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Prospective study of ultraviolet radiation exposure and risk of breast cancer in the United States

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Abstract

Although there are few environmental risk factors for breast cancer, some epidemiologic studies found that exposure to solar UV radiation (UVR) may lower risk. Prior epidemiologic studies are limited by narrow ambient UVR ranges and lack lifetime exposure assessment. To address these issues, we studied a cohort with residences representing a wide range of ambient UVR. Using the nationwide U.S. Radiologic Technologists study (USRT), we examined the association between breast cancer risk and UVR based on ambient UVR, time outdoors, a combined variable of ambient UVR and time outdoors (combined UVR), and sun susceptibility factors. Participants reported location of residence and hours spent outdoors during five age periods. Ambient UVR was derived by linking satellite-based annual UVR estimates to self-reported residences. Lifetime values were calculated by averaging these measures accounting for years spent in that location. We examined the risk of breast cancer among 36,725 participants (n= 716 cases) from baseline questionnaire completion (2003–2005) through 2012–2013 using Cox proportional hazards models. Breast cancer risk was unrelated to ambient UVR (HR for lifetime 5th vs 1st quintile = 1.22, 95% CI: 0.95–1.56, p-trend=0.36), time outdoors (HR for lifetime 5th vs 1st quintile = 0.87, 95% confidence interval (CI): 0.68–1.10, p-trend=0.46), or combined UVR (HR lifetime 5th vs 1st quintile = 0.85, 95% CI: 0.67–1.08, p-trend=0.46). Breast cancer risk was not associated with skin complexion, eye or hair color, or sunburn history. This study does not support the hypothesis that UVR exposure lowers breast cancer risk.

Keywords

Breast cancer; Ultraviolet radiation; Sunlight; Vitamin D; Cancer epidemiology

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Conflicts of interest
None to declare.

This study has been approved annually by human subjects review boards at the University of Minnesota (Minneapolis, MN) and the National Cancer Institute (Bethesda, MD).

1. Introduction

With the exception of skin cancer, breast cancer is the most common malignancy among women in the United States (Cancer Facts & Figures 2015, 2015). The strongest and most consistently identified individual risk factors include age, reproduction-related factors (e.g., parity, age at menarche, age at first childbirth, exogenous hormone use), family history of breast cancer, and lifestyle factors such as alcohol consumption, anthropometry, and physical activity (Claus, Risch, & Thompson, 1991; Kelsey, 1979). Ecological studies have found decreasing breast cancer incidence with increasing proximity to the Equator (Gorham, Garland, & Garland, 1990; Mandal, St-Hilaire, Kie, & Derryberry, 2009; Mohr, Garland, Gorham, Grant, & Garland, 2008). Since latitude is an influential determinant of cutaneous vitamin D production, these ecologic findings supported the hypothesis that exposure to vitamin D reduces breast cancer risk. However, other epidemiological studies of circulating vitamin D and breast cancer risk have been inconsistent and preliminary results from a recent large pooled analysis suggest no association with breast cancer risk (Visvanathan et al., 2015).

Several studies have directly examined the relationship between personal UV radiation (UVR) exposure and breast cancer incidence. However, findings have been inconsistent, supporting either a reduced risk (Anderson, Cotterchio, Kirsh, & Knight, 2011; L. S. Engel et al., 2014; P. Engel, Fagherazzi, Mesrine, Boutron-Ruault, & Clavel-Chapelon, 2011; John, Schwartz, Dreon, & Koo, 1999; John, Schwartz, Koo, Wang, & Ingles, 2007; Yang et al., 2011) or no association (Edvardsen et al., 2011; Fuhrman et al., 2013; Kuper et al., 2009; Lin et al., 2012; Millen et al., 2009). UVR exposure has been estimated in prior studies using a variety of metrics, most commonly either ambient UVR or time outdoors. Many studies reporting an association between UVR and breast cancer have used time outdoors as the metric of UVR exposure (L. S. Engel et al., 2014; John et al., 1999; Millen et al., 2009; Yang et al., 2011) and some evaluated ambient UVR exposure (Anderson et al., 2011; P. Engel et al., 2011; John et al., 1999; Millen et al., 2009). Overall, few studies investigating relationships between UVR-related factors and risk of breast cancer have been prospective (Edvardsen et al., 2011; L. S. Engel et al., 2014; P. Engel et al., 2011; John et al., 1999; Kuper et al., 2009; Millen et al., 2009; Yang et al., 2011) and few of these included a wide range of ambient UVR exposures over the course of a lifetime (Table 1) (Anderson et al., 2011; Kuper et al., 2009; Millen et al., 2009; Yang et al., 2011).

The objective of this study is to assess the relationship between ambient UVR, time spent outdoors, sun sensitivity factors, and subsequent risk of first primary breast cancer using data from the United States Radiologic Technologists (USRT) study. This is the first study to prospectively examine multiple UV radiation-related factors in a large nationwide cohort, which has collected information on personal sun sensitivity characteristics, sun exposure over the lifetime, and detailed lifestyle factors in a population from all 50 states exposed to a wide range of ambient UVR.

2. Methods

2.1 Overview

The United States Radiologic Technologists (USRT) study is a prospective occupational cohort composed of radiologic technologists who were certified by the American Registry of Radiologic Technologists for at least two years between 1926 and 1982. Detailed descriptions of this cohort have been previously published (Boice, Mandel, Doody, Yoder, & McGowan, 1992; Doody, Mandel, Lubin, & Boice, 1998). Briefly, participants were mailed self-administered questionnaires during the following four time periods: 1983–1989, 1994–1998, 2003–2005, and 2012–2013. Informed consent was obtained to collect medical records. The USRT study has been annually approved by human subjects review boards at the University of Minnesota (Minneapolis, MN) and the National Cancer Institute (Bethesda, MD).

