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Breast Cancer Risk and Alcohol Consumption: Results from a Large Case-Control Study

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Bowlin S J (Department of Epidemiology and Biostatistics, School of Medicine, Case Western Reserve University, 10900 Euclid Ave, Cleveland, OH 44106–4945, USA), Leske M C, Varma A, Nasca P, Weinstein A and Caplan L. Breast cancer risk and alcohol consumption: Results from a large case-control study. *International Journal of Epidemiology* 1997; **26:** 915–923.

Background. Alcohol use is associated with breast cancer in many epidemiological studies. Most, however, have measured risk from recent consumption patterns, and only a few include analyses for duration of drinking or age that a woman started to drink. The authors studied the effect of these variables, as well as of recent alcohol consumption patterns, on breast cancer risk.

Methods. Data from a large case-control study conducted in Long Island, New York from 1 January 1984 to 31 December 1986 were used. A total of 1214 women aged 20–79 years with incident breast cancer were interviewed. A control was selected for each case from driver's license files, and matched on age and county of residence. Alcohol consumption was measured as: ever versus never, grams of alcohol per day, age started drinking, and total years drinking.

Results. After adjustment for breast cancer risk factors, the odds ratio for ever versus never drinking was 1.40 (95% confidence interval [CI] 1.09–1.79); odds ratios for $>$0–5 and $\geqslant$5 grams of alcohol use per day, as compared to non-drinkers, were 1.29 (95% CI : 1.00–1.65) and 1.46 (95% CI : 1.13–1.89), respectively. Age when drinking began was not related to breast cancer risk, but the greater the total years of drinking, up to 40 years (odds ratio 1.48, 95% CI : 1.13–1.93), the greater the risk. However, when grams per day and duration of drinking were simultaneously included in the multivariate model, duration was not important as a risk factor. This suggests that intensity of drinking may be the important factor for breast cancer risk. After covariate adjustment, risk from alcohol intake did not differ between pre- and postmenopausal women.

Conclusions. These data support the belief that alcohol is associated with breast cancer risk.

Keywords: alcohol, breast cancer, case-control study

Intense epidemiological research has been directed at understanding the relationship between breast cancer and alcohol consumption.[1] Many reports have found an association but others have not.[1] Most well-defined risk factors such as age, family history of breast cancer, early menarche, late menopause, late age at first full-term birth and benign breast disease are difficult or impossible to alter. On the other hand, alcohol use can be modified and is common among American women.[2] If its association with breast cancer were causal, alcohol use would provide a risk factor to target for primary prevention of breast cancer.

Most epidemiological studies of alcohol and breast cancer have relied on risk assessment from recent consumption patterns.[1] The effect of duration of alcohol consumption, or age when starting to drink have been less studied. These latter variables may add more important information than recent drinking habits in defining risk and establishing causality. This study investigates the association between alcohol use and breast cancer risk in a large case-control study conducted in Long Island, New York. Risk was assessed for recent alcohol use, duration of drinking and age when starting to drink.

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MATERIAL AND METHODS

Case Selection

This case-control study included women residing in Nassau and Suffolk counties in Long Island, New York. The study methodology is described elsewhere.[3] Cases were defined as all females with incident breast cancer, histologically confirmed, in both counties from 1 January 1984 to 31 December 1986. Women between 20 and 79 years old were eligible. Cases were identified by surveillance of all Long Island hospitals' tumour registers and medical records. The New York State Cancer Registry was used to locate county residents with breast cancers diagnosed elsewhere in New York State.

A total of 2140 eligible breast cancer cases were identified during that time; 90% were found through Long Island hospitals; 1616 cases were contacted, of whom 1420 participated, which represented 88% of the contacted women or 67% of the total identified cases. In all 524 cases could not be contacted because of doctor refusal (45%), unable to locate (23%), deceased (14%), and other (18%). Women who were interviewed were younger than those who refused (57.5 years versus 61.1 years, $P < 0.001$); participation rates among those contacted were similar between Nassau and Suffolk County; also, participating cases tended to be of higher socioeconomic status (SES) (measured by New York State Gazetteer coding system) than refusals.[4]

Control Selection

A control was matched to each case by age (±1 year) and by county of residence. The driver's license files of the New York State Department of Motor Vehicles were used to construct a list of potential controls. After a case was interviewed, we attempted to contact and recruit a control from a list of age and county-matched women, in sequence, until a participant was found.

