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Alcohol Intake and Risk of Breast Cancer by Histologic Subtype and Estrogen Receptor Status Among Women Aged 55 to 74 Years

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Abstract

Previous studies suggest that alcohol consumption and risk of breast cancer may differ by histologic subtype and hormone receptor status, though results are not entirely consistent. In this population-based case-control study, we evaluated the association between alcohol consumption and risk of invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), and invasive ductal-lobular carcinoma (IDLC) overall and by estrogen receptor (ER) status, among women aged 55–74 years of age. Using polytomous regression, associations between current alcohol consumption, overall and by type of alcohol, and breast cancer risk were evaluated in 891 controls and 905 IDC, 567 ILC, 489 IDLC cases. Current alcohol use was moderately associated with risk of ILC (odds ratio=1.25, 95% confidence interval: 0.99, 1.58) with a positive dose-response relationship based on average number of drinks per week consumed ($P_{trend}=0.0005$). When further stratified by ER status, alcohol use was positively associated with risk of ER+ ILC ($P_{trend}=0.002$) and ER+ IDC ($P_{trend}=0.02$), but inversely associated with risk of ER– IDC ($P_{trend}=0.01$). No association between alcohol and risk of IDLC tumors was observed. While the link between alcohol consumption and breast cancer risk is well established, our results suggest that the increased risk associated with alcohol is largely limited to ER+ ILC and ER+ IDC. Thus, avoiding or moderating alcohol consumption may be one way that women can lower their risks of these forms of breast cancer.

Keywords

alcohol; breast cancer; risk; ductal; lobular

Introduction

Previous studies have shown that alcohol increases the risk of developing breast cancer with meta-analyses indicating that risk increases 3–10% per 10 grams (~1 drink) of alcohol consumed per day [1–5]. This relationship is thought to be primarily hormonally driven [6] as controlled feeding studies have demonstrated that alcohol metabolism increases estrogen levels in postmenopausal women [7]. However, breast cancer is a heterogeneous disease.

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Evidence from more recent studies suggests that this association may vary by hormone receptor status and histologic subtype, though there are inconsistencies in the literature [4, 8–12]. With respect to hormone receptor status, a meta-analysis based on data from 16 case-control and 4 cohort studies reported that alcohol consumption was associated with a 27% increased risk of ER+ breast cancer, but did not increase risk of ER– breast cancer (p-value comparing the risk associated with ER+ vs. ER–/PR– tumors=0.02) [4]. The association between alcohol consumption and ER+ and ER+/PR+ breast cancers is additionally supported by more recent observational studies [11, 13, 14].

With respect to histology, approximately 70% of postmenopausal breast cancers in the United States are invasive ductal carcinomas (IDC), while 15–20% are invasive lobular carcinomas (ILC) and ~90% or more of all ILCs are ER+ [15]. Relatively few studies have evaluated differences in the association between alcohol use and histologic types of breast cancer. Previous studies have suggested that alcohol use is more strongly associated with risk of lobular cancers than risk of ductal cancers, but most did not find this difference to be statistically significant [9–12, 16, 17]. Fewer studies have assessed the association between alcohol and breast cancer by both histologic and hormone receptor status, but those that did found a stronger association among ER+/PR+ lobular cancers than ER+/PR+ ductal cancers [9, 17].

Though previous studies suggest that alcohol may be more strongly associated with risk of lobular breast cancer, they have been limited by relatively small numbers of lobular cases, an inability to evaluate risk according to type of alcohol consumed, and the lack of assessment of risk according to both histologic type and hormone receptor status combined. Using a population-based case-control study designed specifically to examine the etiologies of ductal and lobular breast cancer, we evaluated the association between alcohol intake and risk of breast cancer by histologic subtype and ER status.

Materials and Methods

We conducted a large population-based study of breast cancer, which has been previously described, with the goal of evaluating differences in risk factors between ductal and lobular breast cancers [18]. Briefly, women aged 55 to 74 years diagnosed with a primary invasive breast cancer from 2000–2008 in the greater Seattle area (King, Pierce, and Snohomish counties) were eligible for this study. Potential cases were identified through the Cancer Surveillance System (CSS), which is a population-based tumor registry serving western Washington State and is a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results program. Case patients with lobular (ICD-O codes 8520, 8522, and 8524) or ductal (ICD-O code 8500) cancers were identified for recruitment to the study. Pathology reports were centrally reviewed to ensure eligibility criteria were met and histology group was re-categorized as appropriate. Due to the lesser frequency of lobular cancers, all eligible lobular cases were recruited, while a random sample of approximately 25% of ductal cases were recruited to the study. The IDC case group was frequency-matched to the lobular case group based on 5-year age groups for each diagnosis year. Of the case patients identified as eligible for this study, 80% were interviewed (17% refused participation and 3% died before interview). Breast cancer cases with histologic subtypes

