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Sun exposure and risk of epithelial ovarian cancer

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Abstract

Purpose—Associations between sun exposure (a primary source of Vitamin D) and risk of ovarian cancer have been inconsistent. Furthermore, studies have not investigated whether sun exposure at different periods in the lifetime of a person results in differences in risk associations, and little is known about differences according to histological subtype.

Methods—Using a population-based case-control study of 1,334 non-Hispanic white women diagnosed with epithelial ovarian cancer in western Washington State between 2002–2009 and 1,679 non-Hispanic white controls, we assessed the relation of epithelial ovarian cancer with constitutional pigmentation characteristics, sun exposure behaviors, and an index of ultraviolet (UV) exposure based on residential history. Information was collected through in-person interviews. Logistic regression was used to compute odds ratios, 95% confidence intervals and trend P values (P_{trend}).

Results—We noted no association with residence-based measures of UV exposure or self-reported sun exposure, either over the lifetime or within specific age intervals. Also, we observed little evidence of association between constitutional pigmentation characteristics and risk, save for a suggestion of increased risk among women who reported increased ability to suntan upon prolonged sun exposure ($P_{\text{trend}} = 0.03$).

Conclusions—Results from this study suggest that sun exposure has little influence on the risk of epithelial ovarian cancer. Additional studies in populations with a wider gradient of sun exposure may yet be warranted.

Keywords

Ovarian cancer; sun exposure; histology; epidemiology

Introduction

Ecological studies comparing rates of ovarian cancer in higher versus lower latitudes suggest a relationship between increasing sun exposure and decreasing incidence of ovarian cancer [1–3]. It is known that exposure of the skin to solar UV-B radiation produces circulating vitamin D, as measured by the 25-Hydroxyvitamin D (25(OH)D) metabolite in serum [4], and that sun exposure is the largest source of vitamin D for most people [5]. Experimental studies indicate that higher levels of vitamin D decrease cell proliferation and

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induce apoptosis in ovarian tissue [6, 7]. Despite these observations, the findings of epidemiological studies examining the relation of sun exposure or vitamin D levels in blood with risk of ovarian cancer have been inconsistent [8–13]. A study of 516 cases and 770 matched controls nested within a pool of seven prospective studies reported no overall association between circulating 25(OH)D levels and the risk of epithelial ovarian cancer [13], while a subsequent comparison within the National Health and Nutrition Examination Survey (NHANES) found lower levels of 25(OH)D among women with a history of ovarian cancer (n=28) than among 7,245 women without such a history [8]. No study has yet explored the possible effects of sun exposure early in life as compared to sun exposure close to the diagnosis of ovarian cancer, as has been done in other cancers [14–16] and few studies have assessed differences in risk according to histological subtype [12].

Using data from a large population-based case-control study, we examined associations of constitutional pigmentation characteristics, self-reported sun exposure, and residential-history based measures of potential UV exposure with risk of epithelial ovarian cancer. We further explored the extent to which early-life and close-to-diagnosis measures of sun exposure influence this risk and characterized associations according to histological subtype.

Methods

A population-based case control study was conducted among residents of 13 counties of Western Washington State. Eligible cases were women diagnosed with primary (borderline or invasive) epithelial ovarian cancer between January 1, 2002 and December 31, 2009, and were able to communicate in English. From 2002–2005, women aged 35–74 years were considered eligible and from 2006–2009, women aged 35–69 years were eligible. They were identified through the Cancer Surveillance System (CSS), a population-based cancer registry participating in the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute [17]; of the potentially eligible women, 61 cases were excluded due to a language barrier. Of the 2,025 eligible cases, 1,502 (74.2%) were interviewed and 1,108 had invasive disease and 394 had borderline tumors. Histologic type was collected and coded by the CSS using the International Classification of Diseases for Oncology (ICD-O) morphology codes [18] and grouped according to the guidelines of the WHO [19] as serous, mucinous, endometrioid, clear cell and “other” epithelial tumors (comprised largely of unspecified adenocarcinoma and carcinoma).

Controls were selected from among English-speaking women with no prior history of ovarian cancer and at least one intact ovary who resided in the 13-county area covered by the CSS. Random digit dialing (RDD) methods were used, with stratified sampling in 5-year age categories and two county strata. From 2002–2005, a 2:1 ratio of controls (35–74 years of age) to women with invasive ovarian cancer was selected using the Waksberg-Mitofsky RDD method [20, 21]. From 2006–2009, a 1:1 ratio of controls (35–69 years of age) to women with invasive disease was used; list-assisted RDD [22] was employed during 2006–2007 and Waksberg-Mitofsky methods during 2008–2009. In total, for 19,092 (78.2%) of the 24,400 telephone numbers belonging to residences, we determined whether an eligible woman resided there; of the 2,351 eligible women identified, 1,849 were interviewed (78.6%) (Table 1). They were assigned a randomly selected calendar year between 2002 and 2009, the *reference date*, and this date was frequency matched to the year of diagnosis for the cases.

