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Does alcohol increase breast cancer risk in African-American women? Findings from a case–control study

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Background: Alcohol is an important risk factor for breast cancer in Caucasian women, but the evidence in African-American (AA) women is limited and results are inconclusive.

Methods: Associations between recent and lifetime drinking and breast cancer risk were evaluated in a large sample of AA women from a case–control study in New York and New Jersey. Multivariable logistic regression models provided odds ratios (ORs) and 95% confidence intervals (CIs).

Results: There was no association between recent drinking and breast cancer risk, even when stratified by menopausal status or by hormone receptor status. A borderline decreased risk with increased lifetime consumption was found (OR = 0.77; 95% CI: 0.58–1.03), which was stronger among women who drank when under 20 years of age (OR = 0.65; 95% CI: 0.47–0.89), regardless of menopausal or hormone receptor status.

Conclusion: Breast cancer risk associated with recent alcohol consumption was not apparent in AA women, while early age drinking seemed to decrease risk. This is the first investigation on recent and lifetime drinking in subgroups and drinking during different age periods in AA women. If findings are replicated, racial differences in biological pathways involving alcohol and its metabolites should be explored.

There is convincing evidence that alcohol consumption even at moderate levels increases breast cancer risk in both pre- and postmenopausal women (World Health Organization/International Agency for Research on Cancer; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 1998; Bandera and Kushi, 2006; World Cancer Research Fund/American Institute for Cancer Research, 2007; World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project Report Summary, 2010; Kushi *et al*, 2012; Seitz *et al*, 2012). A recent review (Seitz *et al*, 2012) of 113 studies reported a modest but significant (relative risk = 1.04; 95% confidence interval (CI): 1.02–1.07) risk for light drinking

(≤ 1 drink per day or ≤ 12.5 g per day ethanol) compared with non-drinkers. The same review also reported breast cancer risk associated with heavy drinking (≥ 3 drinks per day), compared with non-drinkers to be in the range of 40–50% according to the current literature. There was a positive dose–response relationship between alcohol consumption and breast cancer risk, also consistent with the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) expert report that showed 6% increased risk for each 10 g of ethanol consumed per day (World Cancer Research Fund/American Institute for Cancer Research, 2007). Hence, although alcohol should be avoided to minimise breast cancer risk, experts from both the WCRF/AICR

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(World Cancer Research Fund/American Institute for Cancer Research, 2007) and American Cancer Society (Kushi *et al*, 2012) recommend restricting alcohol intake in women to not >1 drink a day for breast cancer prevention, taking into account a potential protective effect for coronary heart disease.

The current evidence on alcohol and breast cancer risk is largely based on studies conducted in Caucasian populations. In a systematic review (Chandran *et al*, 2012) of nutritional factors and breast cancer risk in African-American (AA) women, we found only five studies (two prospective cohorts (Hiatt and Bawol, 1984; Hiatt *et al*, 1988) and three case-control studies (Brinton *et al*, 1997; Kinney *et al*, 2000; Zhu *et al*, 2003)) that presented risk estimates for alcohol and breast cancer risk stratified by race. The observed evidence in AA women was inconsistent and was limited by narrow ranges of alcohol intake and small sample sizes. More recently, a letter to the editor reported on the association between alcohol consumption, anthropometrics and breast cancer risk in a small sample of AA women (Llanos *et al*, 2012). A 53% reduction in breast cancer risk associated with mostly wine consumption was reported, and a 77% reduction in breast cancer risk (for consuming 1–6 drinks compared with <1 drink) was reported among AA women who had low waist-to-hip ratio (Llanos *et al*, 2012).

To our knowledge, there are no studies on alcohol consumption and breast cancer risk among AA women that evaluate associations by menopausal or hormone receptor status, or intake at different ages. Given the limited evidence in AA women for such an important breast cancer risk factor, we investigated the relationship between recent and lifetime alcohol intakes and breast cancer risk in a large sample of AA women participating in the Women's Circle of Health Study (WCHS), a case-control study based in New York (NY) and New Jersey (NJ).

