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Alcohol intake and invasive breast cancer risk by molecular subtype and race in the Carolina Breast Cancer Study

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Abstract

Purpose—Alcohol is an established breast cancer risk factor, but there is little evidence on whether the association differs between African Americans and whites.

Methods—Invasive breast cancers (n=1,795; 1,014 white, 781 African American) and age- and race-matched controls (n= 1,558; 844 white, 714 African American) from the Carolina Breast Cancer Study (Phases I–II) were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for pre-diagnosis drinks per week and breast cancer risk.

Results—African American controls reported lower alcohol intake than white controls across all age groups. Light drinking (0-≤2 per week) was more prevalent among African American controls. Moderate to heavy drinking was more prevalent in white controls. African Americans who reported drinking >7 drinks per week had an elevated risk compared to light drinkers [adjusted OR, 95% CI: 1.62 (1.03–2.54)]. A weaker association was observed among whites [adjusted OR, 95% CI: 1.20 (0.87–1.67)]. The association of >7 drinks per week with estrogen receptor negative [adjusted OR, 95% CI: 2.17 (1.25–3.75)] and triple negative [adjusted OR, 95% CI: 2.12 (1.12–4.04)] breast cancers was significant for African American, but not white women. We observed significantly elevated ORs for heavy intake at ages less than 25 and greater than 50 years of age for African American women only. We found no evidence of statistical interaction between alcohol intake with oral contraceptive use or smoking.

Conclusions—Drinking more than 7 alcoholic beverages per week increased invasive breast cancer risk among white and African American women, with significant increases only among African American women. Genetic or environmental factors that differ by race may mediate the alcohol-breast cancer risk association.

Keywords

Breast Cancer; Alcohol drinking; Race; Subtype; Epidemiology

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INTRODUCTION

Alcohol is an established risk factor for breast cancer, with studies showing elevated risk in those with the highest levels of intake[1–5]. Results regarding never drinkers have been mixed; both null results and increased risk of breast cancer have been observed [1–4,6,7]. However, most of these studies have been conducted primarily on white women[1–3]. There is evidence that drinking patterns differ by race in the United States, with blacks reporting less drinking than whites[6,8–11]. Information on differences in risk by race would support targeted public health messaging regarding alcohol intake.

Comparison of the alcohol-associated risk between African American and white women can be confounded by differing prevalences of breast cancer subtypes within race. African American women have higher rates of estrogen receptor (ER) negative breast cancer, and may be more likely to develop breast cancers that are triple negative (negative for ER, progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (HER2) negative. Given evidence that alcohol may alter hormone metabolism[12], some studies have evaluated risk by ER status, suggesting that alcohol intake is more strongly associated with hormone receptor positive (ER+ or PR+) breast cancers[1,13].

Early experimental studies of alcohol exposure argued that alcohol may be a co-carcinogen, increasing risk only among individuals exposed to other carcinogens. However, this hypothesis was dispelled by longer exposures, wherein lifetime exposure to alcohol produced carcinogenic effects in animals independent of other carcinogenic exposures[10,1]. Investigating the interaction between oral contraceptive use and alcohol intake is important due to biological evidence that alcohol intake may impact levels of bioavailable hormones[15]. Additionally, because smoking may initiate cancer and is more common among alcohol users, it is important to evaluate effect modification of the alcohol-breast cancer risk association by smoking status. Furthermore, few studies have evaluated specific windows of susceptibility to alcohol exposure (i.e., early vs. later life) and none have examined these windows of exposure among African American women.

The current study is an update to the previously published analysis using CBCS Phase I women only (890 cases and 841 controls[6]), incorporating 905 invasive breast cancer cases and 717 controls from Phase II. Increased sample size allows for increased power when stratifying by race, hormone receptor status, and intrinsic breast cancer subtype and allows for evaluation of effect modification by duration of oral contraceptive use, smoking status and multiple age-defined etiologically relevant windows.

METHODS

Study population

The present analysis includes 3,353 participants from the population-based Carolina Breast Cancer Study (CBCS), Phases I (1993–1996) and II (1996–2001). Methods for CBCS have been described in detail elsewhere[16–21]. Briefly, eligible cases were women with a first diagnosis of invasive or in situ breast cancer identified through rapid case ascertainment through the NC Central Cancer Registry. Controls were selected from North Carolina

Department of Motor Vehicles lists for women aged 20 to 64 years and Medicare lists for women aged 65 to 74 years. As previously reported for CBCS, cooperation rates were similar for women of both races. Cooperation rates for women under the age of 50 were 84 percent for white cases and 80 percent for African American cases. Cooperation rates for women 50 and older were 76 percent for white women and 72 percent for African American women[22]. Frequency matching of cases and controls based on race and 5-year age categories was performed. African American and non-African American (>98% white) <50 years of age and ≥50 years of age were sampled accounting for sampling fractions to achieve equal numbers of women in both categories. The current analysis is restricted to invasive cases of breast cancer only resulting in 781 African American and 1,014 white women. We included 714 African American women and 844 white women as controls.

