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Reproductive Factors and Ovarian Cancer Risk in African American Women

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Abstract

Purpose—Reproductive characteristics, the most established ovarian cancer risk factors, differ markedly between African American and White women. Studies in predominantly White populations suggest that associations between reproductive characteristics and ovarian cancer vary by timing of the events and menopause status. This analysis examined associations between number, duration and timing of reproductive events and epithelial ovarian cancer among African American women.

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Methods—Data from a multi-center case-control study of ovarian cancer in African American women (641 cases/752 controls) were used to examine associations with oral contraceptive use and pregnancy characteristics. Odds ratios(OR) and 95% confidence intervals(CI) associated with reproductive characteristics were calculated with logistic regression models.

Results—Oral contraceptive use (OR=0.7, 95%CI 0.5–0.9), parity (OR=0.5, 95% CI 0.3–0.6) and breastfeeding for >12 months (OR=0.3, 95% CI 0.2–0.5) were inversely associated with ovarian cancer. More recent pregnancies and oral contraceptive use had stronger associations with ovarian cancer than pregnancies or oral contraceptive use that occurred earlier in life, especially among pre-menopausal women.

Conclusions—This study provides the first thorough documentation that pregnancy, breastfeeding and oral contraceptive use are inversely associated with ovarian cancer in African American women, similar to what has been observed in White women. The associations with timing of the exposures suggest that these factors have both short and long-term effects.

Keywords

African Americans; breastfeeding; case-control study; oral contraceptives; ovarian cancer; parity; pregnancy

Introduction

Epithelial ovarian cancer has a median age of diagnosis of approximately 63 years.[1] Despite being a disease that is more frequently diagnosed among post-menopausal women, the factors that most influence ovarian cancer risk are reproductive characteristics such as pregnancy, oral contraceptive use and breastfeeding that typically occur when a woman is in her twenties or thirties.[2] Analyses conducted within predominantly White populations suggest that the associations between reproductive characteristics and ovarian cancer depend upon the timing of the exposure and may differ for ovarian cancer diagnosed before and after menopause.[3–12] Most notably, the inverse association with pregnancy seems to be stronger for pre-menopausal women, which may be due to the effect of time since last pregnancy.[3,4,6,8,12] More recent pregnancies have been associated with a greater reduction in ovarian cancer risk that appears to be independent of the total number of pregnancies. These findings suggest that reproductive risk factors may operate through multiple biological pathways that may have both short-term and long-term effects on ovarian cancer risk.

African American women differ markedly from White women in their incidence of ovarian cancer (9.8/100,000 and 12.8/100,000 in African Americans and Whites, respectively)[1] as well as in many of their reproductive characteristics. On average, African American women experience more total pregnancies,[13] an earlier age at first pregnancy,[13] less breastfeeding,[14] and less oral contraceptive use.[15] There are only a few published reports describing the association between reproductive characteristics and ovarian cancer risk in African American women, and all have had very modest sample sizes.[16–19] While these studies have reported inverse associations with pregnancy and oral contraceptive use similar to what has been reported in White women, none of them has presented results stratified by menopausal

status and all were limited in their ability to examine effects by duration, number or timing of the reproductive events.

The purpose of this report is to describe associations between ovarian cancer and the reproductive characteristics of oral contraceptive use, parity, and breastfeeding stratified by menopausal status, using data from a multi-center, case-control study of ovarian cancer in African American women. We present overall associations with ovarian cancer risk as well as examine the effect of the number of pregnancies, the duration of exposure to oral contraceptives and timing of the exposures.

Methods

The data used in these analyses are from the African American Cancer Epidemiology Study (AACES), a population-based, case-control study of ovarian cancer in African American women in 11 geographic regions: North Carolina, South Carolina, Georgia, Alabama, Tennessee, Louisiana, Texas, New Jersey, Ohio, Chicago and Detroit. Duke University is the lead institution for the study. Institutional review board approval was obtained from the Duke University School of Medicine and all participating institutions. The methods of the study have been previously reported [20] and are described here briefly.

Women with ovarian cancer were identified using rapid case ascertainment systems through state cancer registries, Surveillance, Epidemiology and End Results (SEER) registries or individual hospital registries. Inclusion criteria were self-identified African-American/Black race, aged 20–79 years, diagnosis of invasive, epithelial ovarian cancer, no prior history of ovarian cancer and ability to complete an interview in English. Of 1546 eligible cases identified, physician consent was not obtained for 1% of the women, 17% died before they could be contacted, 16% could not be contacted, 23% refused to participate and 42% were enrolled in the study. Controls were selected using random digit dialing, frequency matched to cases on age and geographic region. Eligibility criteria were similar to cases plus they must not have had bilateral oophorectomy or a prior history of ovarian cancer. Of 1450 eligible controls identified, 0.2% died, 24% could not be contacted for an interview, 24% refused to participate and 52% were enrolled in the study. The current analyses are based on women enrolled from December 2010 through January 2016 and include 641 cases and 752 controls.

Data were collected via an interviewer-administered computer-assisted telephone interview (CATI). Survey information included demographic characteristics; reproductive, gynecologic and medical history; hormone use; family history of cancer; and lifestyle characteristics such as smoking, alcohol consumption and physical activity. For the pregnancy characteristics, women provided detailed information on each pregnancy including outcome, duration, date pregnancy ended and breastfeeding information. A full-term pregnancy for the purposes of these analyses was defined as one lasting more than 6 months. Oral contraceptive information was based on a detailed lifetime contraceptive history of the type and timing of each method used.

Menopausal status was based on self-reported menstrual history. Women were categorized as post-menopausal if their menstrual periods had stopped naturally 12 or more months prior to diagnosis/interview or their periods stopped due to chemotherapy or radiation. Women who had started menopausal hormones before their periods stopped and had been taking them for at least two years or thought that they began menopause at least 4 years prior to diagnosis or interview were categorized as post-menopausal. Women who had a pre-menopausal hysterectomy without bilateral oophorectomy were considered post-menopausal if they were 50 years of age or older at diagnosis/interview or, if they were younger than age 50, at least 4 years had passed since they thought they began menopause.