2.2 Study population

The study population included female participants who completed the third (2003–2005) and fourth (2012–2013) questionnaires, and reported no history of cancer (other than non-melanoma skin cancer [NMSC]) at the time of the third questionnaire (N=36,725). Follow-up continued from completion of the third questionnaire until the earlier of first primary cancer diagnosis (excluding NMSC) or completion of the fourth questionnaire.

2.3 Outcome and validation

Incident breast cancers, defined as first primary malignant breast cancer diagnosis after the third questionnaire, were ascertained from the fourth questionnaire through self-report (n=557). Medical records to confirm breast cancer diagnoses were obtained for 368 (66.1%) women, of whom 364 (98.9%) were confirmed. Because the confirmation rate for self-reported breast cancer diagnosis has been high in this study, (Doody et al., 1998) women with non-validated breast cancers (n=189) were also included. We also included 163 cases of malignant breast cancer that were not self-reported on the questionnaire, but were found upon review of medical records, bringing the total number of breast cancer cases to 716.

2.4 UV radiation exposure assessment

Lifetime residential history, lifetime time spent outdoors, and host characteristics of sun sensitivity were ascertained at the baseline of this study (third questionnaire).

Residential history and time spent outdoors in the summer were used to estimate UVR exposure. Participants reported the city and state where they lived for the longest time during five age periods over their lifetime (0–12, 13–19, 20–39, 40–64, 65+). These residential locations were geocoded and linked to the Total Ozone Mapping Spectrometer database, maintained by NASA (“National Aeronautics and Space Administration: Total Ozone Mapping Spectrometer Data Product: Erythemal UV Exposure,” 2004). This database provides estimates of daily noon-time erythemal UVR exposures on a 1.25° longitude by 1° latitude (approximately 110 × 110 km or 69 × 69 miles) grid. Satellite-based annual estimates of UVR have varied little since the start of measurements in the late 1970s, (Lean

et al., 1997) thus, daily noon-time estimates were averaged over years 1978 to 1993 to construct stable estimates. This measure is referred to as ambient UVR.

Participants also reported the typical time spent outside categorically (0, <1, 1–2, 3–4, 5–6 hours/day) on summer weekdays and weekends between 9 AM and 3 PM for the same 5 age periods of their lifetime. We assigned continuous values to each category as follows: 0 was assigned 0.1 hour (since it is unlikely that individuals spent zero time outside), < 1 hour was assigned 0.5 hours, 1–2 hours was assigned 1.5 hours, 3–4 hours was assigned 3.5 hours, and 5–6 hours was assigned 5.5 hours. We then generated a weighted average of weekday and weekend hours to represent time spent outdoors on a typical summer day for each period of life and hereafter refer to this measure as time outdoors.

We also combined ambient UVR and time outdoors by generating a set of variables to better reflect the actual UVR exposure at each location for each time period. To this end, for each period of life, we multiplied the ambient UVR value by the daily number of hours outdoors. We designated this variable combined UVR.

For each of the three exposure metrics, average lifetime exposures were calculated by generating a weighted average based on the values for each period of life, accounting for the number of years in each. This was done for all three methods of exposure assessment: ambient UVR, time outdoors, and combined UVR.

Each metric was analyzed as a categorical variable with five categories. We assigned quintiles based on the distribution of the average lifetime variable for each metric, and used those cutpoints for the specific age periods.

We also assessed the following self-reported characteristics related to sun sensitivity: skin complexion, natural hair color at age 20, eye color, reaction of skin to sunlight after 30 minutes and after prolonged sun exposure, history of blistering sunburn, and Celtic or Gaelic ancestry.

2.5 Lifestyle, reproductive, and family characteristics

We examined other factors associated with breast cancer as potential confounders, including body-mass index (BMI)(kg/m²), physical activity, alcohol consumption, and family history of breast cancer. Physical activity was measured by asking participants to report separately the number of hours they spent per week engaging in moderate (defined as requiring effort but not exhausting) and strenuous (defined as increasing heart rate or causing perspiration) exercise. We then combined these reported values to generate a physical activity variable that represented total hours of combined moderate and strenuous physical activity per week. Reproductive factors known to be associated with breast cancer, including parity, number of live births, menopausal status, history of hormone replacement therapy (HRT), and age at menarche were also assessed. To examine potential surveillance bias, we also ascertained the frequency of dental exams to represent healthcare utilization.

Most of these characteristics were obtained at baseline, or if not available at baseline, then they were ascertained from one of the earlier questionnaires. The exception was reproductive factors, including number of births, menopausal status, and HRT use, which were surveyed

in the fourth questionnaire but used to represent status at baseline. All participants who reported their age at menopause to be older than their age at baseline (n=8781) were considered to be pre-menopausal at baseline, and all women whose age at beginning HRT was older than their age at baseline were also considered not to be using HRT (n=2157) at baseline. In addition, women whose first child was born after baseline were treated as nulliparous at baseline (n=4) in these analyses.