All women provided signed, informed consent before participating in the study, which was approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center. In-person interviews were conducted in relation to events that occurred before a woman’s diagnosis/reference date and included demographic and lifestyle factors, family history of

cancer and reproductive history. Multiple measures related to pigmentation characteristics and sun exposure were collected, including tendency to sunburn on first exposure to summer sun and ability to suntan after prolonged sun exposure, as well as measures of sun-related behaviors. Information on sun-exposure behaviors was collected for each 10-year age period, starting in the teens. Specifically, subjects were questioned about the time spent in the mid-day sun during the summer months, the months per year with a tan and the use of sunscreen in the mid-day sun. A weekly weighted average of daily (summer) sun exposure within each 10-year age period was computed based on questions in which women separately reported time spent in the mid-day sun on weekends and weekdays.

Place of residence (as city, within state or country) was obtained for locations where participants had lived for at least a year after age 25 as well as the age intervals lived at each location. These residential data were linked to latitude and longitudes, which were then linked to a 5-year averaged daily summary measure from NASA's Total Ozone Mapping Spectrometer (TOMS) satellite from 1987–1992 (<http://ozoneaq.gsfc.nasa.gov/TOMSUVExposure.md>) to compute an index of erythema exposure (EE). EE is a measure of the potential for biologic damage due to solar radiation, and is computed for every 1° latitude by 1.25° longitude; factors taken into account include the distance from the sun to the earth, the biological action spectrum for erythema damage, cloud cover, total column ozone, solar zenith angle at a particular time, and the spectral irradiance at the earth's surface under clear skies [23]. As examples, the EE value for Seattle, WA, USA is 1897; low EE areas include Vancouver, BC, Canada (EE value, 1599) and Anchorage, AK, USA (983); high EE areas include Los Angeles, CA, USA (3548) and Miami, FL, USA (4036) [23]. For analysis, we computed the mean EE based on residential history from age 25 to one year before the diagnosis or comparable reference date, as well as the mean EE in the 10 years prior to this latter time point.

Given that production of vitamin D from sunlight is influenced by skin pigmentation, which is correlated with race, analyses were restricted to non-Hispanic whites (1,334 cases (88.8% of those interviewed) and 1,679 controls (90.8% of those interviewed)). Unconditional logistic regression was used to compute odds ratios (OR) and 95% confidence intervals (CI). ORs were adjusted by the matching variables (age at diagnosis/reference date categorized in 5-year intervals, year of diagnosis/reference date and county of residence) as well as number of full term pregnancies and duration of use of hormonal contraceptives. Adjustment for additional potential confounders including body mass index (BMI), tendency to burn upon first seasonal (summer) sun exposure, ability to tan after prolonged sun exposure and mean EE levels did not substantially change the ORs we report, and thus were not included in the final models. Trend p-values were obtained as the p-value associated with the corresponding continuous variable in the logistic model. For the EE related variables, the trend p-values were computed considering the category with the lower level as the reference category. For examination of risk within histologic subtypes of invasive cancers, we excluded women with mucinous cancers as there were too few for meaningful analysis. All analyses were done using the STATA software package (version 10.1, STATA Corporation, College Station, TX) for Macintosh.

Results

Cases were less likely to have had a full term pregnancy, to have taken hormonal contraceptives, or to have undergone tubal ligation (Table 2). In addition, cases tended to report a higher BMI.

In general, there were no clear differences in pigmentation characteristics, including natural skin color, natural hair color and natural eye color, between cases and controls, either overall

or when borderline and invasive tumors were considered separately (Table 3). Relative to women who reported no ability to tan after prolonged sun exposure, women who reported moderate or deep degrees of tanning after such exposure were at a modestly increased risk of ovarian cancer ($P_{\text{trend}}=0.03$). Average EE levels (based on place(s) of residence) from age 25 to the diagnosis/reference date minus 1 year ranged from 1,109 to 4,158 among cases and from 1,127 to 4,321 among controls, with median value 1,897 for both groups. Average EE levels in the decade before the diagnosis/reference date minus 1 year ranged from 1,249 to 3,771 among cases and from 1,123 to 3,769 among controls, with median value 1,897 for both groups. Neither measure was associated with ovarian cancer risk (Table 3). These results changed only slightly when additionally adjusted for tendency to burn, ability to tan, and/or BMI.