Demographic and other descriptive characteristics of cases and controls were compared using a chi-squared test. Unconditional logistic regression analyses were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for parameters related to oral contraceptive use and pregnancy history. Variables included as potential confounders included study site, age (continuous), family history of breast or ovarian cancer in a first degree relative (yes/no), age at menarche (continuous), tubal ligation (yes/no), and body mass index (BMI in kg/m^2, continuous). Analyses that simultaneously examined the timing of exposure and duration of oral contraceptive use or timing and number of pregnancies were restricted to ever users of oral contraceptives and parous women, respectively. To perform tests for trend, categories of the variables were coded as continuous variables. Tests for interaction were conducted by including in the model a product term for menopausal status and the individual reproductive exposure variable. All analyses were conducted using SAS version 9.3 software.

Results

Descriptive characteristics of cases and controls stratified by menopausal status are presented in Table 1. For most characteristics, the direction of the associations were similar for pre- and post-menopausal women, although the magnitude of the differences between cases and controls varied between pre-and post-menopausal cases for several characteristics including family history of cancer, and infertility, which had stronger associations in pre-menopausal women. A notable exception was that post-menopausal cases had higher BMI than controls, which was not the case in pre-menopausal women.

Table 2 presents associations between patterns of oral contraceptive use and ovarian cancer for all women and stratified by menopausal status. The point estimate for ever use of oral contraceptives was 0.7 (95% CI 0.5 – 0. 9) for all women, and was similar for pre- and post-menopausal women, with odds ratios of 0.6 (95% CI 0.4 – 1.2) and 0.7 (95% CI 0.5 – 0.9), respectively, although the association was statistically significant only among the postmenopausal women. Compared to pre-menopausal women, we observed among postmenopausal women that increasing duration of oral contraceptive use was associated with greater reductions in ovarian cancer risk, test for trend p=0.005. Differences in associations by menopausal status were observed in relation to the timing of oral contraceptive use. Among pre-menopausal women, the data suggested that more recent use was associated with greater reduction in risk with significant trends for age at first use (p=0.01), age at last use (p= 0.01) and years since last use (p=0.0009). In contrast, among

post-menopausal women there was not a significant association with age at first use, age at last use and years since last use.

Longer duration of oral contraceptive use tends to correlate with more recent use and later age at last use, but it is inappropriate to include terms for both characteristics of exposure in the same model when unexposed women (i.e., non-users) are the reference group.[21] Therefore, we ran logistic regression models restricted to oral contraceptive users that examined associations with characteristics of timing of exposure while controlling for duration of oral contraceptive use (Table 3). Among pre-menopausal oral contraceptive users, significant inverse trends were observed for later age at first use (p=0.02), later age at last use (p=0.02) and years since last use (p=0.0003) when controlling for duration of use. In contrast, among post-menopausal oral contraceptive users, women with earlier use were at lower risk than those with later use of oral contraceptives, controlling for duration of use.

The effects of pregnancy characteristics on ovarian cancer risk are presented in Table 4. The OR for ovarian cancer was significantly reduced among those who reported at least one full-term pregnancy (OR=0.5, 95% CI 0.3–0.6). The inverse association was stronger for pre-menopausal (OR=0.3, 95% CI 0.2 – 0.5) versus post-menopausal women (OR=0.5, 95% CI 0.4–0.8), with significant trends for decreasing risk with increasing number of pregnancies in pre-menopausal women. Analyses of the timing of pregnancy suggested that later pregnancies, defined either by age at last pregnancy or time since last pregnancy, were associated with reduced ovarian cancer risk. Strong inverse associations were observed for later age at last pregnancy and years since last pregnancy among pre-menopausal women. Among post-menopausal women, no significant trends were observed for these measures, although the smallest odds ratios were observed for more recent pregnancies. A composite variable combining the number of pregnancies and time since last pregnancy showed the smallest odds ratio for pre-menopausal women with 3 or more pregnancies and less than 10 years since the last pregnancy (OR=0.1, 95% CI 0.04–0.4). Duration of breastfeeding was inversely associated with risk among pre-menopausal women whereas no significant trend was observed among postmenopausal women.

Because women with more pregnancies may be more likely to have had more recent pregnancies, we repeated the analyses of the timing of pregnancy restricting the sample to women with at least one full-term pregnancy and included a term for number of pregnancies within each of the models (Table 5). A significant inverse association was observed for each measure of timing of pregnancy (age at first and last pregnancy, years since first and last pregnancy) among pre-menopausal women, suggesting that more recent pregnancies were associated with reduced risk even when taking into account the total number of pregnancies. Among post-menopausal women, we observed no significant trends in the associations between timing of pregnancies and risk of ovarian cancer.

Discussion

The associations between reproductive characteristics and ovarian cancer that we evaluated in the present study have previously been well-established in studies of predominantly White women. In this largest and most thorough investigation yet of these associations in African

American women, our analyses showed that oral contraceptive use and parity are inversely associated with ovarian cancer in African American women. This clearly documents for the first time what would be expected, namely that oral contraceptive use and parity are strongly inversely associated with ovarian cancer risk in both African American and White women.

Previous studies that reported on associations between reproductive characteristics and ovarian cancer in African American women were limited in their ability to examine characteristics of pregnancy or oral contraceptive use because of their small sample sizes (number of cases ranging from 84 to 143). [16–19] While each of the studies reported that parity and oral contraceptive use were inversely associated with ovarian cancer, none of them examined the effect of the timing of the exposures or whether associations differed by age or menopausal status. With the larger sample size in the current study, we were able to demonstrate, as has been shown in several studies of predominantly White populations, that the timing of the exposures appears to influence the associations, with stronger inverse associations with more recent pregnancies or oral contraceptive use as compared to exposures that occurred earlier in life.

Our study enrolled only African American women, so comparisons with findings in White women are necessarily between rather than within studies. There are some differences between our study and many of the studies of predominantly White women, specifically in regard to geographic location. Although our study recruited across a broad geographic region, a large proportion of the study population was from Southern states, reflecting areas with a higher percentage of African Americans in their population. Despite some differences in the geographic location from which study participants were recruited, the women in the present study should be fairly representative of African American women and comparisons with White women would be reasonable.

The overall association with oral contraceptive use was similar for pre and post-menopausal women, but differences in associations by menopausal status were noted when examining timing of exposure. Use later in life, whether measured by age at last use or years since last use, was associated with stronger inverse associations among pre-menopausal women, whereas no such trend was noted among post-menopausal women. Pregnancy related characteristics were more strongly associated with pre-menopausal than postmenopausal disease, and inverse associations appeared stronger for pregnancies at older ages or more recent pregnancies. Because pre-menopausal women have had their pregnancies more recently than post-menopausal women, the stronger association with pregnancy characteristics would be expected.