Tumor subtype for Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal Growth Factor Receptor 2 (HER2) classification was based on a combination of pathology data from hospital records and/or Immunohistochemistry (IHC) performed at the Immunohistochemistry Core Laboratory at the University of North Carolina (when medical record data were missing). Cases were classified as ER+, PR+, or HER2+ if marker expression was recorded as positive in the medical record or if staining was positive based on contemporaneous clinical standards. Additional details regarding staining are provided by O'Brien *et al.* (2010)[23].

Exposure Assessment

The level of alcohol intake was determined by the self-reported drinking in the age category that included diagnosis age (for cases) or enrollment age (for controls). For CBCS, type of alcohol (beer, wine, liquor) and amount (drinks per day, week, month) was queried for the following age ranges for each participant: less than 25 years of age, 25 to 49 years of age, and 50 or more years of age. Alcohol intake most proximal to diagnosis was used as the main variable of interest. Alcohol intake information was missing for 6 white cases and 2 controls and 4 African American cases and 7 controls. These 19 individuals were excluded from all analyses. To be classified as a never drinker, participants had to report being a never drinker for each of the age groups preceding diagnosis. The drinks per week categories were as follows, Never Drinkers, 0 to ≤2 drinks per week (referent) (light drinkers), >2 to ≤7 drinks per week (moderate drinkers), and more than 7 drinks per week (heavy drinkers). Categories were determined using The Dietary Guidelines for Americans[24].

Multivariable analysis

Logistic regression was used to estimate odds ratios (ORs) as the measure of association between alcohol drinking and invasive breast cancer risk. All analyses were done in SAS version 9.3 (SAS Institute, Cary, NC). P-values were two-sided with an alpha of 0.05. To evaluate statistical interaction between oral contraceptive use (never user,<1 year, 1–9 years, 10 or more years), smoking status (never, former, current) and reported drinks per week in association with invasive breast cancer risk, Wald chi-square statistics and p-values for the beta coefficient of the interaction terms between oral contraceptive use, smoking status, and categorical drinks per week were assessed for basic (adjusted for 5-year age groups) and full (adjusted for 5-year age groups, education, marital status, menopausal status (pre/post), HT

use (any/ never), BMI (WHO categories), age at menarche, parity, lactation duration, income, smoking status and duration of oral contraceptive use, with each of the latter two confounders only included when not stratifying on the same. Separate models were fit for African American and white women. Sample size counts in tables are unweighted and the associated proportions account for the sampling design of the study. PROC SURVEYFREQ was used to determine chi-square statistics and p-values for weighted percentages. Potential confounder inclusion was based on substantive area knowledge and Directed Acyclic Graph (DAG) construction for relationships between covariates, alcohol and breast cancer[25,26]. These associations were further investigated in the current dataset for associations with alcohol intake among the controls and case status among the non-drinkers. We report both a basic and a multivariate model because there was no evidence of significant confounding by any of the covariates using the 10% change in estimate backward elimination approach or by using the Likelihood Ratio Test (LRT) approach. The following covariates were used in the logistic regression models based on their hypothesized relationship to both alcohol intake and invasive breast cancer and coded as follows: age at diagnosis or study enrollment modeled as an ordinal variable (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74), marital status (single, married, widowed, divorced), level of education (0–8 years, 9-<12 years (not high school graduate, high school graduate/GED, some college, college graduate (16 years) post-graduate or professional degree), menopausal status (pre-/post-), age at menarche (<11 years, 11–12, 13–14, 15–16, 17 or older), parity (nulliparous, 1, 2, 3, or 4 or more live births), lactation duration (never breast fed, 0–5 months, 6–11 months, 12–24 months, greater than 24 months), postmenopausal hormone therapy (HT) use (never used, 3+ months), recent Body Mass Index (BMI) was calculated as body weight/height squared (kg/m^2) and categorized based on the WHO categories (underweight, <18.5; normal weight, 18.5–24.9; overweight, 25–29.9; class I obese, 30–34.9; class II obese, 35–39.9; and class III obese, 40+), history of mammogram (ever, never) and income (<$20,000, $20,000–50,000, >$50,000). To account for the sampling design of the study, the oversampling of women at younger ages, the CBCS offset term was included in PROC LOGISTIC. Participants without alcohol intake information were excluded from all analyses. For the logistic models, a complete case analysis was used for the basic and multivariate models (resulting in exclusion of approximately 10% of both African American and white women in the multivariate model who were missing any of the covariates). Tests for linear trend were conducted comparing categories of 0 to ≤2 drinks per week (light drinkers, referent), >2 to ≤7 drinks per week (moderate drinkers), and more than 7 drinks per week (heavy drinkers) using an ordinal categorical variable set to 0, 1, or 2, respectively.

