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Alcohol intake over the life course and breast cancer survival in Western New York Exposures and Breast Cancer (WEB) study: Quantity and intensity of intake

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Abstract

Alcohol intake is a risk factor for breast cancer, but the association between alcohol and mortality among breast cancer survivors is poorly understood. We examined the association between alcohol intake from all sources, assessed by cognitive lifetime drinking history, and all-cause and breast cancer mortality among women with breast cancer (N=1097) who participated in a population-based case-control study. Vital status was ascertained through 2006 using the National Death Index. Using Cox Proportional Hazards models, we computed hazard ratios for all-cause and breast cancer mortality in association with alcohol intake. We examined lifetime volume and intensity (drinks per drinking day) of alcohol consumption as well as drinking status during various life periods. Analyses were stratified by menopausal status. After adjustment for total intake, postmenopausal women with consumption of four or more drinks per drinking day over their lifetimes were nearly three times more likely to die from any cause compared to abstainers (HR2.94, 95%CI 1.31,6.62). There was a similar but non-significant association with breast cancer mortality (HR2.68, 95%CI 0.94,7.67). Postmenopausal women who drank one drink or fewer per drinking day between menarche and first birth had a significantly decreased hazard of all-cause (HR0.54, 95%CI 0.31,0.95) and breast cancer mortality (HR0.27, 95%CI 0.09,0.77).

Premenopausal breast cancer survival was not associated with drinking intensity. We observed no associations between drinking status or total volume of alcohol intake and breast cancer or all-cause mortality. High-intensity alcohol consumption may be associated with decreased survival in postmenopausal women with breast cancer. Low-intensity alcohol consumption between menarche and first birth may be inversely associated with all-cause and breast cancer mortality; this period may be critical for development of and survival from breast cancer. Intensity of alcohol intake may be a more important factor than absolute volume of intake on survival in women with breast cancer.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Keywords

breast cancer; alcohol; survival; population-based study

Introduction

Breast cancer is the most common cancer in American women, excluding non-melanoma skin cancer, and is the second-leading cause of death from cancer in American women, after lung cancer [1]. Alcohol intake is an established risk factor in breast cancer etiology [2,3] and is one of the few established modifiable risk factors for this disease. Alcohol may affect breast cancer risk by increasing exposure to endogenous estrogens and androgens, enhancing susceptibility of breast tissue to carcinogens, or inhibition of DNA repair [2]. Although total alcohol consumption is a breast cancer risk factor, resveratrol, found in red wine, may have chemopreventive properties, so red wine consumption may actually reduce breast cancer risk [4]. Little is known about whether alcohol intake affects breast cancer survival. The few studies conducted have had conflicting results: no association [5–8], an inverse association [9], and a modest increase in breast cancer mortality with increasing daily alcohol consumption [10,11]. These studies differed in terms of the time period that was assessed, some examining alcohol intake at the time of enrollment in a prospective cohort study [12,7,5,10], before breast cancer diagnosis and others [11,6,8] closer to the time of breast cancer diagnosis. The window of relevant exposure is not known; lifetime alcohol exposure has not been examined in relation to breast cancer prognosis. It has been demonstrated that dietary exposures experienced in adolescence can affect breast cancer risk decades later [13–15]. Likewise, it is plausible that alcohol exposures experienced earlier in life, during breast maturation, may affect future risk of and mortality from breast cancer. Further, the manner by which alcohol is consumed may affect the physiologic effect. Measures of average consumption do not address differences in impact of drinking intensity. Drinkers who consume seven drinks in two days of a weekend every week may differ from those who drink one drink per day. There is evidence that drinking intensity, the number of drinks per drinking day, affects cardiovascular risk [16–18]. Lifetime alcohol intake and drinking intensity have not been examined in relation to breast cancer mortality. In this study, we examined both total alcohol intake and intensity (drinks per drinking day) over different periods of life in association with mortality in women diagnosed with breast cancer. We hypothesized that higher and more intense lifetime alcohol intakes would be inversely associated with survival among women with breast cancer.