Multiple theories for the genesis of ovarian cancer have been advanced, which variously posit that ovarian carcinogenesis is linked to incessant ovulation, inflammation or levels of gonadotropins or progesterone.[22–27] With increasing recognition that epithelial ovarian cancer is comprised of distinct subtypes and that the fallopian tube may be the cell of origin for many ovarian cancers, there has been a re-examination and modification of these theories. [28–30] For example, Fathalla originally hypothesized that the rupture and subsequent repair of the ovarian surface epithelium with each ovulation led to the development of inclusion cysts that underwent malignant transformation.[22] This mechanism has been

discounted by more recent investigations which have provided evidence that ovarian cancers probably are not derived from surface epithelium cells.[29] An alternative hypothesis is that epithelial cells from the fimbria of the fallopian tube, which are in close contact with the ovaries, may be dislodged and implant in the ovary when the surface epithelium of the ovary is disrupted during ovulation. [29] The inflammatory response that accompanies ovulation may further contribute to ovarian carcinogenesis.[30] Thus, while the carcinogenic mechanism that was originally proposed for incessant ovulation seems less likely, ovulation remains as a key element in the cascade of events leading to ovarian cancer.

Although biological and epidemiologic evidence continues to point to the role of ovulation in ovarian cancer etiology, it has been noted that the reported reduction in risk associated with pregnancies or oral contraceptive use is greater than what can be explained simply by the reduction in number of ovulatory cycles.[24] Our findings that the timing of the exposures appears to modify the reduction in risk corroborates that some other aspects of pregnancy or oral contraceptive use beyond their effect on ovulation play into ovarian cancer risk reduction.

One of the alternative theories of ovarian cancer carcinogenesis focuses on the role of progesterone,[26] which is present in higher levels during pregnancy and is a component of oral contraceptive pills. Progesterone has been shown in experimental systems to induce apoptosis and have a “clearing” effect on transformed cells.[26,27,31] This mechanism suggests that later or more recent exposure to progesterone would have a stronger protective effect for ovarian cancer. Our observations of greater reductions in risk associated with more recent pregnancies or oral contraceptive use, particularly for pre-menopausal women, are consistent with this hypothesis.

Our data suggest that pregnancy and oral contraceptive use have both long-term and shorter term effects on the risk for ovarian cancer. The observation of reduced risk among parous women or oral contraceptive users regardless of age is indicative of a persistent, long-term effect of these exposures. The observations that women with more recent pregnancies or oral contraceptive use had greater reductions in risk than women with earlier exposure, especially among pre-menopausal women, suggest that these exposures also have effects that diminish over time. This effect of timing of the exposures was less prominent among the postmenopausal women, which is not surprising considering that most of these women had not been pregnant or used oral contraceptives in more than 20 years.

We did observe a difference in the distribution of histologic types between pre- and post-menopausal cases, with endometrioid and mucinous sub-types occurring more frequently in the younger women. While the small sample sizes for individual histologic subtypes within our study precluded doing meaningful analyses stratified by histology, it is unlikely that this was an explanation for the observed differences between pre- and post-menopausal women. Studies that have examined risk factors for ovarian cancer by histologic sub-type have tended to find similar associations with oral contraceptives and pregnancy across all histologic sub-types, with the possible exception of a weaker association between OC use and mucinous cancers.[32–35]

A limitation of our analyses is that it is impossible to disentangle the effects of age and menopausal status. Although our analyses were stratified by menopausal status, it cannot be discerned whether the observed differences reflect the endogenous hormonal environment or simply that post-menopausal women were older. Because pregnancies and oral contraceptive use occur only in pre-menopausal women (with rare exceptions for use of oral contraceptives in post-menopausal women), postmenopausal women would have experienced these exposures in the more distant past than pre-menopausal women. The suggestion of stronger associations among pre-menopausal women could reflect the time since exposure rather than differences in the hormonal environment. When analyses were repeated stratifying by age (<50 vs. >50 years), the results were very similar to those obtained when stratifying by menopausal status (data not shown). A related limitation is that the sample size of pre-menopausal women was relatively modest, therefore few of the tests for interaction by menopausal status were statistically significant. A much larger sample size than the one in the present study would be required to determine whether the associations are more strongly related to age or to menopausal status.

An additional potential limitation of the study is the possible selection bias that could result from non-response among both cases and controls. The proportion of women with ovarian cancer that could not be contacted because they were deceased (~17%) is much higher than what has been reported in studies of predominantly white women, suggesting that our case group was not entirely representative of African American women with ovarian cancer. Despite the relatively low response rates among both cases and controls, we did observe the expected associations with most established ovarian cancer risk factors, suggesting that selection bias was not likely a major problem.

The associations between ovarian cancer and oral contraceptive use and parity have been well-established for some time, but the unique contribution of this study is that it is the first to examine in detail the effects of these reproductive characteristics on ovarian cancer risk in African American women. African American women differ from White women with respect to many of these characteristics, including having more pregnancies, earlier age at first pregnancies, and less use of oral contraceptives. Although the characteristics of these exposures differ by race, we showed associations with oral contraceptives and parity that are generally similar to those that have been reported in White women. A possible exception is that the estimates associated with parity were stronger for the pre-menopausal African American women than what has been reported in most other studies, which may reflect a higher average number of pregnancies. The higher average number of pregnancies also may contribute to the lower overall incidence of epithelial ovarian cancer among African American women. In contrast, breastfeeding and oral contraceptive use, while also showing inverse associations with ovarian cancer, have a lower prevalence among African American women. Further evaluation of these associations in studies directly comparing African American and White women taking into account the magnitude of the associations as well as the prevalence of reproductive and other risk factors may provide further insight into reasons for racial differences in ovarian cancer incidence.

Conclusion

The present study clearly documents for the first time that pregnancy, breastfeeding and oral contraceptive use are associated with a substantially reduced risk for ovarian cancer in African American women. These data now provide the evidence-base to support what previously could only be assumed based on data from other populations, namely that these reproductive characteristics are at least as strongly inversely associated with ovarian cancer risk in African American women as they are in women of European ancestry. The effects appear to be affected by the timing of the exposures, especially among pre-menopausal women, suggesting that these factors have both short and long-term effects, which may be mediated by different mechanisms.

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List of Abbreviations

AACES	African American Cancer Epidemiology Study
CATI	computer –assisted telephone interview
CI	confidence interval
OR	odds ratio
SEER	Surveillance Epidemiology and End Results

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TABLE 1

Age-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) comparing characteristics of ovarian cancer cases and controls stratified by menopausal status, the African American Cancer Epidemiology Study (AACES), 2010–2016.