Table 4 shows the association between behavioral sun exposure factors and risk of invasive ovarian cancer separately for two different age intervals. While we observed age-related differences in self-reported sun exposure (e.g., only 10.1% of cases and 9.5% of controls reported having less than 1 hour/day of daily summer sun exposure during the teen age years, while 45.5% of cases and 42.6% of controls reported that degree of exposure in the decade prior to the diagnosis/reference date; 15.6% of cases and 17.3% of controls reported not having a sun tan during the teen age years, versus 30.4% of cases and 28.8% of controls reported no tan in the decade prior to the diagnosis/reference date), and in the use of sun screen (83.6% of cases and 84.1% of controls reported not using sun screen during the teen age years, compared to 31.4% of cases and 29.0% of controls in the decade prior to the diagnosis/reference date), no associations were observed between these factors and risk of invasive ovarian cancer in either period. When we combined the weekly average of sun exposure in summer months with the use of sunscreen, we again did not observe any associations with the risk of ovarian cancer, although the numbers in the individual exposure categories were relatively small for this analysis (data not shown).

We observed little evidence that associations with pigmentation characteristics or EE levels varied markedly by histologic subtype of invasive disease (Table 5). Relative to women who reported no ability to tan after prolonged sun exposure, increased risks were noted in women who reported a greater ability to tan for serous cancers, while little evidence of similar risk increases was noted for the combined group of endometrioid/clear cell cancers or for “other” epithelial cancers. Although risk of serous cancers was weakly increased among women with increasing EE ($P_{\text{trend}}=0.06$), the direction of this effect was opposite to what had been hypothesized, assuming increased EE indicates increased vitamin D synthesis from ultraviolet exposure. In additional stratified analyses, we noted no differences in associations of ovarian cancer risk with behavioral or residence-based measures of sun exposure when we restricted our analyses to groups of women who reported no or mild ability to tan versus women who tanned moderately or deeply (data not shown).

Discussion

This study assessed the relationship between sun exposure and ovarian cancer, using sun exposure as a surrogate of the availability of endogenous vitamin D. For the majority of people, vitamin D is principally synthesized from sun exposure [25], and so sun-related behaviors as well as phenotypic characteristics that are associated with UV-light absorption likely correlate with endogenous levels of vitamin D [26]. Little evidence was found of an association of ovarian cancer risk with either the different measures of pigmentation or the residence-based and behavioral measures of sun exposure in our study.

However, our study may be subject to several limitations. Not all eligible cases or controls could be enrolled; our risk estimates could be influenced if those who chose not to

participate differed from the study subjects in factors related to sun exposure. Errors in reporting pigmentation characteristics, residential history and other sun-related behaviors could also affect our results. While there is little reason to expect that cases and controls would differ in the accuracy of self-report of these exposures (given the limited extent to which they have been addressed in prior ovarian cancer studies), such errors in reporting could nevertheless result in nondifferential misclassification. Some evidence suggests that, although sun exposure behaviors may seem difficult to recall throughout the lifetime of a person, information obtained using standardized interview instruments can provide a valid measure of cumulative sun exposure [24]. Another potential source of bias could be a lack of sun exposure among cases in the months immediately preceding diagnosis due to ill health attributable to the presence of the cancer, which could lead to apparent risk increases associated with reduced sun exposure, particularly for the behavioral measures. We therefore attempted to diminish any influence of such bias by considering only exposure up to one year before the diagnosis/reference date when this was possible. Also, it is possible that unknown or unmeasured confounders could have biased our results.

A large proportion of both cases and controls, particularly in the decade preceding the diagnosis or reference date, had average EE levels equivalent to the EE for the Seattle area, WA, the population center for our study. While little evidence of differences in risk were noted for women who resided either in areas of greater or lesser EE, it is possible that associations with residence-based measures of UV exposure may be more clearly linked with risk in other regions or populations, particularly if study populations with a greater extent of variation in EE levels can be observed.