To examine the association between alcohol intake and breast cancer subtype, we stratified on ER status, Luminal A and B subtype combined, Triple Negative breast cancers and Basal-like subtype. There were too few HER2-positive cases (n= 72) to evaluate the association among these cases. Subtype stratification includes only invasive cases where there was enough tumor tissue for IHC analysis, resulting in 513 African American cases and 629 white cases.

To examine whether alcohol drinking at different ages showed different associations with breast cancer risk (i.e., to evaluate an age-dependent window of alcohol susceptibility), we performed a sensitivity analysis using self-reported information about drinking patterns for

participants over the life course for young age (<25 years), middle age (25-≤49 years of age) and older age (50 or more years of age). In subanalyses, we evaluated confounding by drinking in prior life periods, restricting to women who were 50 or older and who had provided data on young and middle age drinking.

RESULTS

Recent Alcohol Use and Breast Cancer Risk Overall by Race

Frequency of self-reported alcohol drinking among African American and white control participants is shown in Table 1. African Americans were more likely to report being Never Drinkers and had lower alcohol intake than whites across all age groups. During the period prior to enrollment, light drinking (0-≤2) was more prevalent among African Americans, and moderate to heavy drinking remained more prevalent in whites (Table 1). African American women had significantly elevated risk of invasive breast cancer when reporting more than 7 drinks per week prior to diagnosis in both the basic and full model [Basic OR, 95% CI: 1.73 (1.16–2.58); Full OR, 95% CI: 1.62 (1.03–2.54)]. In contrast, white women showed marginally increased risk following adjustment at the highest level of drinking [Basic OR, 95% CI: 1.23 (0.91–1.66); Full OR, 95% CI: 1.20 0.8701.67)] (Table 2).

Recent Alcohol Drinking and Invasive Breast Cancer Subtype

Subtype specific analyses of alcohol-associated risk showed findings similar to breast cancer overall. African American women who drank at least 7 drinks per week showed increased risk of invasive breast cancer for each hormone receptor (ER+, ER−) and intrinsic subtype (luminal A and B combined (ER+ and/or PR+, HER2+/−), triple negative (ER−, PR−, HER2−), and basal-like ((ER−, PR−, HER2−, and EGFR+ or CK5/6+) in both the basic and full models. Odds ratios for more than 7 drinks per week were statistically significant among African American women diagnosed with ER− and triple negative breast cancers (Table 3.) Dose-response patterns tended to be nonlinear for luminal and ER positive breast cancer, with increased risk in the highest category of alcohol drinking among African American and white women. While some of these associations were not significant following adjustment for potential confounders, the magnitudes of the ORs were very similar in the basic and full models (Table 3).

Many papers have used light drinking as a reference category for alcohol intake because of a tendency for alcohol to produce a ‘i-shaped curve’, where risk is higher among both never drinkers and moderate-to-heavy drinkers. We did not observe strong evidence for this curve in our study. Among African Americans, never drinkers were not at elevated risk, and even seemed to be at lower risk of invasive breast cancer subtypes. For white women, we observed suggestive evidence of a j-shaped curve among ER-negative, triple negative, and basal-like cases, but only with regard to the elevation of risk in never drinkers (Table 3). There was no evidence of increased risk among white women who reported moderate or high levels of drinking for any of the subtypes. Among white women, we also observed a significantly decreased risk of triple negative invasive breast cancer for those drinking more than 7 drinks per week and a significantly increased risk of ER− breast cancer among never

drinkers. These associations were significant following adjustment for potential confounders.

Windows of Susceptibility for Alcohol Intake and Invasive Breast Cancer

Among African American women, we observed an increased risk for the highest category of drinking in all three age groups, with statistically significant increases in the younger than 25 years of age and 50 years of age and older categories. For white women, we observed that middle and older age exposure showed the greatest elevation of risk associated with drinking, but none of these elevated ORs were significant. Because previous drinking may confound estimates associated with current or recent use, we conducted an exploratory sensitivity analysis restricting to women diagnosed with invasive breast cancer or enrolled in the study at age 50 or older, adjusting for drinking during the two previous age intervals. Among African American women, there was a significantly increased risk for invasive breast cancer among the never drinkers [Full OR, 95% CI: 2.03 (1.15–3.58)] and the highest category of intake [Full OR, 95% CI: 3.27 (1.16–9.23)] when controlling for lifetime intake. Odds ratios were not substantially changed after adjusting for previous drinking behavior for white women.

Modification of Alcohol-Associated Risk by Oral Contraceptives or Smoking

We did not observe evidence of statistical interaction between recent alcohol intake and oral contraceptive use in the basic or full model for African American or white women (African American, p= 0.06 and p=0.08; white, p=0.70 and p=0.70; basic and full models, respectively). Supplemental Figures 1a and 1b show magnitude of these ORs. Similarly with smoking, we did not observe evidence of statistical interaction (African American, p= 0.99 and p=0.98; white, p=0.08 and p=0.05; basic and full models, respectively). Supplemental Figure 2a and 2b show that confidence intervals were wide for cross-classification of alcohol use and smoking within race strata.

