Tertile 2	44 (28)	2.37 (0.88, 6.36)	188 (87)	1.00 (0.60, 1.67)		57 (33)	1.65 (0.80, 3.42)	344 (179)	0.96 (0.69, 1.33)	
	Tertile 3	46 (19)	1.30 (0.49, 3.47)	138 (53)	0.84 (0.47, 1.50)		51 (19)	0.84 (0.39, 1.83)	306 (145)	0.86 (0.60, 1.23)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, average alcoholic drinks/week, average population density, and average neighborhood income.

[b]Includes both day workers and non-workers.

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio

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Table S5: Characteristics of light measures, for exposure time window 5-30 years before study entry.

Characteristic	n (n_{cases})	DNB (nW/cm^2/sr)	n (n_{cases})	DMSP (nW/cm^2/sr)
Total study population				
Mean (SD)	1786 (862)	29.59 (15.52)	1786 (862)	156.99 (80.85)
Range of Tertile 1	617 (310)	0.00 – 23.14	614 (307)	0.00 – 126.75
Range of Tertile 2	568 (259)	23.17 – 32.26	619 (310)	127.09 – 191.37
Range of Tertile 3	601 (293)	32.26 – 172.91	553 (245)	191.53 – 654.07

DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; SD, standard deviation.

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Table S6. Fully-adjusted logistic regression models examining the relationship between LAN exposure and risk of breast cancer, for exposure time window 5-30 years before study entry.

Measure	Exposure	n (n_{cases})	OR (95% CI)[a]
DNB	Tertile 1	617 (310)	Ref.
	Tertile 2	568 (259)	0.81 (0.63, 1.04)
	Tertile 3	601 (293)	0.96 (0.72, 1.27)
DMSP	Tertile 1	614 (307)	Ref.
	Tertile 2	619 (310)	0.98 (0.77, 1.26)
	Tertile 3	553 (245)	0.84 (0.65, 1.10)

[a]All models adjusted for age, ethnicity, menopausal status, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio.

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Table S7. Fully-adjusted models examining the impact of menopausal status on the relationship between LAN exposure and risk of breast cancer, for exposure time window 5-30 years before study entry.

		Pre-menopausal		Post-menopausal		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	175 (81)	Ref.	442 (229)	Ref.	0.95
	Tertile 2	195 (83)	0.86 (0.55, 1.32)	373 (176)	0.79 (0.58, 1.07)	
	Tertile 3	237 (107)	0.97 (0.63, 1.50)	364 (186)	0.96 (0.69, 1.33)	
DMSP	Tertile 1	199 (90)	Ref.	415 (217)	Ref.	0.88
	Tertile 2	229 (107)	1.00 (0.67, 1.51)	390 (203)	0.98 (0.73, 1.31)	
	Tertile 3	179 (74)	0.92 (0.59, 1.43)	374 (171)	0.81 (0.59, 1.11)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

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Table S8. Fully-adjusted models comparing LAN exposure to risk of breast cancer by night work status, stratified by menopausal status, for exposure time window 5-30 years before study entry.

		Pre-menopausal night worker		Pre-menopausal never night worker[b]			Post-menopausal night worker		Post-menopausal never night worker[b]		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	P-value for interaction	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	32 (16)	Ref.	143 (65)	Ref.	0.99	82 (37)	Ref.	360 (192)	Ref.	0.09
	Tertile 2	39 (19)	0.81 (0.30, 2.22)	156 (64)	0.79 (0.47, 1.35)		53 (22)	0.74 (0.35, 1.58)	320 (154)	0.79 (0.56, 1.10)	
	Tertile 3	57 (27)	1.03 (0.39, 2.71)	180 (80)	1.00 (0.56, 1.76)		55 (32)	1.87 (0.86, 4.05)	309 (154)	0.84 (0.58, 1.21)	
DMSP	Tertile 1	42 (19)	Ref.	157 (71)	Ref.	0.83	82 (38)	Ref.	333 (179)	Ref.	0.17
	Tertile 2	42 (22)	1.17 (0.45, 3.00)	187 (85)	0.94 (0.57, 1.54)		56 (33)	1.87 (0.90, 3.90)	334 (170)	0.87 (0.63, 1.21)	
	Tertile 3	44 (21)	1.20 (0.47, 3.06)	135 (53)	0.87 (0.50, 1.53)		52 (20)	0.96 (0.45, 2.08)	322 (151)	0.77 (0.54, 1.10)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, average alcoholic drinks/week, average population density, and average neighborhood income.