The present study differs in several aspects from previous analytic epidemiologic studies of ovarian cancer risk associated with measures of vitamin D. Most of the previous studies were based on circulating levels of vitamin D (see review [27]) based on a single measurement [8, 13]. Although circulating levels of 25(OH)D have been observed to be stable for about 5 years [28], vitamin D levels are nevertheless expected to vary over the lifetime, given that sun exposure behaviors are very different during the lifetime of a person, as observed in our Table 4. Since the relevant period of exposure influencing the risk of ovarian cancer is unknown, studies based on circulating levels of vitamin D are limited by looking at the exposure at a single point in time. Our study, in contrast, was able to look at behavioral measures of sun exposure over two different periods, and at residential history throughout adulthood. In particular, we were able to look at sun-related behaviors such as time spent in the summer sun early in life, which has been observed to be relevant in other cancers [29]. Studies based on the intake of vitamin D might suffer by not having an accurate assessment of circulating vitamin D levels (as well as differences in this exposure over the lifetime), given that for most people dietary vitamin D represents only a small source of circulating levels of 25(OH)D [5]. The current study further differs from previous ovarian cancer studies of sun exposure in the use of a sun exposure index computed through linking an individual's residential history, assessed at the city level, with objective measures of UV irradiance measured at each 1° latitude and 1.25° longitude). This finer level of detail contrasts with a case-control study on ovarian cancer mortality in which state-level data on place of residence was more broadly categorized as low/medium/high annual mean daily solar radiation [1].

Despite the examination of several measures thought to be correlated with vitamin D synthesis through sun exposure, we found little evidence of association with ovarian cancer risk. Relative to women who reported that they did not tan with prolonged sun exposure, women who were more likely to tan were at increased ovarian cancer risk. Due to the number of tests performed, this association could be due to chance; if not, this increased risk may reflect a lesser extent of vitamin D synthesis among women in whom more melanin

pigment is produced with sun exposure. Risk estimates for variables that examined behavioral measures of sun exposure were similarly null whether exposures were assessed in the teen years or in the recent past, and a lifetime (after age 25) summary variable of EE also failed to detect risk reductions with increased potential sun exposure based on place of residence. While some evidence of a trend in risk associated with EE was noted among women with serous invasive cancer, this association was in the direction opposite to what was hypothesized, and may be due to chance. Our results add to the lack of consistent evidence of the relationship between sun exposure and incidence of ovarian cancer.

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Table 1
Outcomes of telephone screening for control recruitment, western Washington State, 2002–2009.

Total telephone numbers called	84,462	
Ineligible telephone number	53,653	
Business	11,357	
Non-working	36,282	
Non-business (institutions, group quarters, data-lines, cell phones)	6,014	
Unknown if residential telephone number	6,409	
Known residential telephone number	24,400	
Unknown if individual eligible	5,308	
Answering machine on all attempts	2,012	
Refused age/county questions	2,297	
Age/county eligible, ovarian status unknown	488	
Other (language/communication barrier)	511	
Respondent screened	19,092	
Not eligible	16,741	
Did not fit age/county eligibility or frequency matching criteria	16,087	
No ovaries	624	
Prior ovarian cancer	6	
Selected woman had communication barrier	24	
Eligible	2,351	
Not interviewed	502	
Interviewed	1,849	

Table 2

Characteristics of non-Hispanic white women with invasive or borderline epithelial ovarian cancer and controls, western Washington State, 2002–2009.

Characteristics	Cases (N=1,334) n (%)	Controls (N=1,679) n (%)
<i>Age (years)</i>		
35–44	163 (12.2)	177 (10.5)
45–54	443 (33.2)	482 (28.7)
55–64	483 (36.2)	626 (37.3)
65–74	245 (18.4)	394 (23.5)
<i>BMI at age 30 (Kg/m²)</i>		
< 25.0	1,038 (78.3)	1,386 (83.3)
25.0–29.9	168 (12.7)	128 (11.3)
30	120 (9.0)	61 (5.4)
Missing	8	16
<i>Education</i>		
High school or less	325 (24.4)	360 (21.5)
Some college or technical school	504 (37.8)	612 (36.5)
College graduate	303 (22.7)	396 (23.6)
Post-college studies	200 (15.0)	310 (18.5)
Missing	2	1
<i>Full term pregnancies</i>		
0	329 (24.7)	258 (15.4)
1	219 (16.4)	226 (13.5)
2	403 (30.2)	570 (33.9)
3	383 (28.7)	625 (37.2)
<i>Hormonal contraceptive use (years)</i>		
Never	293 (22.0)	283 (16.9)
Less than 6 months	117 (8.8)	108 (6.4)
6 months to less than 5 years	488 (36.6)	609 (36.3)
5 years to less than 10 years	247 (18.5)	356 (21.2)
10 years or more	187 (14.0)	323 (19.2)
Missing	2	0
<i>Tubal ligation</i>		
No	1,098 (82.3)	1,294 (77.1)
Yes	236 (17.7)	385 (22.9)
<i>Family history of breast and ovarian cancer</i>		
Not known	739 (57.8)	975 (59.8)
Breast cancer only	385 (30.1)	540 (33.1)
Ovarian cancer only	85 (6.7)	65 (4.0)
Breast and ovarian cancer	69 (5.4)	50 (3.1)
Missing	56	49

Table 3

Pigmentation characteristics, tendency to burn, ability to tan and erythema exposure (EE)[‡] and risk of epithelial ovarian cancer by tumor type, western Washington State, 2002–2009.