There were 3487 potential controls identified; 2097 potential controls were contacted, and 1420 were matched with cases for a participation rate of 68% among those contacted or 41% among the total identified. It was not possible to contact 1390 women because of inability to locate (88%), deceased (6%), and other (6%). Controls who were interviewed were younger than those who refused (57.4 years versus 63.5 years, $P < 0.001$); participation rates among those contacted were similar between Nassau and Suffolk County. No statistical association was found between participation and SES.[4]

While the 1420 control women had a driver's license, 206 cases did not. Comparison between cases with and without a license revealed significant differences between the groups. Those with a license were younger and had higher incomes; they also reported more alcohol use, benign breast disease, and Jewish religion.[4] These differing characteristics may have distorted the association between alcohol intake and breast cancer in this study. Therefore, only case-control pairs who each possessed a driver's license were included, leaving 1214 pairs in the analysis.

TABLE 1 *Alcohol questions used in the telephone interview, Long Island Breast Cancer Study, 1 January 1984 to 31 December 1986*

1. Prior to (date of diagnosis) did you ever drink alcoholic beverages?
2. Age started drinking alcoholic beverages?
3. Age stopped drinking alcoholic beverages?
   (if still drinking alcohol—code age at diagnosis)
4. Did you usually drink beer, wine or liquor?
5. Approximately how often do you drink alcoholic beverages?
   a) 5–7 days a week
   b) 1–4 days a week
   c) 1–3 days a month
   d) <1/month
   e) never
   f) unknown
6. How many drinks do you usually have at a time?
   a) 1–2 drinks
   b) 3–4 drinks
   c) >4 drinks
   d) unknown

Data Collection

Data were collected with a standardized questionnaire using a telephone interview. Variables included demographics, a lifetime residential history (with emphasis on environmental exposures), medical care, including breast cancer screening practices, reproductive history, hormone use, family history of breast cancer, and lifestyle factors. Questions on alcohol exposure included whether the respondent had ever used alcohol, age started and stopped, type drank, frequency, and number of drinks consumed at a time. Table 1 shows the alcohol questions asked during the interview. For the goals of this report, risk of breast cancer from alcohol was explored comparing ever versus never users, and comparing categories of current alcohol intake, measured in grams per day (g/day). We defined one drink as a shot (measure) of liquor (spirits), 12 ounces of beer, or 5–6 ounces of wine, with one drink approximately equal to 12.5 grams of ethanol. Grams of alcohol per day were calculated as frequency of drinking (based on days) × number of drinks consumed per drinking occasion × 12.5 grams of alcohol in one drink. In these analyses, g/day of alcohol were categorized into 0 g/day, >0–5 g/day, and ⩾5 g/day. Five g/day was, therefore, <½ of

TABLE 2 *Unmatched number of cases and controls in each alcohol category by menopausal status, Long Island Breast Cancer Study, 1 January 1984 to 31 December1986*

Variable	Menopausal status					
	Pre[a]		Post[a]		Combined	
	Case	Control	Case	Control	Case	Control
Ever use alcohol:						
Ever	248	232	676	642	1063	1008
Never	33	49	98	134	148	206
G/day:						
0	35	50	101	137	154	211
>0–5	134	131	343	348	549	550
⩾5	112	100	331	291	510	453
Age started drinking:[b]						
⩽17	22	21	173	156	217	188
18–24	178	145	401	381	667	610
25+	48	66	103	105	181	210
Number years used alcohol:						
0	33	49	98	134	148	207
>0–<20	77	78	26	30	120	116
20–>40	170	152	284	260	571	528
40+	1	2	367	352	374	363
Type of drink:						
None	33	49	98	134	148	206
Beer	6	8	23	17	29	31
Wine	117	108	192	205	363	367
Liquor	27	40	198	185	251	251
Combination	98	75	264	235	422	358

[a] Sample sizes based on case-control pairs concordant on menopausal status.
[b] Among drinkers only.

a drink per day. Risk of breast cancer was also evaluated by type of alcohol drank: beer, wine, liquor or a combination. Women were asked about alcohol intake prior to the date of diagnosis of the case.