other than ductal or lobular were excluded from recruitment to this study. Controls living in the greater Seattle area were frequency-matched to lobular cases by 5-year age groups with a goal of 1:1:1 ratio of ductal and lobular cases and controls (69% of eligible controls were interviewed, 31% refused participation). For analytic purposes we further divided our lobular cases into two groups, invasive lobular carcinomas (ILC) without a ductal component (ICD-O codes 8520 and 8524) and mixed invasive ductal-lobular carcinomas (IDLC) (ICD-O code 8522).

Data collection

Participants in this study were interviewed in person using structured questionnaires in order to collect information on demographic and lifestyle factors, particularly those with known or suspected associations with breast cancer including reproductive history, medical history and medication use, breast cancer screening, and family history. Information on alcohol use was assessed, both overall consumption and consumption of beer, red wine, white wine, and liquor, individually at a variety of time periods in each participant's life. Information collected was limited to exposures which occurred before each participant's reference date. For breast cancer cases, the reference date was defined as the date of breast cancer diagnosis. Reference dates for controls were assigned based on the expected reference date distribution of case participants. Written, informed consent was obtained from all study participants and the study protocol was approved by the Fred Hutchinson Cancer Research Center Institutional Review Board.

Statistical analysis

Our main analysis focused on current alcohol consumption, defined as alcohol use and average number of drinks per week at reference age. Cases and controls were categorized by the average number of drinks per week consumed, both overall and by type (beer, red wine, white wine, and liquor). Participants were excluded from the analyses if they were missing data on alcohol use at reference (n=34; 11 IDC cases, 7 ILC cases, 4 IDLC cases, and 11 controls). The present analyses include 905 IDC cases, 567 lobular cases, 489 IDLC cases, and 891 controls.

Using polytomous regression, we calculated odds ratios (ORs) and their associated 95% confidence intervals (CIs) to compare IDC, ILC, and IDLC cases with controls for current alcohol intake (overall and by type of alcohol). Current alcohol intake was defined as alcohol use at the time of breast cancer diagnosis. Data on amount of alcohol consumed was only assessed for current drinkers. IDLC cases were found to differ from IDC and ILC cases in terms of the relationship between risk and alcohol use and were, therefore, treated as a separate group for all analyses. Controls were frequency-matched to cases based on age at reference, reference year, and county of residence and these factors were additionally controlled for in all models. Effect modification by BMI (<25, ≥25), smoking status (never, ever), and use of menopausal hormone therapy (never/former use, current estrogen only, current estrogen and progestin) were considered; however, no statistically significant effect modification was observed using likelihood ratio tests (P -values>0.05). Variables listed in Table 1, including demographic factors and known breast cancer risk factors, were assessed as potential confounders but no variables were found to change our effect estimates by more

than 10% and were therefore not included in the final model. *P*-values for trends were calculated using continuous variables and a cutoff of 0.05 was used for statistical significance. Analyses were conducted using SAS v9.3 (SAS Institute, Cary, NC).

We additionally stratified cases as ER+ IDC, ER– IDC, ER+ ILC, and ER+ IDLC to further evaluate the role of alcohol in risk of breast cancer. Due to insufficient number of cases, we did not evaluate ER– ILC (n=15) or ER– IDLC (n=13) cases.

Results

Controls and IDC, ILC, and IDLC cases were similar with respect to age distribution, highest education level attained, smoking status, age at menarche, and duration of oral contraceptive use (Table 1). Controls and IDC cases were more likely to be obese (BMI ≥ 30). All cases were slightly more likely to have a family history of breast cancer, to be current smokers, to be older at age of first live birth or nulliparous, and to be using HRT (both estrogen and progestin) at reference compared to controls.

Current alcohol use at reference was moderately associated with risk of ILC (OR=1.25, 95% CI: 0.99, 1.58) but not with IDC or IDLC cancer (Table 2). When number of drinks per week among current drinkers was evaluated, a dose-response relationship was observed between average number of drinks per week at reference and risk of ILC ($P_{trend}=0.0005$; 7 drinks/week compared to never drinkers OR:1.52, 95% CI: 1.11, 2.07). We further evaluated average weekly alcohol intake at reference by type of alcohol among current drinkers. Compared to never drinkers, 4+ liquor drinks per week was significantly associated with ILC (OR=2.05, 95% CI: 1.25, 3.34, $P_{trend}=0.0008$) and IDC (OR=1.66, 95% CI: 1.06, 2.61, $P_{trend}=0.02$). Beer, red wine, and white wine intake of 4+ drinks were all associated with a moderately increased risk of ILC ($P_{trend}=0.08, 0.09, 0.08$, respectively). No associations were observed for beer, red wine, or white wine intake and risk of IDC or IDLC subtypes. Analyses evaluating lifetime alcohol use or alcohol use in the 5 years prior to the reference date yielded similar results as those for current alcohol use.