MATERIALS AND METHODS

The design and procedures followed in the WCHS have been described elsewhere (Ambrosone *et al*, 2009). In summary, the WCHS was a case-control study conducted in NY and NJ. Eligibility criteria for cases included AA or Caucasian females, 20–75 years of age, no previous history of cancer except for non-melanoma skin cancer, able to understand and speak English and newly diagnosed with histologically confirmed invasive breast cancer or ductal carcinoma *in situ* (DCIS). Controls had the same eligibility criteria as cases except that they had no breast cancer. Study recruitment in NY ended in December 2008 while data collection in NJ pertaining to this investigation was completed in March 2012. Cases in NY were identified through hospitals with the largest referral patterns for AA women while in NJ, rapid case ascertainment methodology was employed by the NJ State Cancer Registry to identify eligible cases. African-American controls in NY were recruited through random digit dialling (RDD) and in NJ through RDD supplemented by recruitment through community sources (Bandera *et al*, 2013). Although WCHS included both AA and Caucasian women, because of the plethora of evidence relating alcohol and breast cancer risk in Caucasian women and the scarce literature in AA women, these analyses focus on AA women. Overall, the participation rate for those who were contacted and eligible was 78.7% and 48.2% in AA cases and controls, respectively, and 79% and 49% in Caucasian cases and controls, respectively.

Data collection. Data collection was conducted during an in-person interview, which included the administration of a main study questionnaire querying about demographics, family history, reproductive history, hormone use, lifetime alcohol consumption, physical activity and other lifestyle factors. Participants also completed a Food Frequency Questionnaire (FFQ) that queried

on frequency and portion size for 125 foods and beverages including beer, red wine, white or rose wine, and liquor and mixed drinks consumed during the 12 months before diagnosis for cases and a comparable period for controls. Detailed anthropometric measurements were obtained using a standardised protocol. Data from a total of 803 AA cases and 889 AA controls were included for analyses. All participants provided informed consent, and the study was approved by the Institutional Review Boards of the University of Medicine and Dentistry of New Jersey (now Rutgers University), Mount Sinai School of Medicine and Roswell Park Cancer Institute.

Recent alcohol assessment. The FFQ provided a measure of recent alcohol intake (i.e., in the 12 months before reference date). Measuring alcohol (or ethanol) intake in grams is generally recommended as it includes both size and strength of each drink (World Cancer Research Fund/American Institute for Cancer Research, 2007) and is helpful in standardising ethanol intake across different beverages, which vary in alcohol content. Hence, alcohol intake was calculated as grams (g) of ethanol based on the assumption that there are 14 g of ethanol in a 12 oz can of beer, 1 shot or 1.5 oz of liquor or mixed drink, or 5 oz of wine (Centers for Disease Control and Prevention, 2011). We calculated the consumption of each beverage type as a function of frequency and serving size and expressed in total g per week. The sum of consumption of all the alcoholic beverages was used to estimate total recent alcohol consumption for each participant.

Lifetime alcohol assessment. The interviewer-administered questionnaire ascertained lifetime alcohol consumption and drinking during different life periods: under 20 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60 years and over. For each of these periods, women were queried about how many years they drank and amount of drinks usually consumed during that time. Based on this information, we calculated total drinks consumed during each age interval as well as total lifetime drinks by summing drinks consumed in each age interval.

Statistical analyses. Frequencies were used to compare the distribution of selected characteristics between cases and controls. Mean and median consumption levels of recent alcohol and lifetime consumption were compared between cases and controls, and *P*-values were obtained from the Wilcoxon rank sum test. Multivariable logistic regression analyses were used to compute odds ratios (ORs) and 95% CIs. Total recent alcohol intake and consumption of individual beverages were categorised as 'non-drinker' and 'drinker' as well as '<14 g per week (<1 drink per week)', '14–<28 g per week (1–<2 drinks per week)' and '≥28 g per week (2+ drinks per week)' to evaluate associations for increasing levels of drinking. Total lifetime consumption was analysed as a binary exposure (ever/never) based on the screener question for lifetime drinking as well as 'non-drinker', 'below median drinks' and 'above median drinks' (with median = 3510 drinks) based on computed levels in controls. There were 15 women who reported consuming alcoholic beverages at least once a week for 6 months or more, but had missing information for number of drinks consumed. Drinking during different age intervals was modelled as a binary variable (non-drinker/drinker) during each specific decade.