	Pre-menopausal				Post-menopausal				All Women			
	Cases n=175 n (%)	Controls n=224 n (%)	OR	95% CI	Cases n=466 n (%)	Controls n=528 n (%)	OR	95% CI	Cases n=641 n (%)	Controls n=752 n (%)	OR	95% CI
Age												
20 – 29	7 (4.0)	22 (9.8)			1 (0.2)	1 (0.2)			8(1.3)	23 (3.1)		
30 – 39	27 (15.4)	55 (24.6)			1 (0.2)	2 (0.4)			28(4.4)	57 (7.6)		
40 – 49	90 (51.4)	99 (44.2)			20 (4.3)	22 (4.2)			110 (17.2)	121 (16.1)		
50 – 59	48 (27.4)	46 (20.5)			165 (35.4)	235 (44.5)			213 (33.2)	281 (37.4)		
60 – 69	3 (1.7)	2 (0.9)			177 (38.0)	193 (36.6)			180 (28.1)	195 (25.9)		
70 – 79					102 (21.9)	75 (14.2)			102 (15.9)	75 (10.0)		
Education												
≤ High school graduate	69 (39.4)	69 (30.8)	1.0	Reference	214 (45.9)	211 (40.0)	1.0	Reference	283 (44.2)	280 (37.3)	1.0	
Some post-high school	56 (32.0)	84 (37.5)	0.7	(0.4–1.1)	149 (32.0)	182 (34.5)	0.9	(0.7–1.2)	205 (32.0)	266 (35.4)	0.8	(0.7–1.1)
≥ College graduate	50 (28.6)	71 (31.7)	0.8	(0.4–1.3)	103 (22.1)	134 (25.4)	0.8	(0.06–1.1)	153(23.9)	205 (27.3)	0.8	(0.6–1.1)
Missing						1				1		
Family history of breast or ovarian cancer (1st degree)												
No	128 (75.3)	194 (89.0)	1.0	Reference	333 (73.0)	400 (78.4)	1.0	Reference	461 (73.6)	594 (81.6)	1.0	Reference
Yes	42 (24.7)	24 (11.0)	2.4	(1.3–4.2)	123 (27.0)	110 (21.6)	1.4	(1.0–1.9)	165 (26.4)	134 (18.4)	1.6	(1.2–2.1)
Missing	5	6			10	18			15	24		
Age at menarche (years)												
<12	46 (26.3)	57 (25.5)	1.0	Reference	100 (21.5)	143 (27.1)	1.0	Reference	146 (22.8)	200 (26.6)	1.0	Reference
12 – 13	87 (49.7)	113 (50.5)	0.9	(0.6–1.6)	239 (51.3)	249 (47.2)	1.3	(1.0–1.8)	326 (50.9)	362 (48.1)	1.2	(0.9–1.6)
>13	42 (24.0)	54 (24.1)	0.9	(0.5–1.7)	127 (27.3)	136 (25.8)	1.2	(0.9–1.8)	169(26.4)	190 (25.3)	1.1	(0.8–1.5)
Age at menopause (yrs)												
<45					85 (19.0)	110 (21.1)	1.0	Reference				
45 – 49					108 (24.2)	135 (25.9)	1.0	(0.7–1.5)				
50 – 54					182 (40.7)	203 (39.0)	1.1	(0.7–1.5)				

	Pre-menopausal				Post-menopausal				All Women			
	Cases n=175 n (%)	**Controls n=224 n (%)**	**OR**	**95% CI**	**Cases n=466 n (%)**	**Controls n=528 n (%)**	**OR**	**95% CI**	**Cases n=641 n (%)**	**Controls n=752 n (%)**	**OR**	**95% CI**
>54					72 (16.1)	73 (14.0)	1.1	(0.7–1.7)				
Missing					19	7						
Tubal Ligation												
No	122 (69.7)	148 (66.1)	1.0	Reference	297 (64.0)	301 (57.1)	1.0	Reference	419 (65.6)	449 (59.8)	1.0	Reference
Yes	53 (30.3)	76 (33.9)	0.6	(0.6–1.0)	167 (36.0)	226 (42.9)	0.7	(0.6–1.0)	220 (34.4)	302 (40.2)	0.7	(0.6–0.9)
Missing					2	1			2	1		
Doctor diagnosed female infertility												
No	127 (85.2)	195 (92.4)	1.0	Reference	396 (89.0)	461 (92.2)	1.0	Reference	523 (88.1)	656 (92.3)	1.0	Reference
Yes	22 (14.8)	16 (7.6)	2.5	(1.2–5.3)	49 (11.0)	39 (7.8)	1.6	(1.0–2.6)	71 (12.0)	55 (7.7)	1.9	(1.3–2.8)
Missing	26	13			21	28			47	41		
Body mass index (kg/m^2) 1 year prior to diagnosis/ interview				0.25				0.11				0.11
<25	27 (15.6)	46 (20.5)	1.0	Reference	63 (13.6)	95 (18.0)	1.0	Reference	90 (14.1)	141 (18.8)	1.0	Reference
25 – <30	47 (27.2)	48 (21.4)	1.4	(0.7–2.8)	120 (25.9)	150 (28.5)	1.2	(0.8–1.8)	167 (26.2)	198 (26.4)	1.3	(0.9–1.8)
30 – <35	49 (28.3)	54 (24.1)	1.4	(0.7–2.7)	130 (28.0)	135 (25.6)	1.4	(0.9–2.1)	179 (28.1)	189 (25.2)	1.4	(1.0–2.0)
≥35	50 (28.9)	76 (33.9)	0.9	(0.5–1.7)	151 (32.5)	147 (27.9)	1.6	(1.1–2.4)	201 (31.6)	223 (29.7)	1.4	(1.0–2.0)
Missing	2				2	1			4	1		
Histology												
Serous	84 (52.2)				271 (62.9)			<0.0001 †	355(60.0)			
Endometrioid	31 (19.3)				44 (10.2)				75(12.7)			
Mucinous	17 (10.6)				13 (3.0)				30(5.1)			
Clear cell	5 (3.1)				8 (1.9)				13(2.2)			
Other	24 (14.9)				95 (22.0)				119(20.1)			
Missing	14				35				48			

† p-value comparing histology in pre-menopausal versus postmenopausal cases.