Analyses evaluating current alcohol use were further stratified by ER status (Table 3). We observed a positive association between alcohol use and risk of ER+ ILC (7 drinks compared to never drinkers: OR=1.47, 95% CI: 1.07, 2.01; $P_{trend}=0.002$). Alcohol consumption was positively associated with risk of ER+ IDC ($P_{trend}=0.02$), but inversely associated with risk of ER– IDC ($P_{trend}=0.01$).

Discussion

These data support previous studies and add to the epidemiological evidence that the association between alcohol consumption and risk of breast cancer varies by histologic subtype and ER status. Our results suggest that alcohol consumption (4+ drinks/week), particularly liquor, was associated with an increased risk of ILC. Alcohol consumption was significantly associated with increased risk of ER+ ILC. Alcohol consumption was associated with an increased risk of ER+ IDC and a decreased risk of ER– IDC. Liquor consumption (4+ drinks/week) was also significantly positively associated with risk of IDC.

It is well established that increased estrogen levels are associated with increased risk of breast cancer and studies have shown that alcohol metabolism can increase estrogen levels [19]. A review of the effect of alcohol consumption on hormone levels concluded that natural or synthetic estrogen levels rise in response to alcohol consumption [7]. Compared to IDC tumors, ILC tumors are more commonly ER+ [20] which offers a potential mechanism for the stronger association with ILC cancers. This is further supported by evidence from previous studies showing an association between postmenopausal hormone therapy and risk of ILC [21, 22].

Our study supports the findings of previous studies which have observed that alcohol use is more strongly associated with ILC than IDC; risk estimates from other studies ranged from 1.52–3.30 [9–12, 16, 17] and our results fell well within this range. Most of these studies also observed significant associations for IDC, though effect estimates were generally smaller in magnitude compared to ILC [10–12, 16, 17]; risk estimates varied from 1.06–2.21, similar to what was observed in this study. Consistent with previous studies evaluating the role of histologic subtype and hormone receptor status, our results showed that alcohol consumption was associated with a significantly increased risk of ER+ ILC and with a more moderately increased risk of ER+ IDC. A cohort study observed a significant association between alcohol and ER+/PR+ ILC and ER+/PR+ IDC; however, after multivariable adjustment the latter was no longer statistically significant [9]. In the Nurses' Health Study cohort, the risk estimates for ER+/PR+ IDC and ER+/PR+ ILC were similar in magnitude to those observed in our study for ER+ IDC and ER+ ILC [17]. In that study, statistical heterogeneity in risk estimates was not observed by histologic subtype overall ($P_{\text{heterogeneity}}=0.11$), but heterogeneity was observed when the analyses were limited to ER+/PR+ cases ($P_{\text{heterogeneity}}=0.02$) [17]. In our study, we observed a statistically significant association between liquor consumption and risk of ILC and IDC ($P_{\text{trend}}=0.0008$ and 0.02 , respectively). Risk estimates for red wine, white wine, and beer (4+ drinks/week) for ILC but were weaker than the risk estimate observed for liquor ($OR=2.05$) and the linear trends were moderately significant ($P_{\text{trend}}=0.09$, 0.08 , and 0.08 , respectively). Very low frequencies of high beer consumption in our population may have limited our ability to detect a statistically significant association between beer consumption and risk of breast cancer by histologic type. Two previous studies were identified that evaluated the association between breast cancer subtypes and consumption of different types of alcohol (e.g. beer, wine, and liquor). Neither study noted statistically significant differences in risk by type of alcohol consumed [9, 12]. Two previous studies which assessed the association between alcohol and ER– IDC found no association between alcohol and risk of ER–/PR– IDC [8, 11]. We observed an inverse association between alcohol intake and risk of ER– IDC; however, results are difficult to interpret given the small number of current drinkers with ER– IDC ($n=63$). This may be additional evidence that alcohol acts through a hormonal mechanism, but other non-hormonal pathways may also play a role, such as carcinogenic effects of alcohol and DNA damage [4, 23, 24]. Further studies are needed which are better able to assess these associations by alcohol type, and additionally evaluate the association by hormone receptor status.