Multivariable models were adjusted for age, ethnicity (Hispanic or non-Hispanic), country of origin ('US born', 'Caribbean born', 'other'), education ('<12th grade', 'high school graduate or equivalent', 'some college', 'college graduate', 'post-graduate degree'), age at menarche, age at menopause, menopausal status, parity, age at first birth ('0–19', '20–24', '25–30', '≥31'), breastfeeding, family history of breast cancer, history of benign breast disease, hormone replacement therapy (HRT) use, and oral contraceptive (OC) use. Models were also further adjusted for body

mass index (BMI) and total energy intake, as well as physical activity and recent alcohol consumption (for lifetime alcohol intake). These covariates were selected for inclusion into the model based on their routine adjustment as confounders in the breast cancer literature. Nevertheless, main analyses were repeated after only adjusting for factors that differed significantly in their distribution between cases and controls. If the results remained unchanged, then estimates from the full model are reported to facilitate comparison of results across studies. BMI measures included self-reported BMI 1 year before reference date as well as measurements taken by the interviewer at the time of interview. As measured BMI and BMI based on self-reported weight and height were highly correlated ($r=0.92$), we used the objectively measured BMI values, and substituted missing values for height and/or weight with self-reported values. Subgroup analyses included further stratification by menopausal status, oestrogen receptor (ER)/progesterone receptor (PR) status (using controls as reference in polytomous logistic regression analyses), BMI (stratified as $>25 \text{ kg m}^{-2}$, $25\text{--}29.9 \text{ kg m}^{-2}$, $\geq 30 \text{ kg m}^{-2}$) and smoking status 1 year before reference date (stratified as never smoker, former smoker, current smoker). We were not able to conduct analyses stratified by ER+/PR- and ER-/PR+ tumours as the sample sizes for these subtypes were small.

In sensitivity analyses, models were evaluated after excluding HRT users ($n=219$), DCIS cases ($n=119$) and community controls ($n=339$). There were also 317 women who self-reported recent drinking on the FFQ but reported being a never drinker for the lifetime alcohol question during the interview. Similarly, at least 17 women appeared to have consumed alcohol during their reference age, but did not report drinking on the FFQ. To evaluate the impact of these discrepancies, we repeated analyses after excluding these 334 women.

All analyses were conducted using SAS version 9.2 (Cary, NC, USA).

RESULTS

There were no meaningful differences between cases and controls with regard to frequencies of education, age at menarche, parity, breastfeeding history or BMI (Table 1). A higher proportion of cases reported a family history of breast cancer, personal history of benign breast disease and HRT use. Proportions of OC use and menopausal status were very similar in cases and controls. The distributions of recent and lifetime alcohol intakes for different alcoholic beverages are presented in Table 2. Overall, reported recent alcohol consumption in this study of AA women was very low, with median intake of around 16 g of ethanol in a week in cases and controls who reported being alcohol consumers. Among drinkers, mean intakes of total ethanol from recent drinking and beer were higher among controls than in cases, whereas the opposite was true for ethanol consumed from wine and liquor.

Associations between recent alcohol consumption and breast cancer risk are presented in Table 3. There was no clear relationship between recent alcohol drinking and breast cancer risk, both when evaluated compared with non-drinkers (OR=0.95; 95% CI: 0.77–1.17) or for increasing levels of consumption (OR=0.95; 95% CI: 0.65–1.39, comparing $>28 \text{ g per week vs } <14 \text{ g per week}$). There was also no evidence of an association between drinking any specific alcoholic beverage and disease risk, although the risk estimate for consuming >2 mixed drinks or liquor a week compared with <1 drink was strong, albeit statistically nonsignificant (OR = 1.53; 95% CI: 0.84–2.79).

There was a suggestion of decreased breast cancer risk for women in the highest category of lifetime drinking compared with non-drinkers (OR = 0.77; 95% CI: 0.58–1.03), although the

Table 1. Distribution of selected characteristics for breast cancer among AA women participating in WCHS, $n=1692$