TABLE 2

Odds ratios (ORs) and 95% confidence intervals (CIs) for associations between patterns of oral contraceptive (OC) use and ovarian cancer, stratified by menopausal status, the African American Cancer Epidemiology Study, 2010-2016

	Pre-menopausal				Postmenopausal				All Women			
	Cases n=168 n (%)	**Controls n=218 n (%)**	**OR***	**95% CI**	**Cases n=451 n (%)**	**Controls n=506 n (%)**	**OR***	**95% CI**	**Cases n=619 n (%)**	**Controls 724 n (%)**	**OR***	**95% CI**
OC use												
Non-user†	38 (22.6)	37 (17.0)	1.0	Referent	140 (31.0)	107 (21.2)	1.0	Referent0.	178 (28.8)	144 (19.9)	1.0	Referent
User	130 (77.4)	181 (83.0)	0.6	(0.4–1.2)	311 (69.0)	399 (78.9)	0.7	(0.5–0.9)	441 (71.2)	580 (80.1)	0.7	(0.5–0. 9)
p for interaction‡											0.95	
Years of OC use												
<1	25 (14.9)	36 (16.5)	0.7	(0.3–1.6)	71 (15.7)	73 (14.4)	0.8	(0.6–1.3)	96 (15.5)	109 (15.1)	0.8	(0. 6–1.2)
1 – <5	48 (28.6)	69 (31.6)	0.6	(0.3–1.3)	113 (25.1)	153 (30.2)	0.7	(0.5–0.9)	161 (26.0)	222 (30.7)	0.7	(0.5–0.9)
5 – <10	27 (16.1)	36 (16.5)	0.7	(0.3–1.5)	70 (15.5)	87 (17.2)	0.7	(0.5–1.1)	97 (15.7)	123 (17.0)	0.7	(0.5–1.0)
≥10	30 (17.9)	40 (18.4)	0.6	(0.3–1.2)	57 (12.6)	86 (17.0)	0.6	(0.4–0.9)	87 (14.0)	126 (17.4)	0.6	(0.4–0..9)
p-trend			0.18				0.005				0.004	
p for interaction											0.93	
Age at first OC use												
<20	97 (57.7)	118 (54.1)	0.8	(0.4–1.5)	119 (26.4)	210 (41.5)	0.5	(0.3–0.7)	216 (34.9)	328 (45.3)	0.6	(0.5–0.9)
20 – 24	24 (14.3)	46 (21.1)	0.4	(0.2–0.9)	133 (29.5)	137 (27.1)	0.8	(0.5–1.1)	157 (25.4)	183 (25.3)	0.7	(0.5–1.0)
≥25	9 (5.4)	17 (7.8)	0.4	(0.1–1.1)	59 (13.1)	52 (10.3)	1.0	(0.6–1.5)	68 (11.0)	69 (9.5)	0.8	(0. 6–1.3)
p-trend			0.01				0.84				0.23	
p for interaction											0.01	
Age at last OC use												
<20	33 (19.6)	39 (17.9)	1.0	(0.5–2.2)	34 (7.5)	57 (11.3)	0.5	(0.3–0.9)	67 (10.8)	96 (13.3)	0.7	(0.5–1.1)
20 – 24	40 (23.8)	50 (22.9)	0.7	(0.3–1.5)	99 (22.0)	122 (24.1)	0.7	(0.5–1.1)	139 (22.5)	172 (23.8)	0.7	(0.5–1.0)
25 – 29	20 (11.9)	35 (16.1)	0.5	(0.2–1.2)	69 (15.3)	87 (17.2)	0.7	(0.5–1.1)	89 (14.4)	122 (16.9)	0.7	(0.5–1.0)
≥30	37 (22.0)	57 (26.2)	0.5	(0.2–1.0)	109 (24.2)	133 (26.3)	0.7	(0.5–1.0)	146 (23.6)	190 (26.2)	0.7	(0.5–0.9)
p-trend			0.01				0.08				0.01	
p for interaction											0.50	

	Pre-menopausal				Postmenopausal				All Women			
	Cases n=168 n (%)	Controls n=218 n (%)	OR*	95% CI	Cases n=451 n (%)	Controls n=506 n (%)	OR*	95% CI	Cases n=619 n (%)	Controls 724 n (%)	OR*	95% CI
Years since first use												
>20	104 (61.9)	119 (54.5)	0.7	(0.4–1.4)	305 (67.6)	394 (77.9)	0.67	(0.5–0.9)	409 (66.1)	513 (70.9)	0.7	(0.5–0.9)
≤20	26 (15.5)	62 (28.4)	0.5	(0.2–1.1)	6 (1.3)	5 (1.0)	1.44	(0.4–5.3)	32 (5.2)	67 (9.3)	0.6	(0.3–1.1)
p-trend			0.08				0.03				0.007	
p for interaction											0.24	
Years since last use												
>20	78 (46.4)	66 (30.3)	1.3	(0.6–2.6)	278 (61.6)	356 (70.4)	0.7	(0.5–0.9)	356 (57.5)	422 (58.3)	0.7	(0.5–1.0)
10 – 20	29 (17.3)	56 (25.7)	0.4	(0.2–0.9)	26 (5.8)	32 (6.3)	0.9	(0.5–1.6)	55 (8.9)	88 (12.2)	0.6	(0.4–0.9)
<10	23 (13.7)	59 (27.1)	0.3	(0.2–0.7)	7 (1.6)	11 (2.2)	0.7	(0.3–2.1)	30 (4.9)	70 (9.7)	0.5	(0.3–0.8)
p-trend			0.0009				0.10				0.002	
p for interaction											0.06	
Duration of use/ years since last use												
<5 yrs/any	73 (43.5)	105 (48.2)	0.7	(0.3–1.2)	184 (40.8)	226 (44.7)	0.7	(0.5–1.0)	257 (41.5)	331 (45.7)	0.7	(0.5–1.0)
≥5 yrs/ ≥10 yrs ago	40 (23.8)	46 (21.1)	0.7	(0.3–1.4)	123 (27.3)	165 (32.6)	0.6	(0.4–0.9)	163 (26.3)	211 (29.1)	0.7	(0.5–0.9)
≥ 5yrs/<10 yrs ago	17 (10.1)	30 (13.8)	0.5	(0.2–1.3)	4 (0.9)	8 (1.6)	0.6	(0.2–2.0)	21 (3.4)	38 (5.3)	0.6	(0.3–1.2)
p for interaction											0.81	

*OR adjusted for study site, age, family history of breast or ovarian cancer in first degree relative, age at menarche, tubal ligation, body mass index, and number of full-term pregnancies.