Interestingly, we did not observe an association between alcohol consumption and breast cancers with IDLC histology, even when only ER+ IDLC tumors were evaluated. These

findings support the hypothesis that non-hormonal mechanisms may also play a role in the association between alcohol and breast cancer risk [4]. Alcohol has been shown to have toxic effects and it has been suggested that these effects are mediated by DNA damage, which is a potential mechanism for increased cancer risk [23]. Scientific evidence supports potential non-hormonal mechanisms of alcohol and breast cancer risk through mutagenesis by acetaldehyde and by induction of oxidative damage [25]. Our results also suggest that the association between alcohol and IDLC tumors may differ from IDC and ILC and should potentially be considered as a separate subtype. Most previous studies assessing the association between alcohol consumption and risk of breast cancer by histologic or hormone receptor status have combined ILC cases and IDLC cases for analysis. Three other studies were identified which analyzed IDLC cases as a separate subtype. Similar to our findings, one study, including 424 postmenopausal IDLC cases from the National Institutes of Health-AARP Diet and Health Study cohort, observed no association between alcohol use and risk of IDLC breast cancer [11]. However, the two other studies found significant associations. A study from the PLCO cohort, which included 109 postmenopausal IDLC cases, found a significant increased risk for IDLC tumors, both overall and when limited to ER+/PR+ tumors [8]. Another study, including 261 IDLC cases from the Women's Contraceptive and Reproductive Experiences Study, observed a significant increased risk only among postmenopausal IDLC cases, but not among premenopausal cases [16]. Further studies are needed to better understand this inconsistency.

This study has several noteworthy strengths. This study had a large sample size, comprehensive collection of alcohol use and other breast cancer risk factors, and histology of breast cancer was determined by centralized review of pathology reports. The study design and large sample size allowed for our analyses to evaluate ILC and IDLC cases separately; it also allowed for analysis by type of alcohol consumed. Current alcohol consumption in our population was common among cases (52.7%) and controls (49.6%). There is potential for recall bias in our case-control study; however, our analysis focused on current alcohol use minimizing exposure misclassification. It is also unlikely that there was differential recall among cases by breast cancer histologic subtypes. We found similar associations as those reported here for lifetime alcohol use and alcohol use in the 5 years prior to the reference date. However, it is possible that current alcohol use factored into the recall of previous drinking habits leading to similar associations. The generalizability of this study is high given the case-control study design and high response rates of cases and controls. Although controls had a lower response rate than cases which could result in selection bias, controls who were current drinkers would have had to selectively refuse to participate which is unlikely.

In summary, our results suggest that the association between alcohol consumption and breast cancer varies by histologic subtype and ER status. Evidence of a hormonal mechanism was supported, however, more studies are needed to further evaluate this association and potentially show other mechanisms which may mediate the observed association. These findings offer some understanding of etiological differences of breast cancer by subtype and further indicate differences in risk factor profiles by breast cancer subtype. A better understanding of risk profiles allows for personalized approaches to breast cancer prevention.