	Cases ($n=803$) n (%)	Controls ($n=889$) n (%)	χ^2 P-value
Age at interview (years)			<0.001
20–34	37 (4.6)	71 (8.0)	
35–44	162 (20.2)	182 (20.5)	
45–54	261 (32.5)	320 (36)	
55–64	262 (32.6)	272 (30.6)	
65–76	81 (10.1)	44 (4.9)	
Education			0.11
<High school	118 (14.7)	112 (12.6)	
High school graduate	241 (30)	227 (25.5)	
Some college	213 (26.5)	259 (29.1)	
College graduate	141 (17.6)	180 (20.2)	
Post-graduate degree	90 (11.2)	111 (12.5)	
Country of origin			<0.001
United States	552 (68.7)	711 (80)	
Caribbean countries	189 (23.5)	129 (14.5)	
Other	62 (7.7)	49 (5.5)	
Ethnicity			0.01
Hispanic	45 (5.6)	26 (2.9)	
Non-Hispanic	758 (94.4)	863 (97.1)	
Age at menarche (years)			0.94
<12	228 (28.4)	250 (28.2)	
12–13	365 (45.4)	399 (44.9)	
>13	210 (26.2)	239 (26.9)	
Menopausal status			0.60
Premenopausal	408 (50.8)	463 (52.1)	
Postmenopausal	395 (49.2)	426 (47.9)	
Parity (live births)			0.67
0	124 (15.4)	148 (16.7)	
1–2	414 (51.6)	438 (49.3)	
3–4	200 (24.9)	237 (26.7)	
>5	65 (8.1)	66 (7.4)	
Breastfeeding			0.68
Never	470 (58.5)	529 (59.5)	
Ever	333 (41.5)	360 (40.5)	
Family history			0.08
No	687 (85.6)	786 (88.4)	
Yes	116 (14.4)	103 (11.6)	
Past benign breast disease			<0.001
No	547 (68.3)	685 (77.1)	
Yes	254 (31.7)	203 (22.9)	
HRT use			0.06
Never	682 (85.4)	785 (88.5)	
Ever	117 (14.6)	102 (11.5)	
Oral contraceptive use			0.38
Never	333 (41.5)	387 (43.6)	
Ever	470 (58.5)	501 (56.4)	
BMI			0.73
Underweight/Normal	151 (18.8)	157 (17.7)	
Overweight	235 (29.3)	255 (28.7)	
Obese	416 (51.9)	477 (53.7)	

Abbreviations: AA = African-American; BMI = body mass index; HRT = hormone replacement therapy; WCHS = Women's Circle of Health Study.

Table 2. Comparison of mean and median intakes of recent and lifetime alcohol consumption among AA women in WCHS

	Cases (n = 803)			Controls (n = 889)			P-value
	% Drinkers	Mean ± s.d. (among drinkers)	Median (among drinkers)	% Drinkers	Mean ± s.d. (among drinkers)	Median (among drinkers)	
Recent alcohol intake (g of ethanol per week)	37.36	48.37 ± 86.50	16.54	40.2	54.15 ± 116.26	16.08	0.18
Beer intake (g of ethanol per week)	14.61	23.89 ± 50.47	7	18.36	40.91 ± 107.01	5.92	0.03
Wine intake (g of ethanol per week)	26.9	35.60 ± 66.83	10.79	28.27	35.15 ± 78.23	12.10	0.54
Liquor and mixed drinks (g of ethanol per week)	20.67	24.26 ± 52.28	5.92	22.18	19.50 ± 53.91	5.92	0.55
Lifetime alcohol consumption (number of drinks)	33.13	5955.32 ± 10 085.80	2756	36.04	9966.86 ± 25 628.76	3484	0.09

Abbreviations: AA = African-American; WCHS = Women's Circle of Health Study. P-values are from non-parametric test comparing alcohol consumption among all cases and controls regardless of drinking status. The % of drinkers in each alcohol category reflects the total proportion of alcohol consumers for that category. The proportions are not mutually exclusive.

Table 3. Recent alcohol consumption and breast cancer risk among AA women in WCHS

	Cases (n)	Controls (n)	OR1		OR2	
			Estimate	95% CI	Estimate	95% CI
Total ethanol from recent alcohol intake						
Non-drinker	503	531	Ref		Ref	
Drinker	300	357	0.98	0.79–1.20	0.95	0.77–1.17
< 14 g per week	131	153	Ref		Ref	
14 – <28 g per week	60	70	1.00	0.64–1.56	0.98	0.63–1.53
≥28 g per week	109	134	1.01	0.70–1.46	0.95	0.65–1.39
P for linear trend			0.97		0.80	
Ethanol from recent beer intake						
Non-beer drinker	684	725	Ref		Ref	
Beer drinker	117	163	0.84	0.64–1.10	0.81	0.62–1.06
< 14 g per week	69	92	Ref		Ref	
14 – <28 g per week	22	21	1.65	0.78–3.51	1.67	0.79–3.57
≥28 g per week	26	50	0.77	0.41–1.45	0.79	0.41–1.49
P for linear trend			0.30		0.31	
Ethanol from recent wine intake						
Non-wine drinker	587	637	Ref		Ref	
Wine drinker	216	251	0.98	0.78–1.23	0.94	0.75–1.19
< 14 g per week	109	126	Ref		Ref	
14 – <28 g per week	50	69	0.87	0.54–1.40	0.85	0.53–1.38
≥28 g per week	57	56	1.16	0.71–1.88	1.10	0.67–1.80
P for linear trend			0.45		0.58	
Ethanol from recent liquor/mixed drinks intake						
Non-liquor drinker	637	691	Ref		Ref	
Liquor drinker	166	197	1.08	0.84–1.38	1.06	0.83–1.36
< 14 g per week	109	146	Ref		Ref	
14 – <28 g per week	21	19	1.54	0.75–3.16	1.50	0.73–3.08
≥28 g per week	36	32	1.57	0.88–2.81	1.53	0.84–2.79
P for linear trend			0.13		0.16	