2.6 Statistical analyses

To evaluate the relationship between UVR exposure, sun sensitivity factors and first primary breast cancer, Cox proportional hazards regression analyses were used to calculate HRs and 95% confidence intervals (CIs) with age as the time scale which adjusts for age in all models (Korn, Graubard, & Midthune, 1997). We evaluated risk of breast cancer in relation to categories of time outdoors (<1, 1–1.9, 2–2.9, 3–3.9, and 4 hours/day), quintiles of ambient UVR, and quintiles of combined UVR. We evaluated risk associated with exposure at ages 0–12, 13–19, 20–39, 40–64, and 65+ separately, as well as average lifetime exposure, and mutually adjusted for all other age periods (i.e., all five age periods in one model). The values for ambient UVR, which were derived from residential location, include locations such as Alaska, North Dakota, and Maine in the lowest quintile and Hawaii, Florida, and Texas in the highest quintile. Average lifetime ambient UVR represents an average of several locations and therefore the highest and lowest quintiles may include participants living in a variety of locations.

We also examined risk of breast cancer associated with the following sun sensitivity factors: skin complexion (dark, medium, light), natural hair color at age 20 (dark brown or black, light or medium brown, and blonde, red, or reddish-brown), eye color (brown, green or hazel, blue), reaction of skin to sunlight after 30 minutes (no change in skin color, tanned no sunburn, mild sunburn, and severe or painful sunburn) and after prolonged sun exposure (not tanned, lightly tanned, moderately tanned, deeply tanned), history of blistering sunburn (yes/no), and Celtic or Gaelic ancestry (yes/no).

Multivariable models were adjusted a priori for the following established or suspected breast cancer risk factors (“Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. Collaborative Group on Hormonal Factors in Breast Cancer,” 1997; Kelsey, Gammon, & John, 1993; Krieger, Strong, Makosky, & Weuve, 2003; Magnusson, Colditz, Rosner, Bergstrom, & Persson, 1998; Peters et al., 2009; Xia et al., 2014): birth cohort (before 1930, 1930–1939–1940–1944–1945–1949–1950–1954–1955–1961), BMI (<18.5, 18.5–25, 25–30, >30 kg/m²), race (white, black, Asian/Pacific Islander, other), ever given birth (yes/no), age at first birth (<20, 20–24, 25–29, 30–34, 35), age at menarche (under 11, 11–12, 13–14, 15 and older), ever taken HRT (yes/no), family history of breast cancer (yes/no), physical activity (0, 1–3, 4–7, 7–14, 15 and higher hours/week of moderate and vigorous activity combined), menopausal status (pre- or post-menopausal), ever given birth (yes/no), number of times given birth (0, 1–2, 3–4, 5 and higher), use of oral contraceptives (ever/never), alcohol consumption, and occupational ionizing radiation exposure to the breast (continuous). (Doody et al., 2006; Sigurdson et al., 2009) We

examined whether mutual adjustment for UVR exposure and sun sensitivity factors, as well as mutual adjustment for ambient UVR and time outdoors, altered findings. We also conducted likelihood ratio tests to examine whether marital status, smoking history, or education improved model fit. Missing values were coded as a separate category and included as indicator variables in analyses. P-values for trend were based on likelihood ratio tests of time outdoors, ambient UVR, and combined UVR coded 1 thru 5 and treated as continuous in models.

We conducted several sensitivity analyses. Prior studies have found varying effects of UVR and vitamin D in pre- vs. post-menopausal breast cancer (P. Engel et al., 2011) and in individuals with a family history of breast cancer compared to those with no family history (L. S. Engel et al., 2014). We therefore generated a multiplicative interaction term to test for effect modification between each UVR metric and both menopausal status and family history and repeated the analyses including these terms in separate models. We also repeated the analyses after excluding participants with a history of NMSC (n=3504) as they may have different screening patterns or different patterns of exposure. In addition, we generated a squared term for each UVR exposure metric to explore non-linear relationships. All hazard models satisfied the proportionality assumption as tested using Schoenfeld residuals. We considered two-sided p-values to be significant at $\alpha = 0.05$. Analyses were conducted using SAS 9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

Characteristics of the overall study population are shown in Table 2, and are stratified by UVR exposure in Table 3. The proportions of cases and non-cases are consistent with known risk factors for breast cancer, including positive family history, less exercise, higher BMI, early age at menarche, never giving birth, and being post-menopausal (Table 2). Participant characteristics varied by ambient UVR more than by time outdoors, although certain characteristics, including smoking, exercise, and menopausal status, varied by time outdoors (Table 3). Participant ages ranged from 43–94 years at entry.

None of the sun sensitivity characteristics were associated with risk of breast cancer (Table 4). Constitutional characteristics, including eye color, hair color, and skin complexion were unrelated to breast cancer risk, as was history of blistering sunburns, skin reaction to both short-term and long-term sun exposure, and Celtic heritage (Table 4). Sun sensitivity was also not an effect modifier of UVR and breast cancer risk (Supplementary Figure 1).

The HR for lifetime ambient UVR exposure for the 5th compared to the 1st quintile was 1.22 (95% CI: 0.95–1.56, p-trend = 0.36). Our findings were also null for UVR exposure based on time outdoors (HR for lifetime 5th vs 1st quintile= 0.87 (95% CI: 0.68–1.10, p-trend = 0.46). In addition, we found no association with breast cancer risk by combined UVR (HR for lifetime 5th vs 1st quintile= 0.85 (95% CI: 0.67–1.08, p-trend=0.46). There were also no associations seen between ambient UVR, time outdoors, or combined UVR and breast cancer risk during any of the age periods (Table 5).

For each of the three methods of estimating UVR exposure, we also found no effect modification by menopausal status or family history of breast cancer (data not shown). There was also no difference in risk after additional adjustment for dental x-rays (a surrogate for healthcare utilization), nor did risk estimates change after exclusion of participants with NMSC (data not shown). The squared UVR exposure terms were also not significant (data not shown). Mutual adjustment for ambient UVR and time outdoors did not result in any meaningful differences in HRs, and p-trend remained non-significant for all models (data not shown).