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References

1. Hamajima N, Hirose K, Tajima K, Rohan T, Calle EE, Heath CW Jr, Coates RJ, Liff JM, Talamini R, Chantarakul N, et al. Alcohol, tobacco and breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer*. 2002; 87(11):1234–1245. [PubMed: 12439712]
2. Key J, Hodgson S, Omar RZ, Jensen TK, Thompson SG, Boobis AR, Davies DS, Elliott P. Meta-analysis of studies of alcohol and breast cancer with consideration of the methodological issues. *Cancer Causes Control*. 2006; 17(6):759–770. [PubMed: 16783604]
3. de Menezes RF, Bergmann A, Thuler LC. Alcohol consumption and risk of cancer: A systematic literature review. *Asian Pac J Cancer Prev*. 2013; 14(9):4965–4972. [PubMed: 24175760]
4. Suzuki R, Orsini N, Mignone L, Saji S, Wolk A. Alcohol intake and risk of breast cancer defined by estrogen and progesterone receptor status--a meta-analysis of epidemiological studies. *Int J Cancer*. 2008; 122(8):1832–1841. [PubMed: 18067133]
5. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, et al. Alcohol consumption and site-specific cancer risk: A comprehensive dose-response meta-analysis. *Br J Cancer*. 2015; 112(3):580–593. [PubMed: 25422909]
6. Fernandez SV. Estrogen, alcohol consumption, and breast cancer. *Alcoholism, Clinical and Experimental Research*. 2011; 35(3):389–391.
7. Gill J. The effects of moderate alcohol consumption on female hormone levels and reproductive function. *Alcohol and Alcoholism*. 2000; 35(5):417–423. [PubMed: 11022013]
8. Falk RT, Maas P, Schairer C, Chatterjee N, Mabie JE, Cunningham C, Buys SS, Isaacs C, Ziegler RG. Alcohol and risk of breast cancer in postmenopausal women: An analysis of etiological heterogeneity by multiple tumor characteristics. *Am J Epidemiol*. 2014; 180(7):705–717. [PubMed: 25150269]
9. Li CI, Chlebowski RT, Freiberg M, Johnson KC, Kuller L, Lane D, Lessin L, O'Sullivan MJ, Wactawski-Wende J, Yasmeeen S, et al. Alcohol consumption and risk of postmenopausal breast cancer by subtype: The women's health initiative observational study. *J Natl Cancer Inst*. 2010; 102(18):1422–1431. [PubMed: 20733117]
10. Gago-Dominguez M, Castela JE, Gude F, Fernandez MP, Aguado-Barrera ME, Ponte SM, Redondo CM, Castelo ME, Dominguez AN, Garzon VM, et al. Alcohol and breast cancer tumor subtypes in a spanish cohort. *Springerplus*. 2016; 5:39. [PubMed: 26835221]
11. Lew JQ, Freedman ND, Leitzmann MF, Brinton LA, Hoover RN, Hollenbeck AR, Schatzkin A, Park Y. Alcohol and risk of breast cancer by histologic type and hormone receptor status in postmenopausal women: The nih-aarp diet and health study. *Am J Epidemiol*. 2009; 170(3):308–317. [PubMed: 19541857]
12. Li CI, Malone KE, Porter PL, Weiss NS, Tang MT, Daling JR. The relationship between alcohol use and risk of breast cancer by histology and hormone receptor status among women 65–79 years of age. *Cancer Epidemiol Biomarkers Prev*. 2003; 12(10):1061–1066. [PubMed: 14578143]
13. Chen WY, Rosner B, Hankinson SE, Colditz GA, Willett WC. Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. *JAMA*. 2011; 306(17):1884–1890. [PubMed: 22045766]
14. Deandrea S, Talamini R, Foschi R, Montella M, Dal Maso L, Falcini F, La Vecchia C, Franceschi S, Negri E. Alcohol and breast cancer risk defined by estrogen and progesterone receptor status: A case-control study. *Cancer Epidemiol Biomarkers Prev*. 2008; 17(8):2025–2028. [PubMed: 18708394]
15. Li CI, Daling JR. Changes in breast cancer incidence rates in the united states by histologic subtype and race/ethnicity, 1995 to 2004. *Cancer Epidemiol Biomarkers Prev*. 2007; 16(12):2773–2780. [PubMed: 18086787]

16. Li CI, Daling JR, Malone KE, Bernstein L, Marchbanks PA, Liff JM, Strom BL, Simon MS, Press MF, McDonald JA, et al. Relationship between established breast cancer risk factors and risk of seven different histologic types of invasive breast cancer. *Cancer Epidemiol Biomarkers Prev.* 2006; 15(5):946–954. [PubMed: 16702375]
17. Kotsopoulos J, Chen WY, Gates MA, Tworoger SS, Hankinson SE, Rosner BA. Risk factors for ductal and lobular breast cancer: Results from the nurses' health study. *Breast Cancer Res.* 2010; 12(6):R106. [PubMed: 21143857]
18. Li CI, Daling JR, Tang MT, Haugen KL, Porter PL, Malone KE. Use of antihypertensive medications and breast cancer risk among women aged 55 to 74 years. *JAMA Intern Med.* 2013; 173(17):1629–1637. [PubMed: 23921840]
19. Key TJ, Appleby PN, Reeves GK, Roddam AW, Helzlsouer KJ, Alberg AJ, Rollison DE, Dorgan JF, Brinton LA, Overvad K, et al. The endogenous hormones and breast cancer collaborative group. Circulating sex hormones and breast cancer risk factors in postmenopausal women: Reanalysis of 13 studies. *Br J Cancer.* 2011; 105(5):709–722. [PubMed: 21772329]
20. Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histologic types of breast cancer. *Br J Cancer.* 2005; 93(9):1046–1052. [PubMed: 16175185]
21. Li CI, Daling JR, Haugen KL, Tang MT, Porter PL, Malone KE. Use of menopausal hormone therapy and risk of ductal and lobular breast cancer among women 55–74 years of age. *Breast Cancer Res Treat.* 2014; 145(2):481–489. [PubMed: 24748570]
22. Rosenberg LU, Einarisdottir K, Friman EI, Wedren S, Dickman PW, Hall P, Magnusson C. Risk factors for hormone receptor-defined breast cancer in postmenopausal women. *Cancer Epidemiol Biomarkers Prev.* 2006; 15(12):2482–2488. [PubMed: 17164374]
23. Brooks PJ. DNA damage, DNA repair, and alcohol toxicity--a review. *Alcoholism, Clinical and Experimental Research.* 1997; 21(6):1073–1082.
24. Ristow H, Seyfarth A, Lochmann ER. Chromosomal damages by ethanol and acetaldehyde in *saccharomyces cerevisiae* as studied by pulsed field gel electrophoresis. *Mutation Research.* 1995; 326(2):165–170. [PubMed: 7529880]
25. Dumitrescu RG, Shields PG. The etiology of alcohol-induced breast cancer. *Alcohol.* 2005; 35(3): 213–225. [PubMed: 16054983]