DISCUSSION

In this case-control study of alcohol intake and invasive breast cancer risk among both African American and white women, we found that alcohol intake of more than 7 drinks per week in the time period most proximal to diagnosis significantly increased risk for invasive breast cancer among African American women with a weak increase in risk among white women. We evaluated hormone receptors and intrinsic subtype and found limited evidence for heterogeneity of the risk relationships according to breast cancer characteristics. However, we did observe significantly elevated ORs for ER− and triple negative breast cancers among African American, but not white women. Associations did not vary strongly by age of exposure, and were not strongly modified by oral contraceptive use or smoking status. However, differences in risk according to race suggest other genetic or environmental factors may be important modifiers of the alcohol-breast cancer association.

Previous reports on alcohol intake and invasive breast cancer, including two meta-analyses, have been conducted primarily among white women and have consistently found highest risk in non-drinkers and the heaviest drinkers, regardless of type of beverage

consumed[1–4,7,27–30]. Among white women, this could be due to non-drinkers having comorbidities that necessitate avoiding alcohol. While we do observe slight elevation of risk among white non-drinkers in our study, we did not see this curve morphology among African American women in our study. The absence of elevated risk in the African American non-drinkers could reflect cultural differences where healthy African American women choose not to drink due to religious or cultural reasons[31]. The previous report in Phase I of the CBCS did not find any association between alcohol intake and invasive breast cancer risk, but did not stratify by race[6]. The variability in effect estimates across studies and according to race suggests that unknown modifiers may play an important role in the association between alcohol intake and invasive breast cancer.

Previous studies suggest that alcohol increases risk of ER-positive breast cancer[7,13,27,30,32]. In this study we did not observe a significant increase in ER-positive breast cancer risk for African American or white women. Results for ER-positive breast cancers were similar to those for Luminal A (ER+/PR+/HER2−) and Luminal B (ER+/PR+/HER2+) invasive breast cancers. While the associations in our study were not statistically significant, we note that the direction of association was similar, but lower in magnitude than those of Li *et al.* (2010) in postmenopausal women, the meta-analysis of Suziki *et al.* (2008), the Nurses' Health Study findings by Chen *et al.* (2011), and work by Terry *et al.* (2006) for white women from the Long Island Breast Cancer Study Project[1,7,13,30]. We observed stronger associations between alcohol use and ER− and triple negative breast cancers. Among white women, we observed a suggestion of a protective effect of high alcohol intake relative to triple negative breast cancer, which was also observed in the Women's Health Initiative study[32]. However, this association was qualitatively reversed among African American women, where the highest category of alcohol use was associated with a nearly two fold increased risk of invasive, triple negative breast cancers. There may be many explanations for why associations between alcohol intake and ER− and triple negative breast cancer in this study differ from those previously reported, but alcohol-breast cancer associations have not been well studied in African American women. Notably, associations were similar between triple negative (ER−, PR−, HER2−), and basal-like (ER−, PR−, HER2−, and EGFR+ or CK5/6+), suggesting that a more restrictive definition of basal-like that includes CK5/6+ and EGFR+ did not markedly alter associations.

When we conducted sensitivity analyses to identify age-defined windows of susceptibility to alcohol use, we found that the highest category of alcohol intake (>7 drinks/day) significantly increased risk in the youngest and oldest categories (<25and 50+ years of age) for African Americans, but only the 50+ highest intake category showed an elevated, though not significant, risk for white women (Table 4). Terry *et al.* (2006) also found increased risk in the highest intake category (≥15g/day) among women from 30–40 years of age, 40–50, and 50–60[7], primarily among white women. Similarly, Chen *et al.* (2011) found that previous alcohol intake (>5g/day), current drinking, and cumulative exposure all significantly increased breast cancer risk among white women[30]. Tjonnenland *et al.* (2007) did not report a significant association for increased risk for each 10g/day increase among age periods from 20–40 years of age[2]. We also examined intake in the 50+ category when controlling for drinking in the two prior categories and found significantly elevated risks among African American women for the youngest and oldest age categories (<25 and 50+

years of age) in the categories for 0 drinks per week and more than 7 drinks per week. These data provide little support for a specific window of susceptibility to alcohol use, and are consistent with data suggesting that alcohol may have both early and late effects on the carcinogenic process[12].

Strong differences by race may be caused by a different prevalence of an environmental or genetic modifying exposure. We ruled out two important exposures as effect modifiers in this study. First, we evaluated oral contraceptive use, considering that alcohol intake has been hypothesized to increase levels of bioavailable hormones[15], particularly among women taking oral contraceptives[12,33]. Our results showed weak evidence of interaction between alcohol and oral contraceptives, consistent with Dumeaux *et al.* (2004)[34]. Second, we evaluated smoking status as a possible modifier of alcohol-associated risk. The results among white women were similar to those reported by Hamajima *et al.* (2002) in a large meta-analysis where ever smokers were not at an increased risk of breast cancer when compared to never smokers at any level of intake[29]. We did observe a significantly elevated risk for African American women who reported being current smokers in the highest intake category. Future research should explore other genetic or environmental modifiers that account for differences by race. For example, there is some evidence that there may be genetic differences in alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) by race[35,36], and both genes play important roles in alcohol metabolism.