4. Discussion

In this large nationwide prospective study, we found no evidence that lifetime average time outdoors, lifetime average ambient UV, lifetime average combined UVR, sun sensitivity factors or sunburns were related to breast cancer risk, nor did we find an association between time outdoors, ambient UVR, or combined UVR during any time period throughout life. Results did not differ by menopausal status or by family history of breast cancer.

Other epidemiologic studies have examined the relationship between ambient UVR, based on residential locations (Anderson et al., 2011; P. Engel et al., 2011; Millen et al., 2009) or other metrics, (Edvardsen et al., 2011) and breast cancer risk. All but one (P. Engel et al., 2011) study of ambient UVR exposure have not found an association with breast cancer (Anderson et al., 2011; Edvardsen et al., 2011; Millen et al., 2009).

Study results are mixed on the relationship between risk and time outdoors. A few studies have found inverse associations with personal outdoor exposure (Anderson et al., 2011; L. S. Engel et al., 2014; John et al., 1999; Millen et al., 2009). In a cohort study of farmers' wives in two states Engel et al. found a decreased risk in women who reported spending at least one hour/day outdoors 10 years before enrollment in the study (L. S. Engel et al., 2014). John et al. found occupational time outdoors, but not recreational time outdoors, significantly related to risk in the general population (John et al., 1999). In the Women's Health Initiative Observation Study, Millen et al. found that spending less than 30 minutes outdoors in summer or other seasons was related to a 20% increased risk compared to spending greater than two hours outdoors (Millen et al., 2009). One difficulty with time outdoors as an indicator of UVR exposure is that it is susceptible to residual confounding by physical activity, which has been inversely related to breast cancer risk (Peters et al., 2009). This may be especially problematic in study populations that are likely active outdoors, such as farmers' wives (L. S. Engel et al., 2014) or outdoor workers (John et al., 1999). The study by Millen et al, in contrast, does not focus on a population in which outdoor activities are more likely to be characterized by physical activity. However, their finding that time outdoors is equally protective against risk regardless of season suggests potential residual confounding by physical activity after adjustment.

In addition, one study found an inverse association with a particular type of outdoor exposure, weeks spent on sunbathing vacations, but only during certain early decades of life (Yang et al., 2011). While our study did not investigate vacation time, we found no association with overall summer time outdoors in childhood, adolescence or early adulthood.

To our knowledge, only two studies (Kuper et al., 2009; Yang et al., 2011) have assessed sun sensitivity factors in relation to breast cancer risk and both failed to find any consistent pattern of association. Studies that have examined sunburns as a surrogate for sun exposure have also not observed an association with breast cancer risk (Edvardsen et al., 2011; Kuper et al., 2009; Yang et al., 2011). Our results are consistent with these prior studies.

Our study has several strengths. The study population consists of a large, geographically diverse cohort, representing a wide range of UVR exposures and a large number of breast cancer cases. We used multiple UVR metrics including ambient UVR, time outdoors, and combined UVR, and analyzed average lifetime exposures as well as exposure during specific periods of life, in addition to sun sensitivity factors and sunburns, while most prior studies typically focused on either ambient UVR or various indicators of time outdoors and frequency of sun-seeking vacations. Our results were consistent regardless of the exposure metric assessed, and did not change after adjustment for dental x-rays (a surrogate for healthcare utilization) or exclusion of participants with a NMSC diagnosis, who may have undergone more intensive cancer screening or who may have had different patterns of exposure.

UVR exposures were reported prior to the date of incident breast cancer diagnoses, and thus were not subject to recall bias or reverse causation. To our knowledge, this is the only study on UVR and breast cancer risk in which UVR exposure takes into account both time outdoors and ambient UVR and which examines exposure over the lifetime as opposed to just one point in time.

UVR exposure may influence breast cancer risk through the cutaneous production of vitamin D (Colston, Berger, & Coombes, 1989; Koga, Eisman, & Sutherland, 1988; Welsh, 2004), although a large pooled analysis of serum 25(OH)D in 17 prospective cohorts showed no association between 25(OH)D levels and breast cancer risk (Visvanathan et al., 2015). While our findings do not support the hypothesis of a protective role of vitamin D, we cannot rule out an effect of vitamin D since we did not have information on serum vitamin D levels at baseline. We also did not have information on sun protection behaviors, such as clothing choices, sunscreen use, or staying in the shade, all of which can influence cutaneous vitamin D production. Additionally, most cohort members were post-menopausal women, many of whom were likely taking calcium + vitamin D supplements, but we did not have information on supplement use. A prior study on a subset of this cohort found that a majority of participants were taking supplements, and that supplementation was a key contributing factor to circulating 25(OH)D (Freedman et al., 2013). Therefore, in this cohort, UVR exposure may not be associated with vitamin D levels. We lacked information on other sources of UVR exposure, such as the use of tanning beds. Our measures of UVR exposure (time outdoors, ambient UVR, and sun sensitivity factors) relied on self-reported information (residence and time outdoors over the lifetime). While self-reporting of residential histories is likely accurate, there may be difficulties in identifying a single usual residence over a range of years when a person is highly mobile. In addition, there are inherent difficulties in recalling and synthesizing past behavior, such as time outdoors, over periods of time. We also did not collect data on parental socioeconomic status or socioeconomic status at birth. UVR exposure estimates were missing for some individuals.