†Non-users are the referent group for all comparisons

‡*p* for interaction based on product term for menopausal status and each individual reproductive variable

TABLE 3

Odds ratios (ORs) and 95% confidence intervals (CIs) for associations between patterns of oral contraceptive (OC) use and ovarian cancer among OC users, stratified by menopausal status, the African American Cancer Epidemiology Study (AACES), 2010–2016.

	Pre-Menopausal				Postmenopausal				All Women			
	Cases n=130 n (%)	**Controls n=181 n (%)**	**OR**	**95% CI**	**Cases n=311 n (%)**	**Controls n=399 n (%)**	**OR**	**95% CI**	**Cases n=441 n (%)**	**Controls n=580 n (%)**	**OR**	**95% CI**
Age at first OC use												
<20	97 (74.6)	118 (65.2)	1.0	Reference	119 (38.3)	210 (52.6)	1.0	Reference	216 (48.9)	328 (56.6)	1.0	Reference
20 – 24	24 (18.5)	46 (25.4)	0.5	(0.2–0.9)	133 (42.8)	137 (34.3)	1.6	(1.1–2.3)	157 (35.6)	183 (31.6)	1.1	(0.8–1.5)
≥25	9 (6.9)	17 (9.4)	0.4	(0.2–1.2)	59 (19.0)	52 (13.0)	2.0	(1.2–3.3)	68 (15.4)	69 (11.9)	1.4	(0.9–2.1)
p-trend			0.02				0.004				0.17	
OR for each 5 year duration of OC use			0.9	(0. 7–1.2)			0.9	(0.8–1.1)			0.9	(0.8–1.1)
p for interaction[†]											0.003	
Age at last OC use												
<20	33 (25.4)	39 (21.6)	1.0	Reference	34 (10.9)	57 (14.3)	1.0	Reference	67 (15.2)	96 (16.6)	1.0	Reference
20 – 24	40 (30.8)	50 (27.6)	0.6	(0.3–1.3)	99 (31.8)	122 (30.6)	1.5	(0.9–2.5)	139 (31.5)	172 (29.7)	1.1	(0.7–1.6)
25 – 29	20 (15.4)	35 (19.3)	0.4	(0.2–1.0)	69 (22.2)	87 (21.8)	1.7	(0.9–3.1)	89 (20.2)	122 (21.0)	1.1	(0.7–1.7)
≥30	37 (28.5)	57 (31.5)	0.3	(0.1–0.8)	109 (35.1)	133 (33.3)	1.9	(1.0–3.6)	146 (33.1)	190 (32.8)	1.1	(0.7–1.8)
p-trend			0.02				0.09				0.79	
OR for each 5 year duration of OC use			1.2	(0.9–1.8)			0.8	(0. 7–1.0)			0.91	(0.8–1.1)
p for interaction											0.38	
Years since first use												
>20	104 (80.0)	119 (65.8)	1.0	Reference	305 (98.1)	394 (98.7)			409 (92.7)	513 (88.5)	1.0	Reference
≤20	26 (20.0)	62 (34.3)	0.7	(0.3–1.6)	6 (1.9)	5 (1.3)			32 (7.3)	67 (11.6)	0.9	(0.5–1.6)
OR for each 5 year duration of OC use			0.9	(0.7–1.2)							0.9	(0.8–1.1)
p for interaction											0.08	
Years since last use												
>20	78 (60.0)	66 (36.5)	1.0	Reference	278 (89.4)	356 (89.2)	1.0	Reference	356 (80.7)	422 (72.7)	1.0	Reference
10 – 20	29 (22.3)	56 (30.9)	0.2	(0.1–0.5)	26 (8.4)	32 (8.0)	1.6	(0.8–2.9)	55 (12.5)	88 (15.2)	0.9	(0.6–1.4)

	Pre-Menopausal				Postmenopausal				All Women			
	Cases n=130 n (%)	**Controls n=181 n (%)**	**OR**	**95% CI**	**Cases n=311 n (%)**	**Controls n=399 n (%)**	**OR**	**95% CI**	**Cases n=441 n (%)**	**Controls n=580 n (%)**	**OR**	**95% CI**
<10	23 (17.7)	59 (32.6)	0.2	(0.1–0.4)	7 (2.3)	11 (2.8)	1.4	(0.5–4.1)	30 (6.8)	70 (12.1)	0.7	(0.4–1.3)
p-trend			0.0003				0.20				0.23	
OR for each 5 year duration of OC use			1.3	(0.9–1.8)			0.9	(0.7–1.0)			1.0	(0.8–1.1)
p for interaction											0.03	

*Each model included the term for age or timing of OC use (age at first use, age at last use, years since first use or years since last use) and duration of OC use, site, age, family history of breast or ovarian cancer, age at menarche, tubal ligation, body mass index, and number of full-term pregnancies.

†*p* for interaction based on product term for menopausal status and each individual reproductive variable

TABLE 4

Odds ratios (ORs) and 95% confidence intervals (CIs) for associations between pregnancy characteristics and ovarian cancer, stratified by menopausal status, the African American Cancer Epidemiology Study (AACES), 2010–2015