	All tumors			Borderline tumors			Invasive tumors		
	Controls (N=1,679)	Cases (N=1,334)		Cases (N=351)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	
		n (%)	OR* (95% CI)						
Natural skin color									
Light	1,194 (71.1)	962 (72.3)	1.00 (ref.)	258 (73.7)	1.00 (ref.)	704 (71.8)	1.00 (ref.)		
Medium	480 (28.6)	363 (27.3)	1.07 (0.90–1.26)	91 (26.0)	1.03 (0.78–1.35)	272 (27.7)	1.06 (0.88–1.28)		
Dark	5 (0.3)	6 (0.5)	1.72 (0.51–5.82)	1 (0.3)	0.90 (0.09–8.51)	5 (0.5)	2.15 (0.60–7.74)		
P _{trend}			0.36		0.87		0.38		
Natural hair color (as a teenager)									
Blonde or red	524 (31.2)	438 (32.9)	1.00 (ref.)	122 (34.8)	1.00 (ref.)	316 (32.2)	1.00 (ref.)		
Light brown	348 (20.7)	239 (17.9)	0.81 (0.65–1.00)	57 (16.2)	0.65 (0.46–0.93)	182 (18.5)	0.86 (0.68–1.09)		
Medium or dark brown	774 (46.1)	642 (48.2)	0.96 (0.81–1.14)	167 (47.6)	0.89 (0.68–1.17)	475 (48.4)	0.98 (0.81–1.18)		
Black	33 (2.0)	14 (1.1)	0.52 (0.27–1.02)	5 (1.4)	0.79 (0.28–2.18)	9 (0.9)	0.43 (0.20–0.93)		
P _{trend}			0.46		0.51		0.54		
Natural eye color									
Blue or Grey	655 (39.0)	529 (39.7)	1.00 (ref.)	135 (38.5)	1.00 (ref.)	394 (40.1)	1.00 (ref.)		
Green	232 (13.8)	185 (13.9)	0.98 (0.77–1.24)	47 (13.4)	0.87 (0.59–1.27)	138 (14.0)	1.03 (0.80–1.33)		
Hazel	388 (23.1)	281 (21.1)	0.88 (0.72–1.07)	70 (19.9)	0.88 (0.64–1.23)	211 (21.5)	0.88 (0.71–1.10)		
Brown	404 (24.1)	339 (25.4)	1.01 (0.83–1.23)	99 (28.2)	1.10 (0.81–1.49)	240 (24.4)	0.97 (0.78–1.20)		
P _{trend}			0.77		0.70		0.52		
Tendency to burn [§]									
Painful burn with blistering or peeling	651 (39.1)	530 (39.9)	1.00 (ref.)	131 (37.5)	1.00 (ref.)	399 (40.8)	1.00 (ref.)		
Mild burn then tan	809 (48.5)	619 (46.6)	0.90 (0.76–1.06)	166 (47.6)	0.93 (0.71–1.21)	453 (46.3)	0.87 (0.73–1.04)		
Tan without burn	207 (12.4)	178 (13.4)	1.07 (0.84–1.36)	52 (14.9)	1.35 (0.92–1.98)	126 (12.9)	0.97 (0.74–1.26)		
P _{trend}			0.92		0.33		0.42		
Ability to tan [¶]									