Abbreviations: AA = African-American; BMI = body mass index; CI = confidence interval; HRT = hormone replacement therapy; OC = oral contraceptive; OR = odds ratio; WCHS = Women's Circle of Health Study. OR1: adjusted for age, ethnicity, country of origin, education, age at menarche, parity, age at first birth, breastfeeding status, menopausal status, family history of breast cancer, HRT use, OC use, history of benign breast disease. OR2: further adjusted for total energy intake and BMI. Recent alcohol consumption is measured as alcohol consumption during the 12 months before reference date for cases and controls.

association for ever drinkers compared with never drinkers was null (Table 4). Inverse statistically significant associations were further observed among women who drank alcohol when they were <20 years of age with an OR of 0.65 (95% CI: 0.47–0.89) compared with women who were non-drinkers in that age interval. This association was significant ($P=0.01$) even after adjusting for multiple testing (Bonferroni correction $\alpha=0.01$). Similarly, a reduction in risk was also suggested among women who drank after age 60 (OR = 0.42; 95% CI: 0.17–1.01); however, the sample size was small for drinkers in this age interval, and results could have occurred by chance (P -value = 0.05). There was no association between drinking during any other age interval and breast cancer risk.

When stratified by menopausal status at the time of breast cancer diagnosis/reference date (Table 5), the ORs for premenopausal (OR = 1.21; 95% CI: 0.90–1.62) and postmenopausal women (OR = 0.78; 95% CI: 0.57–1.07) were in the opposite direction, albeit not statistically significant. There was no evidence of an association for increasing levels of consumption in either group. However, the inverse association observed between drinking under 20 years of age and breast cancer risk was observed in both premenopausal and postmenopausal women, although the estimate

was statistically significant in premenopausal women (OR = 0.60; 95% CI: 0.38–0.94). Similarly, the inverse association with drinking under 20 years of age was also found for both ER+/PR+ and ER-/PR- tumours although borderline significance was found among women with hormone receptor-positive cancers (OR = 0.64; 95% CI: 0.41–0.99).

There was no clear evidence of effect modification by BMI or smoking status for both recent and lifetime alcohol consumption, as magnitude of ORs were generally comparable across BMI and smoking categories, with most CIs including the null value (data not shown). However, the inverse association between drinking under 20 years of age and breast cancer risk was stronger among women who were overweight (OR = 0.49; 95% CI: 0.27–0.87) and among never smokers (OR = 0.39; 95% CI: 0.21–0.73).

There was no change in the main findings on lifetime alcohol consumption (overall or drinking under 20 years of age) and breast cancer risk when multivariable models were further adjusted for recent alcohol intake or when both recent and lifetime alcohol risk estimates were also adjusted for physical activity (data not shown). Excluding HRT users, community controls or DCIS cases also did not alter the main conclusions, although the OR for recent drinking compared with non-drinkers among postmenopausal

Table 4. Association between lifetime alcohol consumption, drinking at different age intervals, and breast cancer risk among AA women in WCHS

	Cases (n)	Controls (n)	OR1		OR2	
			Estimate	95% CI	Estimate	95% CI
Lifetime alcohol intake						
Never	537	568	Ref		Ref	
Ever	266	320	0.99	0.80–1.23	0.96	0.78–1.19
Non-drinker ^a	537	568	Ref		Ref	
≤3510 drinks	150	158	1.14	0.87–1.48	1.11	0.85–1.45
>3510 drinks	107	156	0.81	0.61–1.08	0.77	0.58–1.03
Drinking during <20 years						
No	728	760	Ref		Ref	
Yes	75	127	0.68	0.50–0.94	0.65	0.47–0.89
Drinking during 20–29 years						
No	597	634	Ref		Ref	
Yes	206	254	0.98	0.78–1.23	0.94	0.75–1.19
Drinking during 30–39 years						
No	595	627	Ref		Ref	
Yes	197	245	0.94	0.74–1.18	0.91	0.72–1.15
Drinking during 40–49 years						
No	559	582	Ref		Ref	
Yes	141	159	1.02	0.78–1.33	0.99	0.76–1.30
Drinking during 50–59 years						
No	390	388	Ref		Ref	
Yes	72	79	1.02	0.70–1.47	1.00	0.69–1.45
Drinking during ≥60 years						
No	162	130	Ref		Ref	
Yes	10	17	0.44	0.18–1.06	0.42	0.17–1.01