	Pre-Menopausal				Postmenopausal				All Women			
	Cases n=168 n (%)	**Controls n=218 n (%)**	**OR***	**95% CI**	**Cases n=452 n (%)**	**Controls n=507 n (%)**	**OR**	**95% CI**	**Cases n=620 n (%)**	**Controls n=725 n (%)**	**OR**	**95% CI**
Full-term pregnancy												
Never†	60 (35.7)	34 (15.6)	1.0	Reference	101 (22.4)	71 (14.0)	1.0	Reference	161 (26.2)	105 (14.5)	1.0	Reference
Ever	108 (64.3)	184 (84.4)	0.3	(0.2–0.5)	351 (77.7)	436 (86.0)	0.5	(0.4–0.8)	459 (74.0)	620 (85.5)	0.5	(0.3–0.6)
p for interaction‡											0.26	
Full-term pregnancies												
1	31 (18.5)	43 (19.7)	0.4	(0.2–0.9)	73 (16.2)	86 (17.0)	0.6	(0.4–1.0)	104 (16.8)	129 (17.8)	0.6	(0.4–0.8)
2	38 (22.6)	65 (29.8)	0.2	(0.1–0.5)	95 (21.0)	122 (24.1)	0.6	(0.4–0.9)	133 (21.5)	187 (25.8)	0.5	(0.3–0.7)
3	24 (14.3)	42 (19.3)	0.2	(0.1–0.5)	84 (18.6)	119 (23.5)	0.5	(0.3–0. 8)	108 (17.4)	161 (22.2)	0.4	(0.3–0.6)
>3	15 (8.9)	34 (15.6)	0.2	(0.1–0.4)	99 (21.9)	109 (21.5)	0.5	(0.3–0.8)	114 (18.4)	143 (19.7)	0.4	(0.3–0.6)
p-trend			0.04				0.61				<0.08	
p for interaction											0.56	
Age at first pregnancy												
<20	49 (29.3)	64 (29.4)	0.4	(0.2–0.9)	164 (36.3)	201 (39.6)	0.5	(0.4–0.8)	213 (34.4)	265 (36.6)	0.5	(0.4–0.7)
20 – 24	24 (14.4)	54 (24.8)	0.2	(0.1–0.5)	128 (28.3)	135 (26.6)	0.7	(0.4–1.0)	152 (24.6)	189 (26.1)	0.5	(0.4–0.7)
25 – 29	18 (10.8)	31 (14.2)	0.3	(0.1–0.6)	34 (7.5)	57 (11.2)	0.5	(0.3–0.8)	52 (8.4)	88 (12.1)	0.4	(0.3–0.7)
>29	16 (9.6)	35 (16.1)	0.2	(0.1–0. 5)	25 (5.5)	43 (8.5)	0.4	(0.2–0. 8)	41 (6.6)	78 (10.8)	0.4	(0.2–0.6)
Missing	1								1			
p-trend			0.04				0.36				0.15	
p for interaction											0.21	
Age at last pregnancy												
<25	35 (21.0)	54 (24.8)	0.4	(0.2–0.7)	126 (27.9)	131 (25.8)	0.7	(0.4–1.0)	161 (26.0)	185 (25.5)	0.6	(0.4–0.8)
25 – 29	29 (17.4)	42 (19.3)	0.3	(0.2–0.7)	99 (21.9)	132 (26.0)	0.5	(0.3–0. 8)	128 (20.7)	174 (24.0)	0.5	(0.3–0.7)
30 – 34	28 (16.8)	47 (21.6)	0.3	(0.1–0.6)	80 (17.7)	100 (19.7)	0.5	(0.3–0.8)	108 (17.5)	147 (20.3)	0.5	(0.3–0.7)
>34	15 (9.0)	41 (18.8)	0.1	(0.1–0.3)	46 (10.2)	73 (14.4)	0.4	(0.3–0.7)	61 (9.9)	114 (15.7)	0.3	(0.2–0.5)

	Pre-Menopausal				Postmenopausal				All Women			
	Cases n=168 n (%)	**Controls n=218 n (%)**	**OR***	**95% CI**	**Cases n=452 n (%)**	**Controls n=507 n (%)**	**OR**	**95% CI**	**Cases n=620 n (%)**	**Controls n=725 n (%)**	**OR**	**95% CI**
Missing	1								1			
p-trend			0.01				0.10				0.01	
p for interaction											0.53	
Years since first pregnancy												
>20	81 (48.5)	82 (37.6)	0.5	(0.3–1.1)	344 (76.1)	420 (82.8)	0.6	(0.4–0.8)	425 (68.7)	502 (69.2)	0.6	(0.4–0.8)
10 – 20	21 (12.6)	73 (33.5)	0.2	(0.08–0.3)	6 (1.3)	16 (3. 2)	0.3	(0.1–0.9)	27 (4.4)	89 (12.3)	0.3	(0.2–0.4)
<10	5 (3.0)	29 (13.3)	0.1	(0.04–0.4)	1	0			6 (1.0)	29 (4.0)	0.2	(0.08–0.5)
Missing	1								1			
p-trend			0.17				0.63				0.06	
p for interaction											0.20	
Years since last pregnancy												
>20	55 (32.9)	37 (17.0)	0.9	(0.4–2.1)	328 (71.2)	382 (75.4)	0.6	(0.4–0.9)	383 (61.9)	419 (57.8)	0.6	(0.4–0.8)
10 – 20	38 (22.8)	83 (38.1)	0.2	(0.1–0.4)	22 (5.8)	51 (10.1)	0.4	(0.2–0.8)	60 (9.7)	134 (18.5)	0.3	(0.2–0.5)
< 10	14 (8.4)	64 (29.4)	0.2	(0.07–0.3)	1 (0.2)	3 (0.6)			15 (2.4)	67 (9.2)	0.2	(0.1–0.4)
Missing	1								1			
p-trend			0.02				0.26				0.01	
p for interaction											0.20	
# of pregnancies/ yrs since last pregnancy												
<3, ≥10 yrs ago	59 (35.3)	72 (33.0)	0.4	(0.24–0.7)	167 (36.6)	208 (41.0)	0.6	(0.4–0.9)	226 (36.5)	280 (38.6)	0.5	(0.4–0.7)
<3, <10 yrs ago	9 (5.4)	36 (16.5)	0.2	(0.08–0.5)	1	0			10 (1.6)	36 (5.0)	0.3	(0.1–0. 7)
≤3, ≥10 yrs ago	34 (20.4)	48 (22.0)	0.3	(0.1–0.7)	183 (40.4)	225 (44.4)	0.5	(0.3–0.8)	217 (35.1)	273 (37.7)	0.5	(0.3–0.7)
≥3, <10 yrs ago	5 (3.0)	28 (12.8)	0.1	(0.04–0.4)	0	3 (0.6)			5 (0.8)	31 (4.3)	0.2	(0.05–0.4)
Missing	1								1			
Breastfeeding**												
0 months	79 (47.0)	99 (45.4)	0.4	(0.2–0.8)	242 (53.5)	286 (56.4)	0.6	(0.4–0.8)	321 (51.8)	385 (53.1)	0.5	(0.4–0.7)
<6 months	17 (10.1)	39 (17.9)	0.3	(0.1–0.6)	51 (11.3)	70 (13.8)	0.5	(0.3–0.8)	68 (11.0)	109 (15.0)	0.4	(0.3–0.6)
6 – 12 months	7 (4.2)	18 (8.3)	0.2	(0.07–0.6)	28 (6.2)	34 (6.7)	0.6	(0.3–1.1)	35 (5.7)	52 (7.2)	0. 5	(0.3–0.8)

	Pre-Menopausal				Postmenopausal				All Women			
	Cases n=168 n (%)	**Controls n=218 n (%)**	**OR***	**95% CI**	**Cases n=452 n (%)**	**Controls n=507 n (%)**	**OR**	**95% CI**	**Cases n=620 n (%)**	**Controls n=725 n (%)**	**OR**	**95% CI**
>12 months	5 (3.0)	28 (12.8)	0.05	(0.02–0.2)	30 (6.6)	46 (9.1)	0.5	(0.3–0.8)	35 (5.7)	74 (10.2)	0.3	(0.2–0.5)
p-trend			<0.001				0.32				0.02	
p for interaction											0.10	

*OR adjusted for study site, age, family history of breast or ovarian cancer in first degree relative, age at menarche, tubal ligation, body mass index, and duration of oral contraceptive use.