Women were asked at what age they first began to drink and at what age they stopped. Odds ratios (OR) were calculated to determine whether breast cancer was associated with the age the women began drinking and with the duration of alcohol use. Table 2 shows the unmatched number of cases and controls for each alcohol category, by menopausal status.

Statistical Analysis

The conditional logistic regression model for matched case-control studies used in PROC PHREG in the Statistical Analysis System (SAS) program was used for both univariate and multivariate analyses.[5] Univariate analysis was done by including only one independent variable of interest in the model. Multivariate analysis was used to study the association between various measures of alcohol and breast cancer risk, controlling for potential confounders included in the model. Unless otherwise indicated, never drinkers were the reference group for risk calculations.

Variables studied as potential confounders included: religion (Jewish versus other), years of education (⩽12, 13–16, 17+ years), income (median annual family income from the census tracts of the women divided into quartiles from lowest to highest—while family income was not studied directly, Krieger[6] has shown that social class variables measured at the census tract are good proxies for individual-level measurements), marital status (married, single, widowed/separated/divorced), history of benign breast disease (yes versus no), age at menarche (7–11, 12–13, 14+ years), ever pregnant (yes versus no), age at first live birth (never pregnant, <25, 25–29, 30+ years), total weeks of breastfeeding her children (0, >0–24, 25–49, 50+ weeks), family history of breast cancer in first-degree relative (yes versus no), ever smoke cigarettes (yes versus no), pack-years of cigarette smoking (0, >0–14, 15–29, 30+), and Quetelet's Index (0–20, 21–29,

TABLE 3 *Odds ratios and 95% confidence intervals for risk factors and breast cancer, univariate analyses,[a] Long Island Breast Cancer Study, 1 January 1984 to 31 December 1986*

Risk factor	OR[b]	95% CI[b]
Religion:		
Others	1.00	
Jewish	1.05	(0.85–1.28)
Education in years:		
⩽12	1.00	
13–16	1.00	(0.83–1.20)
17+	0.89	(0.72–1.10)
Trend	$P < 0.32$	
Income-quartiles, lowest to highest		
1st	1.00	
2nd	0.89	(0.71–1.12)
3rd	1.02	(0.79–1.31)
4th	1.11	(0.86–1.44)
Trend	$P < 0.19$	
Marital status:		
Married	1.00	
Single	1.46	(0.95–2.24)
Widowed/divorced/separated	1.33	(1.09–1.63)[c]
Family history of breast cancer:		
No	1.00	
Yes	1.70	(1.34–2.17)[c]
History of benign breast disease:		
No	1.00	
Yes	1.47	(1.24–1.74)[c]
Age of menarche:		
7–11	1.00	
12–13	1.01	(0.82–1.26)
14+	1.06	(0.83–1.35)
Trend	$P < 0.62$	
Ever pregnant		
No	1.00	
Yes	0.76	(0.58–0.99)[c]
Age first live birth		
Never pregnant	1.00	
<25	0.72	(0.54–0.96)[c]
25–29	0.77	(0.57–1.04)
30+	0.89	(0.64–1.24)
Trend	$P < 0.81$	
Total weeks spent breast feeding:		
0	1.00	
>0–24	0.85	(0.70–1.04)
25–49	0.59	(0.41–0.87)[c]
50+	0.52	(0.36–0.74)[c]
Trend	$P < 0.0001$	
Menopausal status:		
Pre	1.00	
Post	0.83	(0.60–1.13)
Ever smoke		
No	1.00	
Yes	1.17	(1.00–1.37)
Pack-years of smoking:		
0	1.00	
>0–14	1.31	(1.06–1.61)[c]
15–29	1.11	(0.87–1.43)
30+	1.08	(0.87–1.34)
Trend	$P < 0.41$	
Quetelet's Index		
0–20	1.00	
21–29	0.98	(0.77–1.23)
30+	1.10	(0.82–1.48)
Trend	$P < 0.52$	

[a] The minimum number of pairs used in these analyses due to missing data was 1209 for family history of breast cancer.
[b] OR, odds ratio; CI, confidence interval.
[c] Statistically significant odds ratios.