Methods

Data on lifetime alcohol consumption were collected as part of the Western New York Exposures and Breast Cancer (WEB) Study, a population-based case-control study of women with breast cancer and healthy controls conducted from 1996–2001. The methods for the WEB Study have been described in detail elsewhere [19–21]. Briefly, women with primary, incident histologically confirmed invasive or non-invasive breast cancer (n=1116) were identified by nurse case-finders from records of pathology departments of all hospitals in the region. Diagnosis was confirmed with the woman's physician, the women were contacted, and informed consent was obtained. Eligible women were residents of Erie or Niagara Counties in New York State, between the ages of 35 and 79 at enrollment, able to speak English, with no history of prior cancer diagnosis other than non-melanoma skin cancer. The response rate among cases was 71%. Vital status as of December 31, 2006 was determined for these women from the National Death Index [20]. The WEB study was approved by the Institutional Review Boards of the University at Buffalo School of Medicine and Biomedical Sciences and of all participating hospitals.

Extensive in-person interviews and self-administered questionnaires were used to collect detailed information on medical history, reproductive history, and other risk factors for breast cancer among participants. Demographic factors, such as age, race, and education level; and lifestyle factors, such as smoking status (never, former, current) were self-reported. Diet was self-reported using a modified version of the Health Habits and History food frequency questionnaire [22]. Height and weight were measured when possible and were used to calculate body mass index (BMI). To evaluate lifetime alcohol consumption, the cognitive lifetime drinking history (CLDH) was administered by trained interviewers. The CLDH uses floating intervals to assess type, intensity, and volume of alcohol intake [23]; a participant defines intervals when her drinking habits changed (e.g., during college, after marriage, after the birth of a child). Her alcohol consumption is then probed for each of the identified consumption periods. The CLDH has been shown to have high test-retest reliability [23]. Abstainers were defined as those who did not have 12 or more drinks during any one year of their lives.

Information on cancer characteristics, including stage (tumor-node-metastasis stage) was collected from medical and pathology records of participants. Estrogen receptor (ER) status was determined by a single pathologist from Georgetown University using immunohistochemistry of tumor blocks as described by Allred et al [24]. ER status was determined by medical records where tumor blocks were not available or when hormone receptor status could not be determined. There was good agreement between our assessment and the medical record assessment of ER status ($\kappa=0.66$) [25]. ER status and stage were included as potential confounding variables in analyses. These analyses were limited to women with breast cancer with complete alcohol intake information (N=1097, 93.8% of 1170 total WEB participants with breast cancer). Information on treatment, recurrence, and comorbidities was unavailable.

Hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality and breast cancer mortality associated with alcohol intakes were calculated using Cox proportional hazards models. Alcohol consumption was assessed in several ways: a) drinking status (ever or never) for lifetime, and current or non-current drinkers for the 30 days, and 12 months prior to interview; b) volume of alcohol consumed compared to abstainers during the lifetime, in the period ten to 20 years prior to diagnosis, in the period two to ten years prior to diagnosis, and in the period between menarche and first birth (time of interview for nulliparous women); and c) number of drinks per drinking day (intensity) during the lifetime, in the period ten to 20 years prior to diagnosis, in the period two to ten years prior to diagnosis, and in the period between menarche and first birth (time of interview for nulliparous women). These various time periods were explored in order to deduce how exposures over different life periods may affect survival. Drinks per drinking day, or drinking intensity, refers to the number of drinks (12 ounces of beer, five ounces of wine, or 1.5 ounces of liquor) consumed during one drinking session. These latter analyses were additionally adjusted for total lifetime alcohol intake (oz). We assessed number of drinks per drinking day in the following categories: 0 (abstainer), 1 drink or less, 2–3 drinks, and 4 or more drinks. We categorized volume of alcohol consumed by menopausal status-specific medians of alcohol intake among ever drinkers (for lifetime 1242.9 oz. and 1197.6 oz., for menarche to first birth 510.4 oz. and 110.7 oz., for ten to 20 years prior to diagnosis 372.8 oz. and 196.3 oz., and for two to ten years prior to diagnosis 183.0 oz. and 118.8 oz. for premenopausal and postmenopausal women, respectively). Models were stratified by menopausal status and adjusted for stage of the tumor, age, education level, energy intake, body mass index, smoking status, and race.