[b]Includes both day workers and non-workers.

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Table S9. Fully-adjusted logistic regression models examining the relationship between LAN exposure and risk of breast cancer, including only participants who had residential histories of 10 or more years during the 5-20 years before study entry.

Measure	Exposure	n (n_{cases})	OR (95% CI)[a]
DNB	Tertile 1	516 (253)	Ref.
	Tertile 2	512 (249)	1.01 (0.77, 1.33)
	Tertile 3	491 (227)	1.01 (0.74, 1.39)
DMSP	Tertile 1	521 (258)	Ref.
	Tertile 2	547 (284)	1.04 (0.80, 1.34)
	Tertile 3	451 (187)	0.80 (0.59, 1.08)

[a]All models adjusted for age, ethnicity, menopausal status, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

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Table S10. Fully-adjusted models examining the impact of menopausal status on the relationship between LAN exposure and risk of breast cancer, including only participants who had residential histories of 10 or more years during the 5-20 years before study entry.

		Pre-menopausal		Post-menopausal		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	134 (56)	Ref.	382 (197)	Ref.	0.39
	Tertile 2	149 (71)	1.35 (0.82, 2.22)	363 (178)	0.91 (0.66, 1.24)	
	Tertile 3	193 (81)	1.17 (0.71, 1.92)	298 (146)	0.97 (0.67, 1.40)	
DMSP	Tertile 1	135 (57)	Ref.	386 (201)	Ref.	0.66
	Tertile 2	193 (96)	1.24 (0.78, 1.98)	354 (188)	0.96 (0.71, 1.31)	
	Tertile 3	148 (55)	0.89 (0.53, 1.49)	303 (132)	0.77 (0.55, 1.09)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, night work status, average alcoholic drinks/week, average population density, and average neighborhood income.

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Table S11. Fully-adjusted models comparing LAN exposure to risk of breast cancer by night work status, stratified by menopausal status, including only participants who had residential histories of 10 or more years during the 5-20 years before study entry.

		Pre-menopausal night worker		Pre-menopausal never night worker[b]			Post-menopausal night worker		Post-menopausal never night worker[b]		
Measure	Exposure	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	P-value for interaction	n (n_{cases})	OR (95% CI)[a]	n (n_{cases})	OR (95% CI)[a]	p-value for interaction
DNB	Tertile 1	22 (8)	Ref.	112 (48)	Ref.	0.44	74 (35)	Ref.	308 (162)	Ref.	0.05
	Tertile 2	25 (15)	2.61 (0.72, 9.52)	124 (56)	1.13 (0.62, 2.08)		49 (16)	0.54 (0.24, 1.21)	314 (162)	0.98 (0.69, 1.38)	
	Tertile 3	55 (26)	1.98 (0.62, 6.31)	138 (55)	0.98 (0.50, 1.93)		51 (28)	1.52 (0.68, 3.42)	247 (118)	0.86 (0.57, 1.30)	
DMSP	Tertile 1	26 (8)	Ref.	109 (49)	Ref.	0.15	76 (37)	Ref.	310 (164)	Ref.	0.50
	Tertile 2	37 (23)	2.79 (0.87, 9.00)	156 (73)	0.94 (0.53, 1.68)		51 (27)	1.16 (0.54, 2.48)	303 (161)	0.96 (0.68, 1.34)	
	Tertile 3	39 (18)	1.98 (0.62, 6.30)	109 (37)	0.62 (0.31, 1.23)		47 (15)	0.56 (0.24, 1.28)	256 (117)	0.81 (0.55, 1.19)	

[a]All models adjusted for age, ethnicity, family history of breast cancer, age at menarche, BMI, household income, education, parity and age at first birth, years of oral contraceptive use, age at first mammography screening, smoking status, average alcoholic drinks/week, average population density, and average neighborhood income.

[b]Includes both day workers and non-workers.

CI, confidence interval; DMSP; U.S. Defense Meteorological Satellite Program Operational Linescan System; DNB, Visible Infrared Imaging Radiometer Suite Day-Night Band; OR, odds ratio