30+ kg/m^2). Ordinal variables were tested individually for trend in risk across categories in the univariate analyses. Models were run for all women together and separately for pre- and postmenopausal women. Analyses showed an interaction between alcohol and county of residence. Therefore, multivariate analyses were done separately for Nassau and Suffolk Counties. OR and 95% CI are presented for both univariate and multivariate results. Missing data were assigned the median for continuous data and the mode for categorical data; <1.5% of the data were missing for any variable included in the analysis.

RESULTS

Table 3 shows OR and 95% CI from matched univariate analyses for potential breast cancer risk factors other than alcohol variables. Religion, years of education, household income, age of menarche, menopausal status, and Quetelet's Index had no relationship with breast cancer. Single women and those who were widowed/separated/divorced had higher risk than married women, but only the latter association was statistically significant. Those with a positive family history of breast cancer (OR = 1.70, 95% CI : 1.34–2.17) and of benign breast disease (OR = 1.47, 95% CI : 1.24–1.74) had a higher risk of breast cancer than those who did not give such a history. Ever pregnant (OR = 0.76, 95% CI : 0.58–0.99) and having a first live birth before 25 years of age (OR = 0.72, 95% CI : 0.54–0.96) were associated with lower risk of breast cancer than never being pregnant. As weeks of breastfeeding increased there was a statistically significant decreasing trend in breast cancer risk. Ever smoking cigarettes had a statistically marginal increased risk for disease, with a small OR of 1.17 (95% CI : 1.00–1.37).

TABLE 4 *Odds ratios and 95% confidence intervals for alcohol variables and breast cancer by menopausal status, univariate analyses, Long Island Breast Cancer Study, 1 January 1984 to 31 December 1986*

	Menopausal status					
	Pre		Post		Combined	
	OR[a]	95% CI[a]	OR	95% CI	OR	95% CI
Ever versus never	1.65	(1.02–2.69)[e]	1.43	(1.08–1.90)[e]	1.47	(1.17–1.84)[e]
Use of alcohol	(281)[b]		(774)		(1211)	
G/day						
0	1.00		1.00		1.00	
>0–5	1.52	(0.91–2.52)	1.31	(0.98–1.74)	1.36	(1.07–1.73)[e]
⩾5	1.63	(0.98–2.70)	1.50	(1.11–2.01)[e]	1.52	(1.19–1.93)[e]
	(281)		(774)		(1214)	
Trend	$P < 0.11$		$P < 0.01$		$P < 0.002$	
Age started drinking[c]						
⩽17	0.65	(0.30–1.41)	0.99	(0.69–1.44)	0.79	(0.58–1.08)
18–24	1.17	(0.60–2.29)	1.03	(0.78–1.36)	1.01	(0.79–1.29)
25+	1.00		1.00		1.00	
	(205)		(558)		(883)	
Trend	$P < 0.08$		$P < 0.97$		$P < 0.15$	
Number years used alcohol						
0	1.00		1.00		1.00	
>0–<20	1.43	(0.79–2.59)	1.16	(0.64–2.11)	1.45	(1.00–2.12)
20–<40	1.80	(1.06–3.05)[e]	1.47	(1.07–2.03)[e]	1.53	(1.19–1.98)[e]
40+	[d]		1.39	(1.03–1.89)[e]	1.41	(1.07–1.86)[e]
	(281)		(776)		(1214)	
Trend	$P < 0.03$		$P < 0.02$		$P < 0.004$	
Type of drink						
None	1.00		1.00		1.00	
Beer	1.17	(0.34–4.05)	1.81	(0.92–3.56)	1.31	(0.75–2.28)
Wine	1.62	(0.97–2.71)	1.26	(0.91–1.74)	1.36	(1.05–1.76)[e]
Liquor	0.98	(0.49–1.96)	1.46	(1.05–2.04)[e]	1.39	(1.05–1.85)[e]
Combination	1.92	(1.12–3.29)[e]	1.50	(1.10–2.03)[e]	1.61	(1.25–2.07)[e]
	(281)		(776)		(1214)	

[a] OR, odds ratio; CI, confidence interval
[b] # of case-control pairs; only pairs concordant on menopausal status were used in the pre- and postmenopausal analyses.
[c] Among drinkers only.
[d] Three pairs in this group were included in the 20–<40 years category.
[e] Statistically significant odds ratios.