Results

Among 307 premenopausal women with breast cancer who participated in the WEB study, in the period of follow-up, 43 (14%) died from any cause and of those 37 (12%) from breast cancer (Table 1) (mean follow-up time, 86 months, range 9 to 117 months). Among 790 postmenopausal women, 111 (14%) died from any cause and 55 (7%) from breast cancer as of December 31, 2006 (mean follow-up time, 87.8 months, range 11 to 125 months). Among premenopausal women, deceased women had a higher average BMI and energy intake and were less likely to be never smokers compared to living women. Among postmenopausal women, deceased women were on average older and less educated than living women. Among both premenopausal and postmenopausal women, deceased women were more likely to have a higher stage of cancer and ER negative tumors compared to living women.

Among premenopausal women, wine was the most common alcoholic beverage consumed (n=174, 56.68%), followed by liquor (n=163, 53.09%), beer (n=143, 46.58%), and wine coolers (n=38, 12.38%). Among postmenopausal women, liquor was the most common alcoholic beverage consumed (n=413, 52.28%), followed by wine (n=409, 51.77%), beer (n=281, 35.57%), and wine coolers (n=31, 3.92%). Preliminary analyses showed no differences in association between alcohol intake and mortality among the different types of beverages, so we have reported results for all beverages combined.

For both pre- and postmenopausal women, we observed no associations between all-cause or breast cancer mortality and drinking status in the past 30 days, past 12 months, or over the lifetime (results not shown). There were also no associations between absolute intake of alcohol and death from any cause or from breast cancer for either pre- or postmenopausal women (Table 2).

Intensity of alcohol consumption, drinks per drinking day, adjusted for lifetime intake, was associated with all-cause mortality for postmenopausal women with the highest intensity of drinks per drinking day (Table 3). Compared to abstainers, consumption of 4 or more drinks per drinking day over the lifetime was associated with increased hazards for all-cause mortality among these postmenopausal women diagnosed with breast cancer (HR 2.94, 95% CI 1.31, 6.62, p for trend = 0.01). There was some indication that consumption in the 10–20 years prior to interview was most strongly associated with mortality (HR 2.32, 95% CI 0.98–5.48, p for trend = 0.11). The increased hazards for women consuming 4 or more drinks per drinking day over the lifetime were primarily explained by increased hazards for breast cancer mortality (HR 2.68, 95% CI 0.94, 7.67, p for trend = 0.02). There was a decrease in the hazard ratio for all-cause mortality (HR 0.54, 95% CI 0.31–0.95, p for trend = 0.07) and breast cancer mortality (HR 0.27, 95% CI 0.09–0.77, p for trend = 0.07) among postmenopausal women who consumed 1 drink or less per drinking day between menarche and age at first birth compared to lifetime abstainers. For all other time periods, there were no associations between drinking intensity and all-cause or breast cancer mortality. Drinking intensity was not associated with mortality among premenopausal women.

Discussion

In this study, we examined the association of alcohol intake with all-cause and breast cancer-specific mortality among women who had been diagnosed with incident, primary breast cancer. While most studies have examined only average lifetime or current intake, we were able to examine alcohol intake over the lifetime and during biologically significant periods of time. In addition, we examined intensity (drinks per drinking day) of alcohol intake over these time periods. While total volume of alcohol consumed was not associated with mortality, there was evidence that drinking intensity was. Postmenopausal women who

averaged four or more drinks per drinking day over the lifetime were at risk for increased mortality; the HR for death from breast cancer was similar although the confidence interval included the null. Light drinking but not heavier drinking during the period from menarche to first birth was inversely associated with mortality from any cause and from breast cancer among postmenopausal women. No statistically significant associations were observed between any of the measures of alcohol consumption and mortality in premenopausal women. Some studies suggest that cumulative alcohol consumption over the life course is associated with risk of breast cancer [26,27]. It is plausible that cumulative alcohol consumption is an important factor in its association with mortality, and that premenopausal women are too young to have accumulated sufficient alcohol exposure to have a strong effect on mortality. It may also be possible that there are differences in the tumor biology among the younger women compared to older women and that alcohol does not impact those tumors. For instance, premenopausal women in this study were less likely to have ER-positive cancer compared to postmenopausal women. If alcohol differentially acts on ER-positive tumors, alcohol consumption would have less impact on premenopausal women's survival. In addition, younger women may be at lower risk for comorbidities and competing causes of death which may be exacerbated by alcohol, such as cardiovascular disease, compared to postmenopausal women