	All tumors				Borderline tumors				Invasive tumors			
	Controls (N=1,679)		Cases (N=1,334)		Cases (N=351)		Cases (N=983)		Cases (N=983)		Cases (N=983)	
	n (%)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	n (%)
Freckle or no tan	203 (12.1)	150 (11.3)	1.00 (ref.)	36 (10.3)	1.00 (ref.)	114 (11.6)	1.00 (ref.)	114 (11.6)	1.00 (ref.)	114 (11.6)	1.00 (ref.)	114 (11.6)
Mild tan	389 (23.2)	277 (20.8)	0.92 (0.70–1.21)	73 (20.9)	0.92 (0.58–1.45)	204 (20.8)	0.92 (0.68–1.24)	204 (20.8)	0.92 (0.68–1.24)	204 (20.8)	0.92 (0.68–1.24)	204 (20.8)
Moderate tan	773 (46.1)	638 (47.9)	1.11 (0.87–1.42)	166 (47.4)	1.05 (0.70–1.58)	472 (48.1)	1.13 (0.87–1.48)	472 (48.1)	1.13 (0.87–1.48)	472 (48.1)	1.13 (0.87–1.48)	472 (48.1)
Deep tan	310 (18.5)	267 (20.0)	1.22 (0.92–1.61)	75 (21.4)	1.24 (0.79–1.96)	192 (19.6)	1.21 (0.89–1.64)	192 (19.6)	1.21 (0.89–1.64)	192 (19.6)	1.21 (0.89–1.64)	192 (19.6)
P _{trend}			0.03		0.18		0.05		0.05		0.05	
<i>Mean EE level from age 25 to diagnosis/reference date minus 1 year[£]</i>												
< 1897	415 (24.7)	337 (25.3)	0.89 (0.70–1.13)	97 (27.6)	1.08 (0.74–1.59)	240 (24.4)	0.83 (0.64–1.07)	240 (24.4)	0.83 (0.64–1.07)	240 (24.4)	0.83 (0.64–1.07)	240 (24.4)
1897	499 (29.8)	426 (31.9)	1.00 (ref.)	107 (30.5)	1.00 (ref.)	319 (32.5)	1.00 (ref.)	319 (32.5)	1.00 (ref.)	319 (32.5)	1.00 (ref.)	319 (32.5)
> 1897 and < 2042	343 (20.5)	218 (16.3)	0.78 (0.62–0.97)	54 (15.4)	0.87 (0.60–1.27)	164 (16.7)	0.75 (0.59–0.96)	164 (16.7)	0.75 (0.59–0.96)	164 (16.7)	0.75 (0.59–0.96)	164 (16.7)
2042	420 (25.0)	353 (26.5)	0.97 (0.79–1.19)	93 (26.5)	1.10 (0.79–1.53)	260 (26.4)	0.94 (0.75–1.18)	260 (26.4)	0.94 (0.75–1.18)	260 (26.4)	0.94 (0.75–1.18)	260 (26.4)
P _{trend}			0.98		0.96		0.86		0.86		0.86	
<i>Mean EE level in the 10 years prior to diagnosis/reference date minus 1 year[£]</i>												
< 1897	495 (29.5)	397 (29.8)	0.92 (0.71–1.20)	110 (31.3)	1.14 (0.75–1.74)	287 (29.2)	0.84 (0.63–1.12)	287 (29.2)	0.84 (0.63–1.12)	287 (29.2)	0.84 (0.63–1.12)	287 (29.2)
1897	924 (57.4)	748 (56.1)	1.00 (ref.)	182 (51.9)	1.00 (ref.)	566 (57.6)	1.00 (ref.)	566 (57.6)	1.00 (ref.)	566 (57.6)	1.00 (ref.)	566 (57.6)
> 1897	220 (13.1)	189 (14.2)	1.05 (0.71–1.20)	59 (16.8)	1.21 (0.84–1.73)	130 (13.2)	1.00 (0.76–1.30)	130 (13.2)	1.00 (0.76–1.30)	130 (13.2)	1.00 (0.76–1.30)	130 (13.2)
P _{trend}			0.37		0.68		0.30		0.30		0.30	

[£]EE: mean index of erythema exposure, computed based upon place of residence (see text). Numbers might not add to total due to missing values.

^{*}Adjusted for age, county of residence, calendar year, number of full term pregnancies, and duration of hormonal contraceptives.

[§]Tendency to burn based on first exposure to summer sun (1 hour or more).

[¶]Ability to tan upon prolonged exposure to summer sun.

[£]The EE value for Seattle area, WA, US, is 1897.

Behavioral sun exposure factors and risk of invasive epithelial ovarian cancer in two different age intervals, western Washington State, 2002–2009.