Table 4 shows the univariate analyses, stratified by menopausal status, of breast cancer risk from alcohol. Ever drinkers had a statistically significant increased risk of breast cancer compared to the never drinkers in all the menopausal status groups (OR = 1.47, 95% CI : 1.17–1.84 for the combined group). Risks were increased both in premenopausal (OR = 1.65, 95% CI : 1.02–2.69) and in postmenopausal (OR = 1.43, 95% CI : 1.08–1.90) women. Risk also increased with increasing g/day of alcohol consumed. In the combined group, the OR was 1.36 (95% CI : 1.07–1.73) for women drinking <5 g/day, and was 1.52 (95% CI : 1.19–1.93) for those drinking ⩾5 g/day. Risk was higher in premenopausal women, but the OR and tests of trend were not statistically significant in this group, probably because of small numbers of case-control pairs.

Other variables examined were the total number of years of alcohol consumed, type of drink, and among women who ever drank, age when alcohol was first used. Table 4 shows that age at which women started drinking was not associated with breast cancer. Risk of disease increased with increasing number of years of alcohol consumption, and the test for trend was statistically significant in all menopausal groups. As before, premenopausal women had higher risk than postmenopausal women with those having 20 to <40 years of drinking showing the greatest OR (1.80, 95% CI : 1.06–3.05). No consistent pattern was evident

TABLE 5 *Odds ratios and 95% confidence intervals for alcohol variables and breast cancer by menopausal status, multivariate analyses,*[a] *Long Island Breast Cancer Study, 1 January 1984 to 31 December 1986*

	Menopausal status					
	Pre		Post		Combined	
	OR[b]	95% CI[b]	OR	95% CI	OR	95% CI
Ever versus never	1.45	(0.84–2.50)	1.43	(1.06–1.94)[c]	1.40	(1.09–1.79)[c]
G/day						
0	1.00		1.00		1.00	
>0–5	1.26	(0.71–2.22)	1.32	(0.97–1.80)	1.29	(1.00–1.65)
⩾5	1.54	(0.87–2.74)	1.51	(1.09–2.08)[c]	1.46	(1.13–1.89)[c]
Number years used alcohol:						
0	1.00		1.00		1.00	
>0–<20	1.32	(0.67–2.60)	1.04	(0.56–1.94)	1.33	(0.89–1.98)
20–<40	1.69	(0.94–3.03)	1.57	(1.12–2.21)[c]	1.48	(1.13–1.93)[c]
40+	[d]		1.37	(0.99–1.90)	1.32	(0.98–1.77)
Type of drink:						
None	1.00		1.00		1.00	
Beer	1.02	(0.24–4.33)	1.92	(0.95–3.89)	1.28	(0.72–2.29)
Wine	1.46	(0.82–2.61)	1.32	(0.94–1.85)	1.32	(1.00–1.72)
Liquor	0.72	(0.33–1.58)	1.44	(1.01–2.07)[c]	1.30	(0.96–1.75)
Combo	1.79	(0.97–3.27)	1.52	(1.09–2.12)[c]	1.56	(1.19–2.04)[c]

[a] A separate conditional logistic regression model was developed for each menopausal group and alcohol variable. All models included, in addition to the alcohol variable, the following covariates: religion, income status, marital status, family history of breast cancer, history of benign breast disease, age of menarche, ever pregnant, age first live birth, total weeks spent breastfeeding, and ever smoked.
[b] OR, odds ratio; CI, confidence interval.
[c] Statistically significant odds ratios.
[d] Three pairs in this group were included in the 20–<40 years category.

showing which type of alcoholic beverage increased risk. All types had elevated OR, with the combination of beverages generally showing the highest risk.