Table 1

Demographic and Clinical Characteristics of Breast Cancer Patients by Histologic Subtype and Population-Based Controls

Characteristics	Study Participants, No.(%)			
	Controls (n=891)	Ductal Cases (n=905)	Lobular Cases (n=567)	Ductal-lobular Cases (n=489)
Age, y				
55–59	258 (29.0)	260 (28.7)	155 (27.3)	156 (31.9)
60–64	234 (26.3)	248 (27.4)	159 (28.0)	143 (29.2)
65–69	222 (24.9)	218 (24.1)	143 (25.2)	105 (21.5)
70–74	177 (19.9)	179 (19.8)	110 (19.4)	85 (17.4)
Race/Ethnicity				
Non-Hispanic White	791 (88.9)	816 (90.3)	525 (92.6)	448 (91.8)
African American	28 (3.2)	22 (2.4)	8 (1.4)	7 (1.4)
Asian/Pacific Islander	17 (1.9)	37 (4.1)	10 (1.8)	12 (2.5)
Native American	24 (2.7)	16 (1.8)	10 (1.8)	13 (2.7)
Hispanic White	30 (3.4)	13 (1.4)	14 (2.5)	8 (1.6)
Missing	1	1	0	1
Education				
High School Graduate or less	249 (28.0)	260 (28.7)	162 (28.6)	121 (24.7)
Some College/Technical School	351 (39.4)	337 (37.2)	190 (33.5)	187 (38.2)
College Graduate	170 (19.1)	176 (19.5)	129 (22.8)	100 (20.5)
Post Graduate	121 (13.6)	132 (14.6)	86 (15.2)	81 (16.6)
Annual Household Income, \$US				
<20,000	83 (10.6)	101 (12.6)	62 (12.5)	43 (10.0)
20,000–34,999	140 (17.9)	137 (17.0)	83 (16.7)	89 (20.7)
35,000–69,999	293 (37.5)	278 (34.6)	171 (34.5)	134 (31.1)
70,000–89,999	89 (11.4)	101 (12.6)	73 (14.7)	63 (14.6)
90,000	176 (22.5)	187 (23.3)	107 (21.6)	102 (23.7)
Missing	110	101	71	58
Body Mass Index, kg/m² at Reference				
<25.0	245 (27.7)	269 (29.7)	206 (36.4)	161 (33.0)
25.0–29.9	301 (34.0)	283 (31.3)	170 (30.0)	171 (35.0)
30.0	339 (38.3)	353 (39.0)	190 (33.6)	156 (32.0)
Missing	6	0	1	1
Smoking Status at Reference				
Never	450 (50.5)	452 (49.9)	273 (48.2)	240 (49.1)
Former	353 (39.6)	351 (38.8)	220 (38.8)	195 (39.9)
Current	88 (9.9)	102 (11.3)	74 (13.1)	54 (11.0)
Family History of Breast Cancer				
No	710 (82.4)	666 (76.7)	425 (77.3)	366 (76.9)
Yes	152 (17.6)	202 (23.3)	125 (22.7)	110 (23.1)
Missing	29	37	17	13