Our findings should be interpreted in light of some limitations. CBCS is a case-control study and information on alcohol intake was collected after diagnosis for cases. This could lead to biased classification of alcohol intake. We cannot be certain of the direction of bias, but the Nurses' Health Study showed that recall bias for alcohol intake after breast cancer diagnosis led to underestimation of effect estimates[37]. CBCS did not collect dietary information so we were unable to conduct analysis of how dietary patterns may modify alcohol-associated risk, and we had limited power to evaluate statistical interactions. We therefore emphasized racial differences and evaluated only the most commonly studied effect modifiers of the alcohol-breast cancer association, emphasizing magnitude of change over statistical significance. We were unable to evaluate the effects of drinking more than 7 drinks per week or specific types of alcoholic beverages. Few participants reported intake levels in the higher categories and we had insufficient numbers of participants in each category of specific alcohol beverage type, but previous studies examining beverage type have typically shown strongest associations for the beverage type consumed most commonly. Finally, while we had information on exposure in different age-defined windows, these windows were relatively large and we were unable to account for complex changes in exposure over time within these windows. There was a larger degree of missing data for the analysis restricted to women aged 50 years or older due to oversampling of younger women in the CBCS, but these exploratory sensitivity analyses were included as a preliminary assessment of windows of susceptibility. In spite of these limitations, our study provides compelling evidence of some differences in alcohol-associated risk of breast cancer in African American versus white women.

In summary, we found evidence for modification of the alcohol associated breast cancer risk by race, and for subtype-specific effects of alcohol on triple negative and ER− breast cancer.

Our findings differ from results in predominantly white studies, suggesting a need for research on the genetic and environmental modifiers of alcohol-associated breast cancer risk among African American and white women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Distribution of Alcohol Intake among African American and white controls from the Carolina Breast Cancer Study, Phase I (1993–1996) and Phase II (1996–2001)

	African American N (%)	White N (%)	P-value*
Total	714	844	
Alcohol			
Never	276 (40.4)	230 (22.4)	<0.0001
Ever	438 (59.6)	614 (77.6)	
Drinks per week <25 years of age			
0	372 (51.2)	396 (35.5)	<0.0001
>0–≤2	171 (26.1)	254 (26.6)	
>2–≤7	110 (15.7)	127 (29.7)	
>7	60 (7.0)	65 (8.2)	
Missing	1	2	
Drinks per week 25–<49 years of age			
0	342 (49.5)	273 (30.4)	<0.0001
>0–≤2	194 (30.5)	319 (39.2)	
>2–≤7	104 (12.1)	160 (20.4)	
>7	74 (7.9)	88 (10.0)	
Missing	0	4	
Drinks per week 50+ years of age			
0	252 (70.9)	196 (46.3)	<0.0001
>0–≤2	63 (17.6)	122 (29.7)	
>2–≤7	28 (8.4)	62 (14.6)	
>7	10 (3.1)	42 (9.4)	
Missing	361	422	
Drinks per week prior to enrollment			
Never Drinker	276 (40.4)	230 (22.4)	<0.0001
0–≤2	314 (44.3)	368 (40.5)	
>2–≤7	78 (9.8)	152 (28.1)	
>7	46 (5.5)	94 (9.1)	

*Wald Chi-square test for association excludes missing data and accounts for sampling strata

[a]Frequencies are unweighted and percentages are adjusted for sampling fractions.

Table 2

Odds Ratios (OR) and 95% Confidence Intervals (95% CI) of invasive breast cancer for African American and white women from the CBCS, Phases I (1993–1996) and II (1996–2001)

	African American			White		
	Controls	Cases		Controls	Cases	
Number of drinks per week	**N (%)**	**N (%)**	**OR (95% CI)**	**N (%)**	**N (%)**	**OR (95% CI)**
Basic Model[a]						
Never Drinker	276 (40.4)	293 (37.9)	0.96 (0.77–1.21)	230 (22.4)	272 (31.4)	1.09 (0.86–1.38)
0–≤2	314 (44.3)	337 (43.3)	Ref.	368 (40.4)	434 (39.2)	Ref.
>2–≤7	78 (9.8)	70 (8.7)	0.84 (0.59–1.21)	152 (28.1)	175 (15.8)	0.97 (0.75–1.26)
>7	46 (5.5)	81 (10.1)	1.73 (1.16–2.58)	94 (9.1)	133 (13.6)	1.23 (0.91–1.66)
p-trend			0.03			0.26
Full Model[b]						
Never Drinker	241 (38.6)	261 (37.4)	1.00 (0.77–1.30)	193 (21.1)	235 (29.7)	1.12 (0.86–1.47)
0–≤2	277 (45.5)	302 (43.1)	Ref.	331 (40.5)	404 (40.0)	Ref.
>2–≤7	69 (9.8)	66 (9.2)	0.89 (0.60–1.32)	140 (29.4)	167 (16.6)	0.93 (0.70–1.23)
>7	45 (6.2)	75 (10.4)	1.62 (1.03–2.54)	85 (9.1)	123 (13.7)	1.20 (0.87–1.67)
p-trend			0.15			0.43

[a]Basic Model adjusted for 5-year age groups and the OFFSET option was used to account for sampling design.