Our finding of an increased hazard of death among postmenopausal breast cancer survivors who drank 4 drinks/drinking day in the 10–20 years before diagnosis and over their lifetime compared to abstainers may be possibly explained, in part, by alcohol-related health problems associated with heavy drinking. Indeed, Thun, et al. [28] showed an increase in all-cause mortality among middle-aged and older adults who drink 4 drinks per day. Although we adjusted for total lifetime alcohol consumption, the heaviest drinkers may underreport consumption due to stigma associated with heavy drinking, so our drinking intensity-related estimates may be subject to residual confounding by lifetime alcohol consumption. However, whereas we observed a borderline significant increase in mortality associated with heavy drinking in the 10–20 years prior to diagnosis, there were no associations with more recent heavy drinking, or with total ounces of alcohol consumed over the lifetime.

We observed evidence that light alcohol consumption during the period between menarche and first birth may be associated with decreased breast cancer mortality among postmenopausal women, even after adjustment for total lifetime alcohol intake. There is evidence that this time period is critical in breast development [13]. Thanos, et al. found dietary phytoestrogen intake during adolescence to be inversely associated with adult development of breast cancer [15]. Factors such as diet and, alcohol consumption, during adolescence and young adulthood may influence later breast cancer characteristics and subsequent mortality [15,14]. Because of the importance of young adulthood in healthy breast development, this time may be a critical window for exposure to alcohol in relation to breast cancer. Reding, et al. observed a reduced hazard of death among premenopausal women who were drinkers in the five years prior to breast cancer diagnosis [9]. This supports our hypothesis that some drinking during young adulthood may be protective against mortality in women with breast cancer. We observed a similar, although not statistically significant, association with lifetime alcohol consumption, but observed a J-shaped relationship between intensity of drinking and mortality among premenopausal women for the interval of two to ten years prior to diagnosis. It has been suggested that women who choose not to drink have deficiencies in metabolizing alcohol and other toxins, such as those in chemotherapy, and may therefore have worse clinical outcomes compared to those who are able to metabolize these toxins [9]. In addition, alcohol and folate may interact in breast cancer mortality [9]. However, we were unable to account for lifetime folate status, as the FFQ queried diet in the 1–2 years prior to diagnosis. There may be a

curvilinear relationship between alcohol intake and total mortality, as indicated by Thun, et al. in a study of alcohol intake and total mortality [28].

Consideration of the strengths and limitations of this study are important in interpretation of these findings. One strength of this study was that we used a very detailed and reliable method of assessing lifetime alcohol intake, including separate assessment of quantity and frequency of intake which allowed us to analyze different facets of lifetime alcohol intake. Nonetheless, there is likely error in recall of lifetime intake, which could lead to misclassification of alcohol exposures. We have no reason to believe that error in recall would be associated with vital status, so any misclassification would be likely to attenuate our observed measures of association. Although our study has detailed information on lifetime alcohol consumption, women in the study consumed a generally low volume of alcohol over the lifetime (median number of drinks per drinking day was 1.75). Given our finding that women in the highest category of drinks per drinking day are at increased mortality hazard, if this study were repeated in a population in which women drank more often and more heavily, we may have seen more robust associations between alcohol intake and death. Finally, our follow-up time was a relatively brief 5–10 years. Unfortunately, mortality data are not available after 2006. We observed few mortal events, particularly among premenopausal women, which may have resulted in unstable HR estimates. More events may have been observed, given longer follow-up, which could strengthen our findings. In addition, information on important predictors of mortality, such as comorbidities, physical activity and other health behaviors, and treatment, were unavailable. These factors may be confound the relationships between alcohol intake and mortality, so our estimates may be biased. We did not have data on recurrence in this study, but alcohol intake has previously been shown to be positively associated with breast cancer recurrence [29,11].