4.1 Conclusions

In summary, we found no association between any measure of UVR exposure and breast cancer risk. These results do not support a protective role of UVR exposure, either during key age periods in life or across a lifetime, on the development of breast cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Prior studies of UVR and breast cancer are inconsistent and limited
- We assessed UVR exposure across the lifetime and in three ways
- Conducted a prospective analysis of UVR exposure and breast cancer risk
- No association of any UVR exposure metric at any age with breast cancer risk
- Our findings suggest UVR exposure does not reduce risk of breast cancer

Table 1

Summary of prior studies on UVR exposure and breast cancer risk

First author, year	Study type/study population	No. cases/non-cases	Location	UVR measures	Summary of results
Zamoiski, 2016 (current study)	USRT Cohort	716/36,009	United States	Ambient UVR Time outdoors Combined	Null for all
Engel, 2014	Agricultural Health Study cohort	578/30,443	Iowa and North Carolina	Time outdoors	Decreased risk for time outdoors (in women with no family history of breast cancer)
Lin, 2012	NIH-AARP cohort	8,681/442,253	United States (CA, FL, LA, NJ, NC, PA, GA, MI)	Ambient UVR	Null for ambient UVR.
Edwardsen, 2011	Population-based cohort	948/40,863	Norway	Time outdoors (sunny vacations, solarium use) Ambient UVR Sunburn history	Null for all.
Engel, 2011	Population-based cohort	2,871/64,850	France	Ambient UVR	Decreased risk for highest ambient UVR (in postmenopausal women).
Yang, 2011	Population-based cohort	1,053/48,208	Sweden	Time outdoors (sunny vacations, solarium use) Sun sensitivity factors Sunburn history	Decreased risk for time outdoors. Null for sun sensitivity factors. Null for sunburn history.
Kuper, 2009	Population-based cohort	840/41,049	Sweden	Time outdoors (sunny vacations, solarium use) Sun sensitivity factors Sunburn history	Null for all.
Millen, 2009	WHIOS Cohort	2,535/69,127	United States (23 states + DC)	Time outdoors Ambient UVR	Decreased risk for time outdoors. Null for ambient UVR.
John, 1999	NHANES I Cohort	190/4,819	United States	Time outdoors Ambient UVR Skin pigmentation	Decreased risk for time outdoors. Null for ambient UVR. Null for skin pigmentation.
Anderson, 2011	Case-control	3,101/3,471	Ontario, Canada	Time outdoors Ambient UVR	Decreased risk for time outdoors. Null for ambient UVR.
John, 2007	Case-control	1,788/2,129	San Francisco Bay Area	Time outdoors Skin complexion and pigmentation	Null for time outdoors. Decreased risk for increasing pigmentation (in women with light complexion).

Table 2

Demographic, lifestyle, physical, and reproductive characteristics at baseline in breast cancer cases and non-cases among 36,725 women in the US Radiologic Technologists Study

Characteristic		No breast cancer	Breast cancer
		(n=36,009)	(n=716)
Age at entry, mean (SD)		55.8 (7.6)	57.5 (7.9)
Person-years at risk, mean (SD)		7.8 (1.0)	4.3 (2.3)
Race (%)			
	White	96.6	95.4
	Black	1.9	2.9
	Asian/Pacific Islander	0.7	0.8
	Other or missing	0.8	0.8
Education (%)			
	High school or vocational school	3.2	3.2
	2-year hospital rad tech program	46.1	44.3
	College or graduate school	38.1	42.6
	Missing	12.6	9.9
Marital status (%)			
	Never married	4.6	5.0
	Married	65.1	67.0
	Not married	17.5	17.9
	Missing	12.8	10.1
Smoking status (%)			
	Current smoker	87.7	85.8
	Not current smoker	9.7	11.5
	Missing	2.6	2.8
Alcohol consumption (drinks/week)(%)			
	0	21.7	22.1
	2	51.1	50.1
	3–10	17.4	18.4
	11	4.2	4.2
	Missing	5.7	5.2
BMI (%)			
	<18.5	0.9	0.6
	18.5–25	40.2	40.2
	25–30	29.8	28.2
	>30	21.8	26.1
	Missing	7.3	4.9
Exercise (hours/week) (%)			
	0	8.1	8.9
	1–3	15.1	17.6
	4–7	25.1	22.6

		No breast cancer	Breast cancer
Characteristic		(n=36,009)	(n=716)
Ever given birth (%)	8–14	20.0	19.0
	15	11.4	9.2
	Missing	20.3	22.6
Number of children (%)	No	18.6	20.1
	Yes	80.0	78.1
	Missing	1.4	1.8
Age at first birth (%)	0	19.0	20.7
	1–2	52.0	52.8
	3–4	25.2	22.6
	5+	2.7	2.9
	Missing	1.1	1.0
Age at menarche (%)	Under 20	2.6	1.8
	20–24	30.7	29.9
	25–29	31.1	30.5
	30–34	11.5	11.2
	35 and older	3.9	4.9
	Missing	20.2	21.8
Menopausal status (%)	10 and younger	6.3	7.8
	11–12	42.2	41.5
	13–14	37.3	36.6
	15 and older	7.3	7.8
	Missing	6.9	6.3
Ever used oral contraceptives (%)	Pre-menopausal	27.4	22.1
	Menopausal or post-menopausal	69.0	74.0
	Missing	3.6	3.9
Ever used HRT (%)	No	21.3	26.8
	Yes	72.5	67.7
	Missing	6.2	5.5
Family history of breast cancer (%)	No	51.3	50.1
	Yes	37.2	42.2
	Missing	11.5	7.7
	No	50.3	41.6
	Yes	16.6	23.2

Characteristic	No breast cancer	Breast cancer
	(n=36,009)	(n=716)
Missing	33.1	35.2
Cumulative occupational ionizing radiation to the breast (mGy), mean (SD)	23.2 (28.4)	26.0 (32.5)