Table 5 shows the multivariate analysis results for ever drinking, g/day, total years of alcohol consumption, and type of drink. Separate models were developed for each alcohol factor and for pre- and postmenopausal women. Included as covariates for each model were religion, income status, marital status, family history of breast cancer, history of benign breast disease, age of menarche, ever pregnant, age at first live birth, total weeks breastfeeding, and ever smoked. In the combined and postmenopausal groups, little change in risk from alcohol consumption was seen after controlling for potential confounding; risk was elevated by 40% in ever drinkers, 50% in those drinking ⩾5 g/day. Most OR retained their statistical significance, and dose-response relationships were seen in g/day. In premenopausal women, most OR were reduced after controlling for confounding and became similar in magnitude to those of postmenopausal women. No OR were statistically significant in premenopausal women, possibly due to the smaller sample size. After covariate adjustment, the risk of breast cancer from alcohol intake is not altered by menopausal status. Multivariate analysis for duration of drinking and type of drink and breast cancer risk was similar as in unvariate analysis.

To study how intensity (i.e. g/day) and duration (i.e. total years of consumption) of alcohol exposure may interrelate, we simultaneously included both of these factors as ordinal variables in a multivariate model for the combined group of women. Duration of drinking was no longer significantly related to breast cancer risk ($P = 0.54$). Grams per day was of borderline statistical significance ($P = 0.08$) with OR of 1.15 and 1.33 for >0 to <5 and ⩾5 g/day, respectively. Grams per day and total years of drinking, however, were moderately to strongly correlated (r = 0.60), which may explain why both factors lost statistical significance when placed in the model together. The data suggest that intensity of drinking, and not duration, may be the important risk factor for breast cancer.

The association between alcohol and breast cancer risk appeared stronger in Suffolk County than in Nassau

TABLE 6 *Odds ratios and 95% confidence intervals for alcohol variables and breast cancer by county of residence, multivariate analyses,[a] Long Island Breast Cancer Study, 1 January 1984 to 31 December 1986*

	OR[b]	95% CI[b]
Nassau[c]		
Ever versus never	1.16	(0.81–1.65)
G/day:		
0	1.00	
>0–5	1.17	(0.81–1.69)
⩾5	1.19	(0.82–1.73)
Number years used alcohol:		
0	1.00	
>0–<20	0.99	(0.55–1.79)
20–<40	1.25	(0.85–1.84)
40+	1.10	(0.72–1.67)
Suffolk[c]		
Ever versus never	1.66	(1.16–2.38)[d]
G/day:		
0	1.00	
>0–5	1.38	(0.96–1.99)
⩾5	1.78	(1.21–2.63)[d]
Number years used alcohol:		
0	1.00	
>0–<20	1.67	(0.93–2.98)
20–<40	1.75	(1.17–2.64)[d]
40+	1.54	(0.99–2.40)

[a] Each model included, in addition to the alcohol variable, the following covariates: religion, income status, marital status, family history of breast cancer, history of benign breast disease, age of menarche, ever pregnant, age first live birth, total weeks spent breastfeeding, and ever smoked.
[b] OR, odds ratio; CI, confidence interval.
[c] 661 pairs analysed for Nassau County and 545 for Suffolk County.
[d] Statistically significant odds ratios.

County. This is seen in Table 6, which shows adjusted OR and 95% CI for alcohol measured as ever drinking, g/day, and total years of alcohol consumed for each county separately.

DISCUSSION

There have been several dozen published epidemiological studies of alcohol and breast cancer. Two meta analyses[7,8] and a review[1] have recently been published summarizing these reports. In the present study, risk of breast cancer was increased by 40–45% for women ever drinking alcohol. There was a dose-response relationship with increasing g/day of alcohol consumed; women drinking ⩾5 g/day had a 50% increased risk. Five g/day was less than one-half of an alcoholic drink per day, indicating that moderate levels of consumption increased risk.

Most reports on breast cancer and alcohol consumption lacked data on duration of drinking, and even data on age when alcohol use first began. These variables may add more important information for breast cancer risk than only recent consumption patterns. In this paper, we studied risk by age a woman first began to drink and duration of drinking.

Among the studies which examined the age a woman first started to drink, two found no association between alcohol intake and breast cancer risk.[9,10] Several found higher risks among those who started drinking at younger ages.[11–14] Nasca *et al.* and Holmberg *et al.* found the greatest risk in those who began drinking later in life.[15,16] Several investigators, however, discovered no relationship between age of first starting to drink or early age of alcohol consumption and breast cancer.[17–20] Our study agreed with the latter findings. We cannot rule out, however, that heavy drinking at an early age is associated with breast cancer, because we did not measure the amount of drinking at various ages. The disparity of these studies show further research is needed to understand how age starting to drink relates to breast cancer.