In conclusion, our findings provide evidence that compared to abstainers, lifetime intensity of alcohol intake among postmenopausal women with breast cancer is positively associated with all-cause mortality, and with a trend toward increased breast cancer mortality and suggests a possible inverse association of mortality with light intensity between menarche and first birth. These results add to public health literature that indicates that light drinking during early adulthood may be beneficial, but heavy drinking may be related to increased risk of mortality among women with breast cancer. In addition, lifetime alcohol intake, not just current intake, is associated with mortality. Further studies on this topic are warranted in order to further substantiate these relationships. Specifically, studies with larger sample sizes, more information on co-morbidities, and recurrence, longer follow-up, and a broader range of alcohol intake would help to clarify these observed relationships.

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Descriptive characteristics of women with breast cancer participating in the Western New York Exposures and Breast Cancer (WEB) Study

Table 1

	Premenopausal (N=307)		p ^a	Postmenopausal (N=790)		p ^a
	Living (N=264) N(%)	Deceased (N=43) N(%)		Living (N=679) N(%)	Deceased (N=111) N(%)	
White race	244 (92.4)	39 (90.7)	0.70	633 (93.2)	99 (88.2)	0.13
Education level ^b :						
High school or less	82 (31.1)	19 (44.2)	0.38	332 (48.9)	72 (64.9)	0.004
Some college	98 (37.1)	13 (30.2)		164 (24.2)	25 (22.5)	
College graduate	45 (17.1)	5 (11.6)		77 (11.3)	8 (7.2)	
Post-graduate	39 (14.8)	6 (14.0)		106 (15.6)	6 (5.4)	
Smoking status:						
Never	129 (48.9)	14 (31.8)	0.08	307 (45.3)	50 (45.1)	0.77
Former	96 (36.4)	18 (40.9)		295 (43.5)	46 (41.4)	
Current	39 (14.8)	12 (27.3)		76 (11.2)	15 (13.5)	
Stage:						
2	131 (49.6)	6 (14.0)	<0.0001	409 (60.2)	44 (39.6)	0.0002
>2	100 (37.9)	35 (81.4)		179 (26.4)	43 (38.7)	
Unknown	33 (12.5)	2 (4.7)		91 (13.4)	24 (21.6)	
ER status:						
Negative	84 (31.8)	26 (60.5)	0.001	149 (21.9)	40 (36.0)	0.005
Positive	162 (61.4)	15 (34.9)		462 (68.0)	61 (55.0)	
Unknown	18 (6.8)	2 (4.7)		68 (10.0)	10 (9.0)	
Family history of breast cancer:						
No	191 (72.4)	28 (65.1)	0.60	510 (75.1)	80 (72.1)	0.38
Yes	51 (19.3)	10 (23.3)		131 (19.3)	21 (18.9)	
Unknown	22 (8.3)	5 (11.6)		38 (5.6)	10 (9.0)	
Number of drinks per drinking day:						
0 (Abstainers)	29 (11.0)	7 (16.3)	0.54	124 (18.3)	25 (22.5)	0.03
1	88 (33.3)	13 (30.2)		308 (45.4)	41 (36.9)	
2-3	100 (37.9)	13 (30.2)		199 (29.3)	29 (26.1)	

4	Premenopausal (N=307)				Postmenopausal (N=790)			
	Living (N=264)		Deceased (N=43)		Living (N=679)		Deceased (N=111)	
	N(%)	Median	N(%)	Median	N(%)	Median	N(%)	p ^a
	47 (17.8)		10 (23.3)		48 (7.1)		16 (14.4)	
Age (years)	45	44			62	68		0.0001
BMI (kg/m ²)	25.40	26.82			27.79	28.37		0.40
Daily dietary calories	1437	1742			1424	1368		0.45
Lifetime total oz alcohol	901.33	1085.41			682.10	893.28		0.47
Average drinks per drinking day (lifetime)	2.14	2.16			1.63	1.64		0.71

^aP-values for chi-square tests for categorical variables and Wilcoxon rank sum tests for continuous variable

^bCategories of education computed from years of education: High school or less 12 years, some college 13–15 years, college graduate 16 years, post-graduate >16 years.