Table 4

	Teen age years			Decade prior to diagnosis/reference date		
	Controls (N=1,679)	Cases (N=983)	OR* (95% CI)	Controls (N=1,679)	Cases (N=983)	OR* (95% CI)
	n (%)	n (%)		n (%)	n (%)	
Weekly average of daily sun exposure in summer months						
< 1 hour/day	159 (9.5)	99 (10.1)	1.00 (ref.)	716 (42.6)	446 (45.5)	1.00 (ref.)
1 to < 2 hours/day	304 (18.1)	164 (16.7)	0.90 (0.65–1.25)	504 (30.0)	287 (29.3)	0.92 (0.75–1.11)
2 to < 3 hours/day	273 (16.3)	160 (16.3)	0.93 (0.67–1.30)	224 (13.3)	124 (12.6)	0.85 (0.65–1.10)
3 to < 4 hours/day	345 (20.6)	222 (22.6)	1.09 (0.79–1.49)	145 (8.6)	71 (7.2)	0.88 (0.64–1.22)
4 to < 5 hours/day	224 (13.3)	132 (13.5)	0.97 (0.69–1.38)	53 (3.2)	28 (2.9)	0.79 (0.48–1.30)
5 hours/day	373 (22.2)	204 (20.8)	0.88 (0.64–1.22)	37 (2.2)	25 (2.5)	1.08 (0.63–1.87)
P _{trend}			0.80			0.32
Months with sun tan per year						
Never had a sun tan	290 (17.3)	153 (15.6)	1.00 (ref.)	484 (28.8)	298 (30.4)	1.00 (ref.)
1–3 months	791 (47.1)	479 (48.9)	1.17 (0.92–1.48)	889 (53.0)	499 (50.9)	0.95 (0.79–1.15)
4–6 months	426 (25.4)	260 (26.5)	1.12 (0.87–1.46)	234 (13.9)	136 (13.9)	0.94 (0.72–1.23)
7–9 months	105 (6.3)	46 (4.7)	0.86 (0.57–1.30)	40 (2.4)	24 (2.4)	0.96 (0.56–1.66)
10–12 months	67 (4.0)	42 (4.3)	1.15 (0.73–1.80)	31 (1.8)	23 (2.3)	1.33 (0.74–2.40)
P _{trend}			0.95			0.87
Use of sun screen						
Never or rarely	1412 (84.1)	821 (83.6)	1.00 (ref.)	487 (29.0)	309 (31.4)	1.00 (ref.)
Less than half the time	120 (7.1)	66 (6.7)	0.97 (0.70–1.35)	187 (11.1)	111 (11.3)	0.89 (0.67–1.19)
About half the time	73 (4.3)	53 (5.4)	1.05 (0.72–1.55)	234 (13.9)	154 (15.7)	1.08 (0.83–1.40)
More than half the time	32 (1.9)	17 (1.7)	0.87 (0.47–1.62)	247 (14.7)	112 (11.4)	0.71 (0.53–0.94)
Always or nearly always	42 (2.5)	25 (2.5)	0.95 (0.56–1.61)	523 (31.2)	297 (30.2)	0.91 (0.74–1.13)
P _{trend}			0.82			0.23

Numbers might not add to total due to missing values.

* Adjusted for age, county of residence, calendar year, number of full term pregnancies, and duration of hormonal contraceptives.

Table 5

Pigmentation characteristics, tendency to burn, ability to tan, and erythral exposure (EE)[‡] and risk of invasive ovarian cancer by histological subtype, western Washington State, 2002–2009.

	Serous invasive tumors			Endometroid/dear cell invasive tumors			Other epithelial (non-mucinous) invasive tumors		
	Controls (N=1,679)	Cases (N=577)		Cases (N=234)	Cases (N=144)		Cases (N=144)	OR* (95% CI)	OR* (95% CI)
	n (%)	n (%)	OR* (95% CI)	n (%)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	OR* (95% CI)
<i>Natural skin color</i>									
Light	1,194 (71.1)	404 (70.1)	1.00 (ref.)	182 (77.8)	99 (69.2)	1.00 (ref.)	99 (69.2)	1.00 (ref.)	1.00 (ref.)
Medium	480 (28.6)	170 (29.5)	1.12 (0.90–1.39)	49 (20.9)	44 (30.8)	0.80 (0.56–1.15)	44 (30.8)	1.18 (0.81–1.74)	1.18 (0.81–1.74)
Dark	5 (0.3)	2 (0.3)	2.02 (0.38–10.88)	3 (1.3)	0 (0.0)	6.71 (1.40–32.15)	0 (0.0)	--	--
P _{trend}			0.26			0.61			0.45
<i>Natural hair color (as a teenager)</i>									
Blonde or red	524 (31.2)	188 (32.6)	1.00 (ref.)	76 (32.5)	40 (28.0)	1.00 (ref.)	40 (28.0)	1.00 (ref.)	1.00 (ref.)
Light brown	348 (20.7)	94 (16.3)	0.73 (0.55–0.98)	54 (23.1)	28 (19.6)	1.00 (0.67–1.49)	28 (19.6)	1.03 (0.61–1.71)	1.03 (0.61–1.71)
Medium or dark brown	774 (46.1)	289 (50.1)	0.99 (0.79–1.24)	101 (43.2)	75 (52.4)	0.84 (0.59–1.18)	75 (52.4)	1.25 (0.83–1.88)	1.25 (0.83–1.88)
Black	33 (2.0)	6 (1.0)	0.47 (0.19–1.18)	3 (1.3)	0 (0.0)	0.80 (0.22–2.87)	0 (0.0)	--	--
P _{trend}			0.80			0.27			0.57
<i>Natural eye color</i>									
Blue or Grey	655 (39.0)	236 (40.9)	1.00 (ref.)	103 (44.0)	44 (30.6)	1.00 (ref.)	44 (30.6)	1.00 (ref.)	1.00 (ref.)
Green	232 (13.8)	79 (13.7)	0.99 (0.72–1.34)	24 (10.3)	31 (21.5)	0.63 (0.38–1.04)	31 (21.5)	2.10 (1.28–3.44)	2.10 (1.28–3.44)
Hazel	388 (23.1)	122 (21.1)	0.86 (0.66–1.11)	52 (22.2)	29 (20.1)	0.85 (0.58–1.24)	29 (20.1)	1.13 (0.69–1.84)	1.13 (0.69–1.84)
Brown	404 (24.1)	140 (24.3)	1.00 (0.77–1.28)	55 (23.5)	40 (27.8)	0.81 (0.56–1.18)	40 (27.8)	1.42 (0.90–2.25)	1.42 (0.90–2.25)
P _{trend}			0.68			0.29			0.29
<i>Tendency to burn[§]</i>									
Painful burn with blistering or peeling	651 (39.1)	232 (40.4)	1.00 (ref.)	90 (38.6)	68 (47.6)	1.00 (ref.)	68 (47.6)	1.00 (ref.)	1.00 (ref.)
Mild burn then tan	809 (48.5)	264 (46.0)	0.89 (0.72–1.10)	120 (51.5)	53 (37.1)	0.88 (0.64–1.21)	53 (37.1)	0.61 (0.41–0.89)	0.61 (0.41–0.89)
Tan without burn	207 (12.4)	78 (13.6)	1.00 (0.73–1.37)	23 (9.9)	22 (15.4)	0.80 (0.48–1.34)	22 (15.4)	0.99 (0.59–1.67)	0.99 (0.59–1.67)
P _{trend}			0.66			0.32			0.28
<i>Ability to tan[¶]</i>									