A few studies have evaluated the association between duration of alcohol use and breast cancer.[15,17,19] All failed to show an association. In the present study, the risk of breast cancer increased as total years of drinking increased; after 40 years, however, no further increase was seen. While first age at drinking was not important for risk, our results on duration of drinking suggested that risk increased as the years of alcohol consumed during a woman's life increased. However, when g/day of drinking and duration were simultaneously included in the multivariate model, duration was no longer statistically significant. This may have occurred because the two variables were highly correlated (r = 0.60), or because intensity of drinking (i.e. g/day) was the important contributor to risk, and not duration. Further studies specifically designed to separate the effect of intensity and duration of drinking on breast cancer risk are needed.

We did not expect an interaction of alcohol and breast cancer risk by county of residence. Suffolk County had higher risks from alcohol consumption than Nassau County. This pattern was also found from this data set in the association of oral contraceptive use and breast cancer.[21] Nassau and Suffolk County participants did not differ in their distribution of ever drinking, g/day, or type of drinks. Intercounty drinking pattern differences would not explain the county interaction. Other breast cancer risk factors that differ by county are known. Based on control data, Nassau county women have a higher educational and income level, higher proportion who are Jewish, higher rates of benign

breast disease, and an older age at first live birth than Suffolk county women. How these differences may explain why the breast cancer and alcohol association was stronger in Suffolk than in Nassau County is not clear.

Strengths of this study are its size and the measures of alcohol consumption used in the analysis. However, biases particular to this study and common to case-control studies may be present. Our participation rate was lower for controls than for cases (see MATERIAL AND METHODS), and we had only a few variables to assess fully the selection biases. Participating cases and controls were younger than those who did not participate. The mean difference in age between those who were interviewed and those who refused was small (4–6 years). This difference, while statistically significant, was probably not large enough to cause a severe selection bias, and being non-differential for case-control status, did not bias the association of alcohol and breast cancer. Among those contacted, the participating cases tended to be of higher SES than those who refused, but for controls no differences were seen. Higher SES groups tend to use alcohol more often than lower SES groups.[2] Alcohol use in the cases may have been greater compared to controls because of this selection bias resulting in overestimating the OR. Although statistically significant, the difference in SES between participating and non-participating cases was small and probably only slightly biased the OR.

While the selection biases for these variables appear to be small, the possibility of biases concerning other characteristics cannot be excluded, especially among controls. The influence of other potential selection biases is not measurable or known. The results of our study, however, agree with those of many other studies with high participation rates,[13,17,22–26] thus suggesting that these biases had modest effects.

Cases may have recalled alcohol consumption more accurately than controls. Giovannucci *et al.* however, showed that retrospective data collection and any associated recall bias for alcohol consumption had only minor effects on alcohol reporting and risk estimates, as compared to prospectively collected data.[27] Interviewers were not masked to case-control status, and may have differentially assessed alcohol exposure between the two groups. However, the alcohol questions were part of an extensive and lengthy interview measuring many potential risk factors for breast cancer. At the time data were collected, the association between alcohol and breast cancer was not well recognized, and both subjects and interviewers were not aware of the hypothesis of this report. These considerations lessen the likelihood of recall or interviewer bias.

We controlled for the major risk factors for breast cancer. Other potential biases in case-control studies are unmeasured confounders and unmeasurable factors contributing to selection bias. We attempted to measure most known and suspected variables related to breast cancer. While these biases may exist, the possibility was minimized by a careful study design.

Many case-control and cohort studies have found an association between alcohol use and breast cancer. Assuming the relationship is real and causal, an important question is how much breast cancer in women similar to those in our study is attributable to alcohol consumption. This study allows this calculation. We assume an OR of 1.4 for women ever drinking alcohol compared to never drinkers, and a prevalence of ever drinking in a population of women similar to our sample (estimated from the control group) of 83%. Applying formulas given by Kelsey,[28] results show that 25% of breast cancer among these women between 20 and 79 years old is attributable to ever drinking alcohol. Alcohol use is a common exposure and breast cancer is common among women. If the alcohol-breast cancer hypothesis is correct, many breast cancers would be preventable by reducing alcohol consumption.

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