[b]Full Model adjusted for 5-year age groups, education, marital status, menopausal status (pre-/post-), HT use (any/ never), BMI (WHO Categories), age at menarche, parity, lactation duration, income, duration of oral contraceptive use, smoking status and the OFFSET option was used to account for sampling design.

[c]Percentages adjusted for sampling probabilities.

Table 3

Odds Ratios (OR) and 95% Confidence Intervals (95% CI) of alcohol intake and invasive breast cancer by hormone receptor and intrinsic subtype for African American and white women from the CBCS, Phases I (1993–1996) and II (1996–2001)

	African American						White					
	Basic Model			Full Model			Basic Model			Full Model		
	Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)
Number of drinks per week						ER+						
Never Drinker	276 (40.4)	132 (38.2)	0.87 (0.65–1.17)	241 (38.6)	117 (37.2)	0.89 (0.64–1.24)	230 (22.4)	149 (29.0)	0.90 (0.69–1.18)	191 (21.1)	127 (27.3)	0.96 (0.70–1.32)
0–≤2	314 (44.3)	159 (45.7)	Ref.	277 (45.6)	143 (45.5)	Ref.	368 (40.5)	263 (39.5)	Ref.	331 (40.5)	246 (40.3)	Ref.
>2–≤7	78 (9.8)	27 (7.5)	0.73 (0.44–1.19)	69 (9.8)	26 (8.0)	0.73 (0.43–1.24)	152 (28.1)	110 (17.1)	1.01 (0.75–1.35)	140 (29.4)	106 (18.2)	0.95 (0.69–1.29)
>7	46 (5.5)	32 (8.6)	1.59 (0.96–2.65)	44 (6.1)	31 (9.3)	1.25 (0.70–2.22)	94 (9.1)	83 (14.3)	1.23 (0.88–1.73)	85 (9.1)	77 (14.3)	1.18 (0.81–1.70)
p-trend			0.26			0.93			0.25			0.56
Number of drinks per week						ER−						
Never Drinker	276 (40.4)	136 (36.4)	1.02 (0.76–1.36)	241 (38.6)	125 (36.7)	1.06 (0.76–1.49)	230 (22.4)	101 (34.9)	1.38 (1.00–1.89)	191 (21.1)	89 (33.6)	1.34 (0.92–1.94)
0–≤2	314 (44.3)	158 (41.8)	Ref.	277 (45.6)	142 (41.2)	Ref.	368 (40.4)	147 (39.3)	Ref.	331 (40.5)	136 (40.5)	Ref.
>2–≤7	78 (9.8)	39 (10.2)	0.96 (0.62–1.49)	69 (9.8)	36 (10.4)	1.06 (0.65–1.74)	152 (28.1)	57 (14.2)	0.93 (0.64–1.34)	140 (29.4)	53 (14.5)	0.91 (0.61–1.36)
>7	46 (5.5)	44 (11.6)	1.89 (1.18–3.02)	44 (6.1)	40 (11.7)	2.17 (1.25–3.75)	94 (9.1)	36 (11.5)	1.00 (0.64–1.55)	85 (9.1)	32 (11.5)	1.08 (0.66–1–77)
p-trend			0.02			0.01			0.84			0.97
Number of drinks per week						Luminal A and B						
Never Drinker	276 (40.4)	110 (39.1)	0.87 (0.64–1.19)	241 (38.6)	98 (38.6)	0.86 (0.61–1.23)	230 (22.4)	104 (27.1)	0.84 (0.62–1.13)	191 (21.1)	89 (25.0)	0.87 (0.62–1.24)
0–≤2	314 (44.3)	133 (46.6)	Ref.	277 (45.6)	117 (45.9)	Ref.	368 (40.4)	202 (41.8)	Ref.	331 (40.5)	187 (42.3)	Ref.
>2–≤7	78 (9.8)	17 (5.9)	0.54 (0.30–0.95)	69 (9.8)	16 (6.2)	0.54 (0.29–1.00)	152 (28.1)	84 (17.1)	0.99 (0.72–1.37)	140 (29.4)	82 (18.4)	0.98 (0.69–1.37)
>7	46 (5.5)	25 (8.4)	1.46 (0.84–2.51)	44 (6.1)	25 (9.4)	1.38 (0.75–2.54)	94 (9.1)	60 (14.0)	1.15 (0.80–1.67)	85 (9.1)	56 (14.3)	1.14 (0.76–1.72)
p-trend			0.69			0.79			0.50			0.68