†Never pregnant women are referent category for all comparisons

‡*p* for interaction based on product term for menopausal status and each individual reproductive variable

**Duration of breastfeeding among parous women. Reference group is women with no full-term pregnancy.

TABLE 5

Odds ratios (ORs) and 95% confidence intervals (CIs) for associations between pregnancy characteristics and ovarian cancer among parous women, stratified by menopausal status, the African American Cancer Epidemiology Study (AACES), 2010–2015

	Pre-Menopausal				Postmenopausal				All			
	Cases n=108 n (%)	Controls n=184 n (%)	OR*	95% CI	Cases n=351 n (%)	Controls n=436 n (%)	OR	95% CI	Cases n=459 n (%)	Controls n=620 n (%)	OR	95% CI
Age at first pregnancy												
<20	49 (45.8)	64 (34.8)	1.0	Reference	164 (46.7)	201 (46.1)	1.0	Reference	213 (46.5)	265 (42.7)	1.0	Reference
20 – 24	24 (22.4)	54 (29.4)	0.4	(0.2–0. 9)	128 (36.5)	135 (31.0)	1.2	(0.8–1.7)	152 (33.2)	189 (30.5)	1.0	(0.7–1.3)
25 – 29	18 (16.8)	31 (16.9)	0.5	(0.2–1.2)	34 (9.7)	57 (13.1)	0.8	(0.5–1.3)	52 (11.4)	88 (14.2)	0.7	(0.5–1.1)
≥30	16 (15.0)	35 (19.0)	0.3	(0.1–0.6)	25 (7.1)	43 (9.9)	0.7	(0.4–1.2)	41 (9.0)	78 (12.6)	0.6	(0.4–1.0)
Missing	1								1			
p-trend			0.004				0.22				0.02	
OR for each additional birth			0.6	(0.5–0.9)			0.9	(0.8–1.1)			0.8	(0.7–1.0)
p for interaction†											0.18	
Age at last pregnancy												
<25	35 (32.7)	54 (29.4)	1.0	Reference	126 (35.9)	131 (30.1)	1.0	Reference	161 (35.2)	185 (29.8)	1. 0	Reference
25 – 29	29 (27.1)	42 (22.8)	1.0	(0.5–2.1)	99 (28.2)	132 (30.3)	0.8	(0.5–1.1)	128 (28.0)	174 (28.1)	0.8	(0. 6–1.1)
30 – 34	28 (26.2)	47 (25.5)	1.0	(0. 5–2.1)	80 (22.8)	100 (22.9)	0.8	(0.5–1.2)	108 (23.6)	147 (23.7)	0.9	(0.6–1.2)
≥35	15 (14.0)	41 (22.3)	0.4	(0.1–0.9)	46 (13.1)	73 (16.7)	0.7	(0.4–1.1)	61 (13.3)	114 (18.4)	0.6	(0.4–0.9)
Missing	1								1			
p-trend			0.04				0.12				0.03	
OR for each additional birth			0.8	(0.6–1.1)			1.0	(0.9–1.2)			0.9	(0.8–1.1)
p for interaction											0.49	
Years since first pregnancy												
>20	81 (75.7)	82 (46.3)	1.0	Reference	344 (98.0)	420 (96.3)	1.0	Reference	425 (92.8)	502 (81.9)	1.0	Reference
10 – 20	21 (19.6)	73 (41.2)	0.3	(0.2–0.7)	6 (1.7)	16 (3.7)	0.5	(0.2–1.5)	27 (5.9)	89 (14.5)	0.5	(0.3–0.8)
<10	5 (4.7)	22 (12.4)	0.3	(0.08–1.3)	1 (0.3)	0			6 (1.3)	22 (3.6)	0.5	(0.2–1.4)
Missing	1	7							1	7		

	Pre-Menopausal				Postmenopausal				All			
	Cases n=108 n (%)	**Controls n=184 n (%)**	**OR***	**95% CI**	**Cases n=351 n (%)**	**Controls n=436 n (%)**	**OR**	**95% CI**	**Cases n=459 n (%)**	**Controls n=620 n (%)**	**OR**	**95% CI**
p-trend			0.009								0.008	
OR for each additional birth			0.7	(0.5–0. 9)			0.96	(0.8–1.1)			0.9	(0.8–1.0)
p for interaction											0.11	
Years since last pregnancy												
>20	54 (51.9)	36 (21.4)	1.0	Reference	323 (93.4)	382 (87.6)	1.0		377 (83.8)	418 (69.2)	1.0	Reference
10 – 20	38 (36.5)	82 (48.8)	0.3	(0.1–0.6)	23 (6.7)	51 (11.7)	0.8	(0.4–1.4)	61 (13.6)	133 (22.0)	0.6	(0.4–0.9)
< 10	12 (11.5)	50 (29.8)	0.2	(0.08–0.7)	0	3 (0.8)			12 (2.7)	53 (8.8)	0.3	(0.2–0.7)
Missing	2	13							2	13		
p-trend			0.01								0.002	
OR for each additional birth			0.8	(0.6–1.1)			1.0	(0.8–1.1)			0.9	(0.8–1.1)
p for interaction											0.06	

*Models included terms for pregnancy-related characteristic (i.e., age at first pregnancy, age at last pregnancy, years since first pregnancy, years since last pregnancy or breastfeeding), parity, age, race, family history of breast or ovarian cancer, age at menarche, tubal ligation, body mass index, oral contraceptive (OC) duration and site. Parity was 1 degree of freedom coded 1-2-3-4, with 4+ included as 4.

†*p* for interaction based on product term for menopausal status and each individual reproductive variable