Characteristics	Study Participants, No.(%)			
	Controls (n=891)	Ductal Cases (n=905)	Lobular Cases (n=567)	Ductal-lobular Cases (n=489)
Age at Menarche				
11	197 (22.1)	194 (21.5)	127 (22.4)	120 (24.6)
12–13	486 (54.6)	536 (59.4)	318 (56.2)	269 (55.1)
14	98 (11.0)	93 (10.3)	67 (11.8)	60 (12.3)
>14	110 (12.4)	80 (8.9)	54 (9.5)	39 (8.0)
Missing	0	2	1	1
Duration of Oral Contraceptive Use				
Never	248 (27.9)	281 (31.1)	181 (32.1)	142 (29.1)
<6 months	62 (7.0)	81 (9.0)	50 (8.9)	38 (7.8)
6 months – <5 years	280 (31.5)	244 (27.0)	175 (31.0)	142 (29.1)
5 – <10 years	145 (16.3)	145 (16.1)	78 (13.8)	85 (17.4)
10+ years	154 (17.3)	152 (16.8)	80 (14.2)	81 (16.6)
Missing	2	2	3	1
Age at First Live Birth, y				
Nulliparous	90 (10.1)	138 (15.3)	67 (11.8)	64 (13.1)
<20	176 (19.8)	167 (18.5)	103 (18.2)	78 (16.0)
20–24	382 (42.9)	329 (36.4)	216 (38.1)	195 (40.0)
25–29	171 (19.2)	189 (20.9)	121 (21.3)	92 (18.9)
30–34	72 (9.0)	82 (10.7)	60 (12.0)	59 (13.9)
Missing	0	0	0	1
Number of Full-Term Pregnancies Among Parous women				
1–2	395 (49.3)	378 (49.3)	257 (51.4)	225 (53.1)
3	226 (25.4)	192 (21.2)	154 (27.2)	113 (23.2)
4+	180 (20.2)	197 (21.8)	89 (15.7)	86 (17.6)
Missing	0	0	0	1
Type of Menopause				
Natural	508 (58.6)	589 (66.9)	377 (68.2)	328 (68.8)
Induced	142 (16.4)	106 (12.0)	82 (14.8)	60 (12.6)
Simple hysterectomy	217 (25.0)	186 (21.1)	94 (17.0)	89 (18.7)
Missing	24	24	14	12
Age at Menopause, y				
<45	124 (19.4)	98 (14.4)	47 (10.7)	46 (12.3)
45–49	144 (22.5)	162 (23.8)	119 (27.2)	91 (24.3)
50–52	174 (27.2)	191 (28.1)	109 (24.9)	105 (28.1)
53–55	130 (20.3)	145 (21.3)	100 (22.8)	87 (23.3)
56	67 (10.5)	85 (12.5)	63 (14.4)	45 (12.0)
Missing	252	224	129	115
Recency of Menopausal Hormone Therapy Use				
Never	253 (28.6)	323 (35.9)	146 (25.9)	121 (24.7)
Former	309 (34.9)	249 (27.7)	154 (27.3)	106 (21.7)
Current Unopposed Estrogen	202 (22.8)	163 (18.1)	119 (21.1)	104 (21.3)

Characteristics	Study Participants, No.(%)			
	Controls (n=891)	Ductal Cases (n=905)	Lobular Cases (n=567)	Ductal-lobular Cases (n=489)
Current Estrogen and Progestin	121 (13.7)	165 (18.3)	145 (25.7)	158 (32.3)
Missing (14)	6	5	3	0
AJCC Stage				
Stage I	N/A	524 (57.9)	251 (44.3)	245 (50.1)
Stage III	N/A	296 (32.7)	213 (37.6)	199 (40.7)
Stage III-IV	N/A	79 (8.8)	92 (16.6)	39 (8.1)
Unknown or Unstaged	N/A	6	11	6

Current Alcohol Use Overall and by Type and Risk of Invasive Ductal, Invasive Lobular, and Invasive Ductal-Lobular Breast Cancer