	African American						White					
	Basic Model			Full Model			Basic Model			Full Model		
	Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)
Number of drinks per week	Triple Negative											
Never Drinker	276 (40.4)	82 (36.1)	0.98 (0.69–1.38)	241 (38.6)	77 (37.5)	1.05 (0.70–1.57)	230 (22.4)	54 (37.3)	1.41 (0.94–2.11)	191 (21.1)	47 (35.2)	1.44 (0.89–2.33)
0–≤2	314 (44.3)	99 (43.0)	Ref.	277 (45.6)	87 (41.7)	Ref.	368 (40.4)	78 (40.4)	Ref.	331 (40.5)	75 (44.3)	Ref.
>2–≤7	78 (9.8)	22 (9.3)	0.89 (0.52–1.51)	69 (9.8)	19 (9.0)	0.96 (0.52–1.75)	152 (28.1)	27 (14.9)	0.83 (0.51–1.35)	140 (29.4)	24 (14.7)	0.80 (0.47–1.38)
>7	46 (5.5)	26 (11.6)	1.83 (1.06–3.19)	44 (6.1)	24 (11.9)	2.12 (1.12–4.04)	94 (9.1)	10 (7.3)	0.50 (0.25–1.10)	85 (9.1)	8 (5.8)	0.51 (0.23–1.15)
p-trend			0.07			0.07			0.03			0.05
Number of drinks per week	Basal-like											
Never Drinker	276 (40.4)	35 (30.8)	0.78 (0.49–1.25)	241 (38.6)	33 (31.8)	0.80 (0.46–1.38)	230 (22.4)	26 (37.8)	1.28 (0.75–2.19)	191 (21.1)	24 (37.8)	1.17 (0.61–2.25)
0–≤2	314 (44.3)	57 (48.5)	Ref.	277 (45.6)	51 (47.3)	Ref.	368 (40.4)	45 (45.5)	Ref.	331 (40.5)	43 (47.7)	Ref.
>2–≤7	78 (9.8)	10 (8.3)	0.66 (0.32–1.38)	69 (9.8)	10 (9.1)	0.82 (0.37–1.80)	152 (28.1)	10 (10.8)	0.52 (0.25–1.08)	140 (29.4)	8 (8.2)	0.50 (0.21–1.15)
>7	46 (5.5)	14 (12.5)	1.59 (0.79–3.21)	44 (6.1)	12 (11.8)	1.52 (0.46–1.38)	94 (9.1)	5 (5.9)	0.44 (0.16–1.16)	85 (9.1)	5 (6.4)	0.69 (0.61–2.25)
p-trend			0.31			0.44			0.02			0.13

[a] Basic Model adjusted for 5-year age groups and the OFFSET option was used to account for sampling design.

[b] Full Model adjusted for 5-year age groups, education, marital status, menopausal status (pre-/post-), HT use (any/ never), BMI (WHO Categories), age at menarche, parity, lactation duration, income, duration of oral contraceptive use, smoking status and the OFFSET option was used to account for sampling design.

[c] Percentages adjusted for sampling probabilities.

Table 4

Odds Ratios (OR) and 95% Confidence Intervals (95% CI) of invasive breast cancer at different age periods of alcohol intake for African American and white women from the CBCS, Phases I (1993–1996) and II (1996–2001)