Demographic and other characteristics of study participants according to low, medium, high lifetime average ambient UVR and lifetime average time outdoors at study entry

Table 3

Characteristic	Lifetime average time outdoors ^a			Lifetime average ambient UVR ^b		
	Low time outdoors (n=17, 973)	High time outdoors (n=17, 973)	P-value ^c	Low UVR (n=18, 381)	High UVR (n=17, 826)	P-value ^c
Lifetime average time outdoors (hours/day), mean (SD)	1.4 (0.5)	3.1 (0.8)	<0.01	2.3 (1.1)	2.2 (1.1)	<0.01
Lifetime average ambient UVR, mean (SD) ^d	119.1 (25.4)	117.3 (24.5)	<0.01	98.9 (6.8)	138.2 (21)	<0.01
Age at entry, mean (SD)	56.5 (7.8)	55 (7.2)	<0.01	55.5 (7.5)	56.2 (7.6)	<0.01
Person-years at risk, mean (SD)	7.8 (1.2)	7.8 (1.2)	0.01	7.8 (1.2)	7.8 (1.2)	0.2
Birth Cohort (%)						
Before 1930	2.4	1.4		1.8	2.0	
1930–1939	12.5	9.5		10.5	11.8	
1940–1944	14.4	11.9		12.4	14.0	
1945–1949	21.5	20.4	<0.01	20.5	21.3	<0.01
1950–1954	27.7	28.9		28.4	28.1	
1955–1961	21.5	28.0		26.4	22.9	
Race (%)						
White	96.3	97.1		98.4	94.8	
Black	2.1	1.6		1.1	2.7	
Asian/Pacific Islander	0.8	0.5	<0.01	0.1	1.2	<0.01
Other or missing	0.9	0.9		0.3	1.4	
Education (%)						
High school or vocational school	3.2	3.2		2.9	3.5	
2-year hospital rad tech program	46.0	46.7		50.7	41.8	
College or graduate school	37.9	39.2	0.64	35.1	42.0	<0.01
Missing	12.9	10.9		11.3	12.6	
Marital status (%)						
Never married	4.7	4.6	0.54	4.4	4.9	<0.01

Characteristic	Lifetime average time outdoors ^a			Lifetime average ambient UVR ^b		
	Low time outdoors (n=17, 973)	High time outdoors (n=17, 973)	P-value ^c	Low UVR (n=18, 381)	High UVR (n=17, 826)	P-value ^c
Married	64.8	66.6		68.4	62.7	
Not married	17.3	17.8		15.7	19.5	
Missing	13.2	11.0		11.5	12.8	
Smoking status (%)						
Not current smoker	88.9	86.5		88.2	87.2	
Current smoker	8.0	11.5	<0.01	9.3	10.1	0.01
Missing	3.2	2.0		2.5	2.7	
Alcohol consumption (drinks/week) (%)						
0	23.7	19.4		18.4	25.0	
2	51.2	51.1		54.6	47.5	
3–7	15.9	18.9	<0.01	17.5	17.3	<0.01
11	3.7	4.8		3.8	4.7	
Missing	5.5	5.8		5.7	5.7	
BMI (%)						
<18.5	1.0	0.9		0.8	1.0	
18.5–25	40.7	39.8		39.4	41.2	
25–30	29.8	29.8	<0.01	30.1	29.4	<0.01
>30	21.8	21.8		21.7	21.9	
Missing	6.7	7.8		8.0	6.5	
Exercise (hours/week) (%)						
0	9.5	6.7		7.5	8.8	
1–3	17.6	12.9		15.3	15.0	
4–7	25.8	24.5	<0.01	25.8	24.4	<0.01
8–14	17.7	22.5		20.1	20.0	
15	8.0	14.8		11.4	11.4	
Missing	21.5	18.6		19.9	20.4	
Ever given birth? (%)						
No	18.6	18.7		16.6	20.7	
Yes	80.0	80.0	0.42	82.1	77.9	<0.01

Characteristic	Lifetime average time outdoors ^a			Lifetime average ambient UVR ^b		
	Low time outdoors (n=17, 973)	High time outdoors (n=17, 973)	P-value ^c	Low UVR (n=18, 381)	High UVR (n=17, 826)	P-value ^c
Missing	1.4	1.3		1.3	1.4	
Number of children (%)						
0	18.9	19.1		17.0	21.1	
1–2	51.8	52.5		51.3	53.0	
3–4	25.3	24.8	0.08	27.6	22.5	<0.01
5+	2.9	2.5		3.1	2.3	
Missing	1.0	1.1		1.1	1.1	
Age at first birth (%)						
Under 20	2.7	2.5		1.7	3.5	
20–24	31.2	30.1		31.8	29.5	
25–29	30.7	31.6	0.13	33.1	29.1	<0.01
30–34	11.3	11.6		11.6	11.3	
35 and older	3.9	4.0		3.6	4.3	
Missing	20.2	20.2		18.2	22.3	
Age at menarche (%)						
10 and younger	6.3	6.4		6.3	6.5	
11–12	43.1	41.2		42.1	42.1	
13–14	36.9	37.8	<0.01	37.8	36.9	0.2
15 and older	6.9	7.8		7.2	7.5	
Missing	6.8	6.9		6.7	7.1	
Menopausal status (%)						
Pre-menopausal	25.2	29.6		30.3	24.3	
Menopausal or post-menopausal	71.3	66.9	<0.01	66.6	71.8	<0.01
Missing	3.6	3.5		3.2	3.9	
Ever used oral contraceptives (%)						
No	22.5	20.1		23.3	19.3	
Yes	71.4	73.9	<0.01	70.9	74.2	<0.01
Missing	6.1	6.1		5.8	6.5	
Ever used HRT (%)						