Table 2

Controls (n=891)		Ductal Cases (n=905)		Lobular Cases (n=567)		Ductal-lobular Cases (n=489)	
No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a
Alcohol Use							
Never	323 (36.3)	312 (34.5)	1 [Ref]	186 (32.8)	1 [Ref]	178 (36.4)	1 [Ref]
Former	126 (14.1)	123 (13.6)	1.01 (0.76, 1.36)	70 (12.4)	0.97 (0.69, 1.37)	58 (11.9)	0.80 (0.56, 1.15)
Current	442 (49.6)	470 (51.9)	1.09 (0.89, 1.33)	311 (54.9)	1.25 (0.99, 1.58)	253 (51.7)	0.99 (0.78, 1.26)
Average #Drinks/Week at Reference							
<4 Drinks	242 (27.2)	239 (26.4)	1.01 (0.79, 1.28)	143 (25.2)	1.04 (0.79, 1.37)	126 (25.8)	0.91 (0.68, 1.21)
4-<7 drinks	64 (7.2)	77 (8.5)	1.22 (0.84, 1.76)	52 (9.2)	1.46 (0.97, 2.21)	36 (7.4)	0.96 (0.61, 1.51)
7 drinks	136 (15.3)	154 (17.0)	1.16 (0.88, 1.54)	116 (20.5)	1.52 (1.11, 2.07)	91 (18.6)	1.15 (0.83, 1.60)
P _{trend}		0.17		0.0005		0.40	
Average #Beer/Week at Reference							
<4	142 (15.9)	146 (16.1)	1.05 (0.79, 1.39)	101 (17.8)	1.26 (0.92, 1.73)	71 (14.5)	0.86 (0.61, 1.21)
4+	15 (1.7)	21 (2.3)	1.44 (0.73, 2.85)	15 (2.7)	1.78 (0.85, 3.74)	10 (2.0)	1.12 (0.49, 2.56)
P _{trend}		0.12		0.08		0.72	
Average #Red Wine/Week at Reference							
<4	191 (21.4)	189 (20.9)	1.00 (0.77, 1.30)	128 (22.6)	1.18 (0.88, 1.58)	114 (23.3)	1.02 (0.76, 1.38)
4+	73 (8.2)	64 (7.1)	0.88 (0.60, 1.27)	59 (10.4)	1.43 (0.96, 2.12)	41 (8.4)	0.98 (0.64, 1.51)
P _{trend}		0.76		0.09		0.33	
Average #White Wine/Week at Reference							
<4	221 (24.8)	215 (23.8)	1.00 (0.78, 1.27)	150 (26.5)	1.21 (0.91, 1.59)	120 (24.5)	0.92 (0.69, 1.24)
4+	74 (8.3)	87 (9.6)	1.20 (0.85, 1.70)	56 (9.9)	1.36 (0.92, 2.01)	46 (9.4)	1.06 (0.70, 1.60)
P _{trend}		0.48		0.08		0.75	
Average #Liquor/Week at Reference							
<4	245 (27.5)	225 (24.9)	0.93 (0.73, 1.18)	154 (27.2)	1.10 (0.83, 1.44)	113 (23.1)	0.79 (0.59, 1.06)
4+	35 (3.9)	56 (6.2)	1.66 (1.06, 2.61)	40 (7.1)	2.05 (1.25, 3.34)	27 (5.5)	1.34 (0.79, 2.30)
P _{trend}		0.02		0.0008		0.07	

^aOR (95% CI) adjusted for age, reference year, and county of residence

Table 3

Current Alcohol Use and Risk of Invasive Ductal, Invasive Lobular, and Invasive Ductal-Lobular Breast Cancer by ER Status

Controls (n=891)		ER+ Ductal Cases (n=735)		ER- Ductal Cases (n=156)		ER+ Lobular Cases (n=538)		ER+ Ductal-Lobular Cases (n=459)	
No.(%)		No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a	No.(%)	OR (95% CI) ^a
Alcohol Use									
Never	323 (36.3)	249 (33.9)	1 [Ref]	60 (38.5)	1 [Ref]	178 (33.1)	1 [Ref]	167 (36.4)	1 [Ref]
Former	126 (14.1)	88 (12.0)	0.91 (0.66, 1.26)	33 (21.2)	1.39 (0.86, 2.23)	70 (13.0)	1.02 (0.72, 1.44)	52 (11.3)	0.77 (0.53, 1.12)
Current	442 (49.6)	398 (54.2)	1.16 (0.94, 1.44)	63 (40.4)	0.72 (0.49, 1.05)	290 (53.9)	1.22 (0.96, 1.55)	240 (52.3)	1.01 (0.79, 1.29)
Average #Drinks/Week at Reference									
<4 Drinks	242 (27.2)	200 (27.2)	1.07 (0.83, 1.38)	37 (23.7)	0.76 (0.48, 1.18)	134 (24.9)	1.02 (0.77, 1.35)	122 (26.6)	0.94 (0.70, 1.25)
4-<7 drinks	64 (7.2)	67 (9.1)	1.34 (0.92, 1.97)	8 (5.1)	0.62 (0.28, 1.36)	49 (9.1)	1.45 (0.96, 2.21)	32 (7.0)	0.92 (0.57, 1.46)
7 drinks	136 (15.3)	131 (17.8)	1.25 (0.93, 1.67)	18 (11.5)	0.69 (0.39, 1.21)	107 (19.9)	1.47 (1.07, 2.01)	86 (18.7)	1.17 (0.84, 1.63)
P _{trend}			0.02		0.01		0.002		0.36

^a OR (95% CI) adjusted for age, reference year, and county of residence