	African American						White					
	Basic Model			Full Model			Basic Model			Full Model		
	Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)
Number of drinks per week	Age less than 25 years											
0	373 (51.3)	401 (51.8)	1.08 (0.83–1.41)	330 (50.2)	357 (51.5)	1.06 (0.79–1.43)	396 (35.4)	452 (52.8)	0.98 (0.79–1.22)	338 (33.8)	397 (51.3)	1.01 (0.79–1.28)
>0–≤2	171 (26.1)	164 (20.9)	Ref.	149 (26.4)	150 (21.3)	Ref.	256 (26.7)	328 (28.9)	Ref.	227 (26.4)	303 (29.2)	Ref.
>2–≤7	110 (15.7)	127 (15.8)	1.18 (0.84–1.65)	97 (15.9)	111 (15.4)	1.06 (0.73–1.53)	127 (29.7)	144 (11.0)	0.83 (0.62–1.12)	118 (31.4)	138 (11.8)	0.76 (0.5–1.04)
>7	60 (7.0)	92 (11.6)	1.67 (1.13–2.48)	55 (7.5)	85 (11.9)	1.63 (1.05–2.54)	65 (8.2)	91 (7.3)	1.00 (0.70–1.45)	62 (8.4)	87 (7.8)	0.96 (0.66–1.41)
p-trend			0.01			0.16			0.44			0.63
Number of drinks per week	Age 25 to 49 years											
0	342 (49.5)	361 (46.5)	1.07 (0.83–1.37)	300 (47.7)	322 (46.0)	1.05 (0.79–1.40)	273 (30.4)	311 (35.3)	1.06 (0.84–1.33)	230 (40.1)	272 (33.6)	1.08 (0.83–1.40)
>0–≤2	194 (30.5)	191 (24.3)	Ref.	171 (31.7)	174 (24.6)	Ref.	319 (39.3)	374 (32.8)	Ref.	290 (29.2)	350 (33.7)	Ref.
>2–≤7	104 (12.1)	121 (15.7)	1.17 (0.84–1.64)	91 (12.0)	109 (15.7)	1.12 (0.77–1.62)	160 (20.4)	199 (19.4)	1.09 (0.84–1.41)	143 (20.6)	187 (20.3)	1.10 (0.83–1.45)
>7	74 (7.9)	106 (13.6)	1.49 (1.03–2.14)	69 (8.6)	96 (13.7)	1.36 (0.90–2.05)	88 (9.9)	125 (12.6)	1.24 (0.90–1.69)	81 (10.2)	114 (12.3)	1.16 (0.83–1.63)
p-trend			0.02			0.28			0.17			0.34
Number of drinks per week	Age 50 and greater											
0	252 (70.9)	293 (74.4)	1.34 (0.90–2.00)	209 (69.6)	247 (73.9)	1.52 (0.94–2.46)	194 (46.3)	194 (45.5)	1.09 (0.79–1.51)	158 (45.4)	166 (44.4)	1.04 (0.70–1.54)
>0–≤2	63 (17.6)	58 (14.3)	Ref.	56 (18.3)	51 (14.7)	Ref.	122 (29.7)	113 (26.2)	Ref.	101 (29.4)	99 (26.5)	Ref.
>2–≤7	28 (8.4)	20 (5.1)	0.82 (0.41–1.61)	24 (8.5)	17 (5.2)	0.90 (0.41–2.01)	61 (14.6)	61 (14.2)	1.08 (0.69–1.67)	55 (15.7)	56 (15.0)	0.98 (0.59–1.61)
>7	10 (3.1)	25 (6.2)	2.95 (1.30–6.71)	10 (3.6)	21 (6.2)	2.85 (1.09–7.45)	42 (9.4)	59 (14.2)	1.58 (0.98–2.53)	35 (9.5)	53 (14.2)	1.37 (0.79–2.40)

	African American						White					
	Basic Model			Full Model			Basic Model			Full Model		
	Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)
p-trend			0.04			0.22			0.07			0.23

[a]Basic Model adjusted for 5-year age groups and the OFFSET option was used to account for sampling design.

[b]Full Model adjusted for 5-year age groups, education, marital status, menopausal status (pre-/post-), HT use (any/ never), BMI (WHO Categories), age at menarche, parity, lactation duration, income, duration of oral contraceptive use, smoking status and the OFFSET option was used to account for sampling design.

[c]Percentages adjusted for sampling probabilities.

Table 4a

Odds Ratios (OR) and 95% Confidence Intervals (95% CI) of invasive breast cancer at different age periods of alcohol intake for African American and white women from the CBCS, Phases I (1993–1996) and II (1996–2001) among women aged 50 years and older controlling for drinking before the age of 50 years

	African American						White					
	Basic Model			Full Model			Basic Model			Full Model		
	Controls	Cases		Controls	Cases		Controls	Cases		Controls	Cases	
	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)	N (%)	N (%)	OR (95% CI)
Number of drinks per week												
0	251 (70.8)	293 (74.4)	1.68 (1.05–2.71)	209 (69.6)	247 (73.9)	2.03 (1.15–3.58)	194 (46.3)	193 (45.5)	1.12 (0.68–1.84)	158 (45.4)	166 (44.4)	1.03 (0.58–1.81)
>0–≤2	63 (17.7)	58 (14.3)	Ref.	56 (18.3)	51 (14.7)	Ref.	122 (30.0)	113 (26.7)	Ref.	101 (29.4)	99 (26.5)	Ref.
>2–≤7	28 (8.4)	20 (5.1)	0.80 (0.39–1.68)	24 (8.5)	17 (5.2)	1.05 (0.44–2.49)	60 (14.2)	59 (13.9)	0.85 (0.50–1.44)	55 (15.7)	56 (15.0)	0.76 (0.41–1.40)
>7	10 (3.1)	25 (6.2)	2.95 (1.21–7.18)	10 (3.6)	21 (6.2)	3.27 (1.16–9.23)	42 (9.5)	59 (13.9)	1.04 (0.56–1.95)	35 (9.5)	53 (14.2)	0.96 (0.46–2.00)
p-trend			0.17			0.28			0.78			0.92

[a] Basic Model adjusted for 5-year age groups and the OFFSET option was used to account for sampling design.

[b] Full Model adjusted for 5-year age groups, education, marital status, menopausal status (pre-/post-), HT use (any/ never), BMI (WHO Categories), age at menarche, parity, lactation duration, income, duration of oral contraceptive use, smoking status and the OFFSET option was used to account for sampling design.

[c] Percentages adjusted for sampling probabilities.