Characteristic	Lifetime average time outdoors ^a			Lifetime average ambient UVR ^b		
	Low time outdoors (n=17, 973)	High time outdoors (n=17, 973)	P-value ^c	Low UVR (n=18, 381)	High UVR (n=17, 826)	P-value ^c
No	49.6	53.0		55.6	46.8	
Yes	39.0	35.7	<0.01	33.2	41.7	<0.01
Missing	11.4	11.3		11.3	11.5	
Family history of breast cancer (%)						
No	50.4	50.0		51.0	49.4	
Yes	16.6	17.0	0.65	16.5	17.0	0.01
Missing	33.0	33.0		32.6	33.6	
Cumulative occupational ionizing radiation dose to the breast (mGy), mean (SD)	24.5 (31.2)	21.8 (25.5)	<0.01	21.7 (27.6)	24.8 (29.5)	<0.01

^aLow and high average lifetime time outdoors defined by dividing cohort at the median.

^bLow and high average lifetime ambient UVR defined by dividing cohort at the median.

^cP-values determined from Chi-square tests (for categorical variables) and two-sample T-tests (for continuous variables).

^dUnits are arbitrary.

Table 4

Risk of breast cancer according to sun sensitivity characteristics among white women in the United States Radiologic Technologists study, 2003–05 through 2012–13 (n=35,456)

Characteristic ^a	Breast cancer cases, n	Person years	HR (95% CI) ^b
Skin complexion			
Dark or medium	317	129912	ref
Light	300	114966	1.06 (0.91 – 1.24)
Eye color			
Brown	196	73342	ref
Green or hazel	244	98696	0.93 (0.77 – 1.12)
Blue	178	72009	0.91 (0.74 – 1.12)
Natural hair color at age 20			
Dark brown or black	151	63923	ref
Light or medium brown	347	139554	1.10 (0.91 – 1.33)
Blonde, red, or reddish-brown	182	70379	1.12 (0.90 – 1.39)
Skin reaction to 30 minutes of sunlight			
Tanned without sunburn or no change in skin color	69	32034	ref
Mild sunburn	350	142002	1.19 (0.92 – 1.54)
Severe or painful sunburn	262	100462	1.21 (0.93 – 1.58)
Skin reaction to prolonged sunlight			
Lightly tanned or not tanned	181	74713	ref
Moderately tanned	335	129429	1.11 (0.93 – 1.33)
Deeply tanned	159	69745	1.01 (0.82 – 1.25)
Ever had a blistering sunburn			
No	242	99568	ref
Yes	439	174945	1.05 (0.90 – 1.23)
Celtic or Gaelic ancestry			
No	355	146590	ref
Yes	160	57112	1.07 (0.89 – 1.30)

^aParticipants with unknown or missing information are not presented.

^bHRs and 95% CIs computed using Cox proportional hazard models with age as the time scale, adjusted for birth cohort (before 1930, 1930–1939–1940–1944–1945–1949–1950–1954–1955–1961), BMI (<18.5, 18.5–25, 25–30, >30 kg/m²), ever given birth (yes/no), age at first birth (<20, 20–24, 25–29, 30–34, 35), age at menarche (under 11, 11–12, 13–14, 15 and older), ever taken HRT (yes/no) family history of breast cancer (yes/no), exercise (0, 1–3, 4–7, 7–14, 15 and higher hours/week), menopausal status (pre- or postmenopausal), number of births (0, 1–2, 3–4, 5 and higher), use of oral contraceptives (ever/never), alcohol consumption (0, 1–2, 3–10, 11 and higher drinks/week), and ionizing radiation exposure to the breast (continuous).

Risk of breast cancer associated with ambient UVR exposure, time outdoors, and combined UVR according to age at exposure among 36725 women in the United States Radiologic Technologists study, 2003–05 through 2012–13^a