Table 2

Death from any cause and death from breast cancer in association with total alcohol intake category for the total lifetime and for different time periods.^{a,b}

Premenopausal (N=307)				Postmenopausal (N=790)				Premenopausal (N=307)				Postmenopausal			
n deceased	n alive	HR	95% CI	n deceased	n alive	HR	95% CI	n died from breast cancer	n did not die from breast cancer	HR	95% CI	n died from breast cancer	n did not die from breast cancer	HR	95% CI
Death from any cause															
Total lifetime alcohol intake															
None	7	29	Ref	25	124	Ref	Ref	7	29	Ref	Ref	14	135	Ref	Ref
Low	17	119	1.00 (0.36, 2.73)	36	285	0.84 (0.49, 1.41)	0.84 (0.49, 1.41)	13	123	0.71 (0.25, 2.06)	0.71 (0.25, 2.06)	19	302	0.65 (0.32, 1.34)	0.65 (0.32, 1.34)
High	19	116	0.74 (0.26, 2.10)	50	270	1.19 (0.70, 2.01)	1.19 (0.70, 2.01)	17	118	0.65 (0.22, 1.92)	0.65 (0.22, 1.92)	22	298	0.88 (0.42, 1.84)	0.88 (0.42, 1.84)
Total alcohol intake, menarche to age at first birth (time of interview for nulliparous women)^c															
None	7	29	Ref	25	124	Ref	Ref	7	29	Ref	Ref	14	135	Ref	Ref
Low	15	121	0.83 (0.30, 2.31)	55	266	1.15 (0.70, 1.90)	1.15 (0.70, 1.90)	13	123	0.67 (0.23, 1.92)	0.67 (0.23, 1.92)	27	294	0.92 (0.47, 1.82)	0.92 (0.47, 1.82)
High	21	114	0.92 (0.32, 2.63)	31	289	0.76 (0.44, 1.33)	0.76 (0.44, 1.33)	17	118	0.70 (0.24, 2.10)	0.70 (0.24, 2.10)	14	306	0.50 (0.22, 1.12)	0.50 (0.22, 1.12)
Total alcohol intake, ten to 20 years prior to diagnosis															
None	7	29	Ref	25	124	Ref	Ref	7	29	Ref	Ref	14	135	Ref	Ref
Low	15	120	0.92 (0.33, 2.56)	38	287	0.86 (0.51, 1.44)	0.86 (0.51, 1.44)	12	123	0.68 (0.23, 1.99)	0.68 (0.23, 1.99)	19	306	0.65 (0.32, 1.32)	0.65 (0.32, 1.32)
High	22	115	0.82 (0.29, 2.31)	48	268	1.17 (0.69, 1.99)	1.17 (0.69, 1.99)	18	118	0.68 (0.23, 2.02)	0.68 (0.23, 2.02)	22	294	0.89 (0.42, 1.87)	0.89 (0.42, 1.87)
Total alcohol intake, two to ten years prior to diagnosis															
None	7	29	Ref	25	124	Ref	Ref	7	29	Ref	Ref	14	135	Ref	Ref
Low	16	121	0.80 (0.29, 2.22)	44	277	0.98 (0.59, 1.63)	0.98 (0.59, 1.63)	12	125	0.57 (0.19, 1.67)	0.57 (0.19, 1.67)	22	299	0.77 (0.39, 1.56)	0.77 (0.39, 1.56)
High	20	114	0.99 (0.34, 2.84)	42	278	0.99 (0.58, 1.69)	0.99 (0.58, 1.69)	18	116	0.87 (0.29, 2.62)	0.87 (0.29, 2.62)	19	301	0.69 (0.32, 1.48)	0.69 (0.32, 1.48)

^a Hazard ratios and 95% confidence intervals adjusted for smoking status, stage, age, education level, calories, bmi, and race.