Abbreviations: AA = African-American; BMI = body mass index; CI = confidence interval; HRT = hormone replacement therapy; OC = oral contraceptive; OR = odds ratio; WCHS = Women's Circle of Health Study. OR1: adjusted for age, ethnicity, country of origin, education, age at menarche, parity, age at first birth, breastfeeding status, menopausal status, family history of breast cancer, HRT use, OC use, history of benign breast disease. OR2: further adjusted for total energy intake and BMI.

^aFifteen women had missing data for number of drinks consumed.

Table 5. Recent and lifetime alcohol consumption stratified by menopausal status and hormone receptor status in AA women

	Premenopausal (n = 871)			Postmenopausal (n = 821)			ER + /PR +			ER - /PR -		
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	Ca	OR	95% CI	Ca	OR	95% CI
Recent alcohol intake												
Non-drinker	225/267	Ref		278/264	Ref		202	Ref		114	Ref	
Drinker	183/195	1.21	0.90–1.62	117/162	0.78	0.57–1.07	121	0.93	0.70–1.23	61	0.89	0.62–1.27
< 14 g per week	81/87	Ref		50/66	Ref		53	Ref		22	Ref	
14–<28 g per week	32/41	0.81	0.45–1.48	28/29	1.14	0.55–2.36	26	1.01	0.57–1.81	13	1.25	0.57–2.77
≥28 g per week	70/67	1.18	0.71–1.95	39/67	0.73	0.39–1.35	42	0.86	0.52–1.44	26	1.20	0.61–2.39
P for linear trend	0.38			0.23			0.53			0.69		
Lifetime alcohol intake												
Never	285/304	Ref		252/264	Ref		213	Ref		109	Ref	
Ever	123/159	0.90	0.66–1.24	143/161	1.07	0.79–1.46	110	0.98	0.74–1.31	66	1.14	0.80–1.63
Non-drinker	285/304	Ref		252/264	Ref		213	Ref		109	Ref	
≤3510 drinks	77/92	1.00	0.69–1.46	73/66	1.33	0.89–2.00	68	1.23	0.87–1.74	35	1.21	0.78–1.89
>3510 drinks	44/65	0.74	0.47–1.17	63/91	0.82	0.55–1.22	39	0.70	0.47–1.06	29	1.02	0.63–1.63
Drinking at <20 years												
No	370/391	Ref		358/369	Ref		293	Ref		159	Ref	
Yes	38/72	0.60	0.38–0.94	37/55	0.74	0.46–1.20	30	0.64	0.41–0.99	16	0.61	0.34–1.07

Abbreviations: AA = African-American; BMI = body mass index; Ca = case; CI = confidence interval; Co = control; ER = oestrogen receptor; HRT = hormone replacement therapy; OC = oral contraceptive; OR = odds ratio; PR, progesterone receptor. ORs are adjusted for age, ethnicity, country of origin, education, age at menarche, age at menopause (only for postmenopausal women), menopausal status (for analyses by hormone receptor status), parity, age at first birth, breastfeeding status, family history of breast cancer, HRT use, OC use, history of benign breast disease, total energy intake, BMI.

women changed from 0.78 to 0.64 when excluding community controls (data not shown). Results from the main analyses did not change in parsimonious models (data not shown).

DISCUSSION

In this case-control study involving a large sample of AA women, neither recent, light to moderate alcohol intake nor lifetime drinking significantly increased breast cancer risk, even after stratifying by menopausal or hormone receptor status. Drinking under 20 years of age was associated with a reduced disease risk when compared with non-drinkers during that age interval, which remained regardless of menopausal status and tumour receptor status. The inverse relationship observed for drinking during adolescence was also significant among overweight women and non-smokers, although magnitude of associations were generally similar across BMI and smoking levels.