Table 5

Average lifetime	Time outdoors				Ambient UVR				Combined UVR			
	Hours/day	Cases	HR (95% CI) ^b	Quintile ^c	Cases	HR (95% CI) ^b	Quintile ^d	Cases	HR (95% CI) ^b	Cases	HR (95% CI) ^b	
Age range 0–12	<1	80	ref	Q1	116	ref	Q1	156	ref			
	1–1.9	241	0.88 (0.70–1.10)	Q2	159	1.41 (1.11–1.79)	Q2	143	0.96 (0.77–1.21)			
	2–2.9	238	0.96 (0.76–1.20)	Q3	140	1.21 (0.94–1.54)	Q3	132	0.92 (0.73–1.16)			
	3–3.9	104	0.95 (0.76–1.20)	Q4	150	1.26 (0.99–1.61)	Q4	153	1.06 (0.85–1.33)			
	4	41	0.87 (0.68–1.10)	Q5	144	1.22 (0.95–1.56)	Q5	120	0.85 (0.67–1.08)			
	p-trend		0.46	p-trend		0.36	p-trend		0.46			
13–19	<1	63	ref	Q1	156	ref	Q1	90	ref			
	1–1.9	110	1.11 (0.81–1.52)	Q2	191	1.48 (1.20–1.83)	Q2	92	1.29 (0.96–1.73)			
	2–2.9	113	1.34 (0.98–1.83)	Q3	131	1.17 (0.92–1.48)	Q3	54	1.41 (1.00–1.98)			
	3–3.9	183	1.30 (0.97–1.75)	Q4	98	1.38 (1.05–1.82)	Q4	134	1.32 (1.01–1.73)			
	4	232	1.15 (0.85–1.55)	Q5	112	1.36 (1.00–1.86)	Q5	312	1.26 (0.98–1.61)			
	p-trend		0.42	p-trend		0.09	p-trend		0.20			
20–39	<1	83	ref	Q1	163	ref	Q1	125	ref			
	1–1.9	147	1.04 (0.79–1.36)	Q2	188	1.37 (1.10–1.69)	Q2	133	1.16 (0.91–1.49)			
	2–2.9	162	1.08 (0.82–1.43)	Q3	136	1.13 (0.89–1.43)	Q3	89	1.38 (1.04–1.83)			
	3–3.9	126	0.89 (0.66–1.20)	Q4	98	1.23 (0.93–1.63)	Q4	100	0.86 (0.65–1.13)			
	4	180	1.00 (0.72–1.38)	Q5	107	1.06 (0.76–1.48)	Q5	235	0.97 (0.75–1.26)			
	p-trend		0.58	p-trend		0.68	p-trend		0.22			
	<1	212	ref	Q1	145	ref	Q1	272	ref			
	1–1.9	184	0.81 (0.66–1.00)	Q2	150	1.27 (1.01–1.60)	Q2	141	0.94 (0.76–1.15)			
	2–2.9	184	1.05 (0.85–1.31)	Q3	130	1.10 (0.86–1.42)	Q3	95	1.08 (0.85–1.38)			
	3–3.9	64	0.92 (0.68–1.25)	Q4	104	1.27 (0.96–1.70)	Q4	64	0.78 (0.58–1.04)			

Average lifetime	Hours/day	Time outdoors			Ambient UVR			Combined UVR		
		Cases	HR (95% CI) ^b	Quintile ^c	Cases	HR (95% CI) ^b	Quintile ^d	Cases	HR (95% CI) ^b	
40–64	4	55	0.79 (0.56–1.11)	Q5	162	1.14 (0.84–1.54)	Q5	109	0.97 (0.75–1.26)	
	p-trend		0.58	p-trend		0.46	p-trend		0.52	
	<1	285	ref	Q1	143	ref	Q1	355	ref	
	1–1.9	211	1.17 (0.98–1.42)	Q2	148	1.32 (1.05–1.67)	Q2	144	1.19 (0.97–1.45)	
	2–2.9	117	1.08 (0.86–1.37)	Q3	124	1.17 (0.91–1.50)	Q3	58	0.89 (0.67–1.18)	
65+	3–3.9	41	0.93 (0.66–1.33)	Q4	94	1.10 (0.82–1.46)	Q4	50	0.87 (0.64–1.18)	
	4	43	1.09 (0.76–1.57)	Q5	187	1.27 (0.96–1.70)	Q5	78	1.03 (0.78–1.37)	
	p-trend		0.81	p-trend		0.27	p-trend		0.66	
	<1	67	ref	Q1	31	ref	Q1	73	ref	
	1–1.9	37	1.05 (0.68–1.61)	Q2	12	0.57 (0.29–1.11)	Q2	17	0.97 (0.56–1.68)	
	2–2.9	11	0.94 (0.48–1.84)	Q3	22	1.03 (0.58–1.84)	Q3	10	0.93 (0.47–1.85)	
	3–3.9	13	1.19 (0.62–2.30)	Q4	27	1.37 (0.74–2.51)	Q4	7	0.74 (0.33–1.66)	
	4	11	1.60 (0.75–3.41)	Q5	42	1.05 (0.55–1.98)	Q5	20	1.36 (0.76–2.43)	
	p-trend		0.34	p-trend		0.47	p-trend		0.60	

^aParticipants with missing UVR exposure information were excluded only from the specific models examining the missing exposure. The number of individuals excluded in each analysis due to missing UVR exposure information is set forth below. Time outdoors: Average lifetime 779, 0–12 years 1047, 13–19 years 1026, 20–39 years 925, 40–64 years 987, 65+ years 31327.

lifetime 518, 0–12 years 1528, 13–19 years 1438, 20–39 years 1480, 40–64 years 1586, 65+ years 31676.

Combined UVR: Average lifetime 779, 0–12 years 1908, 13–19 years 1865, 20–39 years 1823, 40–64 years 1917, 65+ years 31938

Most participants (87%) were younger than 65 years at baseline, which accounts for most of the “missing” data in the 65+ age group.

^bHRs and 95% CIs computed using Cox proportional hazard models with age as the time scale, adjusted for birth cohort (before 1930, 1930–1939–1940–1944–1945–1949–1950–1954–1955–1961), race (white, black, Asian or Pacific Islander, American Indian or Alaska native, other), BMI (<18.5, 18.5–25, 25–30, >30 kg/m²), ever given birth (yes/no), age at first birth (<20, 20–24, 25–29, 30–34, 35), age at menarche (under 11, 11–12, 13–14, 15 and older), ever taken HRT (yes/no) family history of breast cancer (yes/no), exercise (0, 1–3, 4–7, 7–14, 15 and higher hours/week), menopausal status (pre- or post-menopausal), number of births (0, 1–2, 3–4, 5 and higher), use of oral contraceptives (ever/never), alcohol consumption (0, 1–2, 3–10, 11 and higher drinks/week), and ionizing radiation exposure to the breast (continuous). Trend tests were conducted by modeling categorical values as ordinal.

^cCutpoints are as follows (units are arbitrary): 97.0, 104.8, 117.9, 140.4

^dCutpoints are as follows (units are arbitrary): 149.6, 213.9, 280.1, 369.1