^b Low and high alcohol intake defined by menopause-specific cutpoints: for lifetime 1242.9 oz. and 1197.6 oz. for menarche to first birth 510.4 oz. and 110.7 oz., for ten to 20 years prior to diagnosis 372.8 oz. and 196.3 oz., for two to ten years prior to diagnosis 183.0 oz. and 118.8 oz. for premenopausal and postmenopausal women, respectively.

Table 3

Hazard ratios and 95% confidence intervals for death from any cause and death from breast cancer by average number of drinks per drinking day (intensity) for different time periods and for category of lifetime total alcohol intake^a

Premenopausal (N=307)			Postmenopausal (N=790)			Premenopausal (N=307)			Postmenopausal		
n deceased	n alive	HR 95% CI	n deceased	n alive	HR 95% CI	n died from breast cancer	n did not die from breast cancer	HR 95% CI	n died from breast cancer	n did not die from breast cancer	HR 95% CI
Death from any cause											
Drinks per drinking day, lifetime											
0	7	29	Ref	25	124	Ref	7	29	Ref	14	135
1 or less	13	88	1.10 (0.39, 3.16)	41	308	0.89 (0.53, 1.51)	13	88	0.98 (0.33, 2.87)	18	331
2-3	13	100	0.54 (0.18, 1.63)	29	199	1.07 (0.60, 1.91)	10	103	0.32 (0.10, 1.02)	13	215
4 or more	10	47	0.65 (0.18, 2.37)	16	48	2.94 (1.31, 6.62)	17	50	0.27 (0.06, 1.17)	10	54
p for trend			0.42			0.01			0.06		0.02
Drinks per drinking day, menarche to age at first birth (time of interview for nulliparous women)											
0	9	67	Ref	63	258	Ref	9	67	Ref	33	288
1 or less	7	48	1.62 (0.54, 4.79)	16	156	0.54 (0.31, 0.95)	7	48	1.67 (0.60, 4.97)	4	168
2-3	16	104	1.31 (0.53, 3.21)	24	212	0.60 (0.37, 0.98)	13	107	1.00 (0.39, 2.54)	14	222
4 or more	11	45	1.34 (0.46, 3.90)	8	51	0.84 (0.38, 1.83)	8	48	0.79 (0.25, 2.54)	4	55
p for trend			0.09			0.07			0.65		0.06
Drinks per drinking day, ten to 20 years prior to diagnosis											
0	11	70	Ref	41	261	Ref	10	71	Ref	22	280
1 or less	11	63	1.52 (0.59, 3.91)	28	219	1.00 (0.60, 1.67)	10	64	1.47 (0.54, 4.01)	10	237
2-3	13	96	0.83 (0.32, 2.15)	33	170	1.59 (0.96, 2.63)	11	98	0.71 (0.25, 1.97)	18	185
4 or more	8	35	0.66 (0.20, 2.16)	9	29	2.32 (0.98, 5.48)	6	37	0.44 (0.12, 1.65)	5	33
p for trend			0.45			0.11			0.25		0.22
Drinks per drinking day, two to ten years prior to diagnosis											
0	18	90	Ref	48	287	Ref	14	94	Ref	24	311
1 or less	8	75	0.68 (0.26, 1.77)	34	228	1.06 (0.66, 1.70)	8	75	0.91 (0.33, 2.48)	14	248
2-3	10	87	0.60 (0.24, 1.48)	24	146	1.28 (0.75, 2.17)	9	88	0.69 (0.26, 1.89)	14	156
4 or more	7	12	2.36 (0.69, 8.04)	5	18	1.62 (0.57, 4.60)	6	13	2.59 (0.67, 9.94)	3	20

	Premenopausal (N=307)		Postmenopausal (N=790)		Premenopausal (N=307)		Postmenopausal
n deceased	n alive	HR 95% CI	n deceased	n alive	n died from breast cancer	n did not die from breast cancer	n did not die from breast cancer
					HR 95% CI	HR 95% CI	HR 95% CI
p for trend		0.10			0.72	0.21	0.71

^aAdjusted for smoking status, stage, age, education level, calories, BMI, race, and total lifetime oz. alcohol.