Despite a larger sample size compared with previous studies, the overall null findings for recent alcohol intake and breast cancer risk were in general agreement with the current evidence in AA women (reviewed in Chandran *et al*, 2012). There were also no meaningful differences in risk by beverage type, except for a stronger OR observed with increasing levels of liquor consumption. In a small case-control study of AA women, an inverse association was observed between alcohol intake (mostly consisting of wine) and breast cancer risk (Llanos *et al*, 2012). In our study, we observed nonsignificant opposite relationships in premenopausal and postmenopausal women for drinkers compared with non-drinkers, which also could have contributed to the null findings when combining all women, although there was limited power to detect a significant association. The likelihood of spurious associations because of relatively small numbers especially among alcohol consumers cannot be discounted. As this is the first study to present risk estimates stratified by menopausal status in AA women, findings need replication.

In this study, we also found a borderline inverse association between lifetime alcohol consumption and breast cancer risk. The only other study on lifetime consumption in AA women reported null results albeit with an OR below 1 (OR = 0.7; 95% CI: 0.3–1.6) for average lifetime consumption of over 182 g per week (Kinney *et al*, 2000), but drinking in our study was much lower. It is possible that the inverse association in our study was driven by drinking during a particular lifetime period, during which time alcohol consumption may not have a detrimental effect or perhaps alcohol intake was only a marker for other factors that may reduce risk. The marginal inverse relationship observed for lifetime drinking in AA women appeared to be reflected mostly through alcohol consumption under age 20 including the adolescent period. This association remained statistically significant even when adjusted for multiple testing. Excluding HRT users also did not alter the inverse relationship. It is unlikely that this finding was affected by the participant's current age because not only was this age category applicable to all participants, but the association was found in both premenopausal and postmenopausal women. However, findings related to lifetime consumption could be spurious in view of potential recall bias described later; hence should be interpreted with caution. Some past studies mostly involving Caucasian populations have reported no risk increase for drinking at 10–15 years (Marcus *et al*, 2000), 15–20 years (Berstad *et al*, 2008), 16 years (Freudenheim *et al*, 1995), 18 years (Smith *et al*, 1994) and below 22 years (Garland *et al*, 1999), while other studies have shown increased risks associated with drinking below 30 years of age (Harvey *et al*, 1987) and during ages 18–40 years (Chen *et al*, 2011). Terry *et al* (2006) observed an inverse relationship between breast cancer risk and drinking >15 g of alcohol per day (compared with non-drinkers) under age 20 (OR = 0.66; 95% CI: 0.41–1.06) and between 20 and 30 years (OR = 0.57; 95% CI: 0.36–0.89) in women who were overweight or obese, and the sample included Caucasian women. Similarly, although the interaction between smoking and alcohol intake on breast cancer risk was not significant, perhaps the stronger inverse

finding in non-smokers could be because of reduced exposure to toxic compounds in the absence of tobacco. However, mechanisms to explain both an increased and decreased risk of breast cancer associated with smoking have been postulated (Terry and Rohan, 2002) and, the evidence remains inconclusive. Hence, the inverse finding in non-smokers cannot be emphasised.

Racial differences in oestrogen (Taioli *et al*, 1996) and ethanol (Yu *et al*, 1995) metabolism have been noted, such that even when AA have reported heavier drinking habits, on average, they had lower levels of urinary ethanol as compared with Caucasian drinkers, which could be due to identified racial differences in distributions of genetic polymorphisms related to ethanol metabolism (Dumitrescu and Shields, 2005). A variant in the regulatory region of CYP2E1 has been associated with increased metabolic activity of this gene (McCarver *et al*, 1998), which could increase concentrations of acetaldehyde. The incidence of this variant has been shown to be higher in AA than in Caucasians with greater levels of metabolic activity observed mostly among obese individuals or among those who had recently consumed ethanol (McCarver *et al*, 1998). However, animal studies have also shown that CYP2E1 could metabolise both ethanol and acetaldehyde (Terelius *et al*, 1991), which could potentially result in lowered levels of acetaldehyde in the body, thus reducing toxicity. Research on the role of alcohol in promoter methylation of tumour-suppressor genes has indicated an inverse association between *p16* promoter methylation and lifetime drinking as well as drinking intensity (Tao *et al*, 2011). This inverse relationship was more prominent for intakes at earlier age periods. Hence, race-specific investigations on biological mechanisms involved in the impact of ethanol intake and oestrogen levels on breast tissue are warranted.