	Serous invasive tumors		Endometroid/clear cell invasive tumors		Other epithelial (non-mucinous) invasive tumors	
	Cases (N=577)		Cases (N=234)		Cases (N=144)	
	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)	n (%)	OR* (95% CI)
Freckle or no tan	203 (12.1)	63 (10.9)	1.00 (ref.)	30 (12.8)	19 (13.2)	1.00 (ref.)
Mild tan	389 (23.2)	122 (21.2)	1.05 (0.73–1.50)	47 (20.1)	32 (22.2)	0.86 (0.47–1.58)
Moderate tan	773 (46.1)	282 (49.0)	1.26 (0.91–1.75)	117 (50.0)	58 (40.3)	0.76 (0.44–1.33)
Deep tan	310 (18.5)	109 (18.9)	1.29 (0.89–1.87)	40 (17.1)	35 (24.3)	1.26 (0.69–2.30)
P _{trend}		0.07		0.84		0.50
<i>Mean EE level from age 25 to diagnosis/reference date minus 1 year[£]</i>						
<1897	415 (24.7)	141 (24.4)	0.86 (0.62–1.15)	59 (25.2)	34 (23.6)	0.63 (0.36–1.10)
1897	499 (29.8)	176 (30.5)	1.00 (ref.)	81 (34.6)	50 (34.7)	1.00 (ref.)
>1897 and <2042	343 (20.5)	105 (18.2)	0.86 (0.62–1.17)	34 (14.5)	22 (15.3)	0.60 (0.35–1.02)
2042	420 (25.0)	155 (26.9)	1.01 (0.77–1.33)	60 (25.6)	38 (26.4)	0.80 (0.50–1.29)
P _{trend}		0.47		0.78		0.90
<i>Mean EE level in the 10 years prior to diagnosis/reference date minus 1 year[£]</i>						
<1897	495 (29.5)	166 (28.8)	0.82 (0.58–1.16)	63 (26.9)	52 (36.1)	1.36 (0.77–2.40)
1897	964 (57.4)	328 (56.8)	1.00 (ref.)	145 (62.0)	75 (52.1)	1.00 (ref.)
> 1897	220 (13.1)	83 (14.4)	1.16 (0.85–1.59)	26 (11.1)	17 (11.8)	1.01 (0.57–1.81)
P _{trend}		0.06		0.83		0.39

[£]EE: mean index of erythema exposure, computed based upon place of residence (see text). Numbers might not add to total due to missing values.

^{*}Adjusted for age, county of residence, calendar year, number of full term pregnancies, and duration of hormonal contraceptives.

[§]Tendency to burn based on first exposure to summer sun (1 hour or more).

[¶]Ability to tan upon prolonged exposure to summer sun.

[£]The EE value for Seattle area, WA, US, is 1897.