Certain limitations of the study should be noted. The main issue was the limited consumption of alcohol in our study because of light drinking (<1 drink per day). Alcohol consumption in AA women has been generally lower than reported intakes in Caucasian women (Liu *et al*, 1996; US Department of Health and Human Services; Centers for Disease Control and Prevention; National Center for Health Statistics, 2012), which was also found in our study. Although the prevalence of recent alcohol consumption in our study (39%) is similar to national estimates reporting 32% of AA women as current regular drinkers (US Department of Health and Human Services; Centers for Disease Control and Prevention; National Center for Health Statistics, 2012), only 10% of women reported having more than half a drink per day, which is lower than levels reported among AA women in the Carolina Breast Cancer Study (Kinney *et al*, 2000). Therefore, we could not assess breast cancer risk associated with drinking patterns, heavy drinking (3 or more drinks per day) or binge drinking. There was also limited power to detect associations in stratified analyses. Low alcohol consumption in our study was not restricted to AA women. In our study, associations between recent drinking, lifetime consumption and breast cancer risk were mostly null in Caucasian women, possibly because of limited range of intake (median among drinkers was <3 drinks per week) even in this group (data not shown). Although majority of studies in Caucasians have shown increased breast cancer risk with increasing levels of drinking, few studies have also shown inverse or nonsignificant associations (Rosenberg *et al*, 1990; Friedenreich *et al*, 1993; Freudenheim *et al*, 1995).

Recall bias is also often an issue in case-control studies especially for exposures such as lifetime alcohol consumption where there could be possible errors in recalling alcohol intake from the distant past. There is some evidence showing that alcohol consumption recall (Giovannucci *et al*, 1993) is similar for breast cancer cases and controls. A validation study reported that recall of alcohol intake for 20 years in the past was good but not reports at 18 years of age (Dwyer *et al*, 1989). Another study reported that recall of alcohol intake at different age periods: 16–19 years, 20–29

years, 30–39 years, and recent consumption was very good (Longnecker *et al*, 1992). Specifically, a reliability study (Liu *et al*, 1996) using NHANES data reported that correlations for alcohol recalled from 10 years in the past for AA women were moderate and were only slightly lower than correlations observed in Caucasian women. Nevertheless, since adolescent drinking has been illegal in the United States for several years, incorrect reporting of drinking when under 20 years of age is likely. Hence, the observed inverse association between drinking under 20 years and the marginal decreased risk for overall lifetime drinking and breast cancer risk should be viewed with caution.

Mode of data collection (interviewer-administered vs self-report) could also affect reporting for certain exposures such as alcohol. In our study, >300 women reported to be non-drinkers on the interviewer-administered questionnaire, but disclosed alcohol intake in the self-administered FFQ, whereas only 17 women seem to have the opposite discrepancy. However, results were similar when we used the FFQ and interviewer-administered responses. Moreover, assessment of alcohol intake using self-reported methods has been shown to be both valid and reliable (Feunekes *et al*, 1999; Del Boca and Darkes, 2003). Nevertheless, analyses were repeated after excluding women with inconsistent data, and while there was a loss in precision as expected, study conclusions did not change.

Cases may also have changed their alcohol intake after their diagnosis and incorrectly report recent consumption. In our study, as compared with controls, greater proportion of AA cases had quit drinking since diagnosis (33.9% vs 19.4%), and a lesser proportion of cases had started drinking more (5.4% vs 18%). Drinking levels could be systematically different among controls than cases, especially with higher socioeconomic status generally observed among RDD controls. Finally, to evaluate potential selection bias arising from community control recruitment, analyses were repeated excluding them. But, main results did not substantially change. Moreover, a combination of community and RDD controls appeared to be more representative of the underlying population with regard to characteristics such as education, income, and marital status (Bandera *et al*, 2013). Response rates as low as 50% are not uncommon in population studies (Hartge, 2006), and case participation for studies of cancer have shown to be lower than for studies of other diseases (Olson, 2001).

Strengths of the study include the large sample of AA women allowing further evaluation by important subgroups as well as collection of both recent and lifetime drinking data. To our knowledge, this is the first and largest study of AA women to evaluate the association between both recent and lifetime alcohol intakes and breast cancer risk along with assessment of risk associated with drinking during different life periods, and stratification by several important factors.

To conclude, recent moderate alcohol intake was not associated with breast cancer risk in AA women. Lifetime drinking, particularly early age drinking, appeared to decrease risk. However, as this is the first study to report these findings in AA women, and in light of potential biases that have been discussed, no definitive conclusions can be drawn at this time. Hence, until future research is conducted to explore the role of alcohol as well as potential gene-environment interactions to evaluate racial differences in response to intake, expert guidelines of limiting alcohol consumption for cancer prevention should continue to be recommended.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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