American Journal of
EPIDEMIOLOGY

Volume 149
Number 2
January 15, 1999

Sponsored by The Society for Epidemiologic Research

ORIGINAL CONTRIBUTIONS

Alcohol Consumption and Risk of Breast Cancer: The Framingham Study Revisited

Yuqing Zhang,[1] Bernard E. Kreger,[1,2] Joanne F. Dorgan,[3] Greta L. Splansky,[4] L. Adrienne Cupples,[5] and R. Curtis Ellison[1,4]

Although many studies report that moderate-to-heavy alcohol intake increases breast cancer risk, the effect of light alcohol consumption remains controversial, and a consistent pattern of association with different types of alcoholic beverages is not evident. The authors examined the relation of average alcohol consumption and of different beverages to the risk of breast cancer in the Framingham Study (Framingham, Massachusetts). Of 2,764 women followed more than 40 years in the Original Cohort from 1948 to 1993 and 2,284 followed up to 24 years in the Offspring Cohort from 1971 to 1993, 221 and 66 incident breast cancer cases occurred, respectively. Breast cancer incidence decreased from 3.60 per 1,000 person-years to 2.47, 2.30, and 2.33 in increasing categories of average alcohol consumption (none, <5.0, 5.0–<15.0, and ≥15.0 g/day) among the Original Cohort and from 3.07 to 1.26, 1.24, and 2.22, respectively, among the Offspring Cohort. With the two cohorts combined, multivariate-adjusted rate ratios of breast cancer in each increased category of alcohol consumption were 1.0 (nondrinkers), 0.8 (95% confidence interval (CI) 0.6–1.1), 0.7 (95% CI 0.5–1.1), and 0.7 (95% CI 0.5–1.1), respectively. Breast cancer was not associated with wine, beer, or spirits consumption when assessed separately. The findings suggest that the light consumption of alcohol or any type of alcoholic beverage is not associated with increased breast cancer risk. *Am J Epidemiol* 1999;149:93–101.

alcohol drinking; breast neoplasms; cohort studies

Editor's note: *For a discussion of this paper and for the authors' response, see pages 102 and 105, respectively.*

Over the past decade, the relation of alcohol consumption to the risk of breast cancer has been studied extensively. The results from a meta-analysis published in 1994 suggest that a daily intake of two drinks of any alcoholic beverage increases the risk by 24 percent (1). The effect of light alcohol consumption (e.g., alcohol drinkers who consume up to one drink per day) on the risk of breast cancer, however, remains controversial (2–24). Many studies also examined the intake of different types of alcoholic beverages, that is, beer, wine, and spirits, in relation to the risk of breast cancer. Some found an increased risk with all types of alcoholic beverages (13, 16, 17), while others reported that an adverse effect was strong for only one or two types of beverages (3, 8, 12, 21–24). A consistent pattern of association with different types of alcoholic beverages is not evident (1, 25).

Received for publication December 22, 1997, and accepted for publication May 28, 1998.

Abbreviation: CI, confidence interval.

[1] Sections of Preventive Medicine and Epidemiology, Evans Department of Medicine, Boston University School of Medicine, Boston, MA.
[2] General Internal Medicine, Evans Department of Medicine, Boston University School of Medicine, Boston, MA.
[3] Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD.
[4] Framingham Heart Study of the National Heart, Lung, and Blood Institute, Framingham, MA.
[5] Department of Epidemiology and Biostatistics, Boston University School of Public Health, Boston, MA.
Reprint requests to Dr. Yuqing Zhang, Section of Preventive Medicine and Epidemiology, Boston University School of Medicine, 80 East Concord Street, Boston, MA 02118.

In an earlier report (19), based on 26 years of follow-up of 2,636 women in the Framingham Original Cohort, we did not find that alcohol consumption was associated with an increased risk of breast cancer. In the current analyses, we extended the follow-up of the Original Cohort to more than 40 years and assessed the effect of average alcohol consumption over the entire study period. We also evaluated such an association among more than 2,500 women in the Framingham Offspring Cohort who have been followed for more than 20 years. In addition, we investigated the relation of different types of alcoholic beverage consumption to the risk of breast cancer for both cohorts.

MATERIALS AND METHODS

Study population

The Framingham Study began in 1948 in Framingham, Massachusetts. The original cohort, hereafter referred to as the "Original Cohort," included 2,873 women, aged 28–62 years at the first examination. Subjects have been examined biennially since then. At each examination, participants receive a medical history interview, a physical examination, and a series of laboratory tests. In 1971, examination was begun on many of the children of the Original Cohort and their spouses. Of 5,124 subjects aged 12–60 years who were enrolled in the Framingham Offspring Study, hereafter referred to as the "Offspring Cohort," 2,641 are women. Subjects in the Offspring Cohort have been followed in 4-year cycles, with evaluations similar to those of the Original Cohort.

Assessment of alcohol consumption

Information on alcohol consumption has been collected repeatedly from both the Original Cohort and the Offspring Cohort. At two early examinations (examinations 2 and 7) of the Original Cohort, women were asked how many 2-oz cocktails, 8-oz glasses of beer, and 4-oz glasses of wine they consumed in a month. At subsequent examinations (examinations 12–15 and 17–21) of the Original Cohort, and at all examinations (examinations 1–4) of the Offspring Cohort, women were asked about the number of 1.5-oz cocktails, 12-oz glasses (or cans) of beer, and 5-oz glasses of wine they consumed in a week. Total alcohol consumption (grams per day) has been computed by multiplying the average amounts of alcohol in beer, wine, and mixed drinks times the amount drunk. Since there was a secular change in the alcohol content of liquor commonly consumed (from 100 to 80 percent proof) and the type of wine generally consumed (from fortified to table wine), as well as a change in the average serving sizes of drinks, we used two different conversion formulas to calculate the total ethanol content according to when the data were collected. For examinations 2 and 7 of the Original Cohort, the total ethanol content (grams per day) was calculated based on (1.0 × the number of cocktails per month + 0.4 × the number of beers per month + 0.67 × the number of glasses of wine per month) × 28.35/30. For all later examinations in the Original Cohort and all examinations in the Offspring Cohort, the ethanol content was estimated as (0.57 × the number of cocktails per week + 0.44 × the number of beers per week + 0.40 × the number of glasses of wine per week) × 28.35/7.

Ascertainment of cases

The methods used to identify cancer cases in the Framingham Study have been described in detail by Kreger et al. (26). Briefly, cases were identified initially by self-report at each examination, surveillance of admissions to the only local hospital, and review of all death records. Participants who missed a regularly scheduled examination were contacted by telephone or mail to solicit information regarding medical events during the time interval since their last examination. For the nonrespondents or subjects whose vital status was unknown, the National Death Index was searched to obtain vital status and cause of death. Pertinent medical records (pathology reports, operation notes, autopsies) were obtained from hospitals and physicians. Framingham records for each suspected cancer case were then reviewed to confirm the diagnosis and to determine the date of earliest diagnosis, the location in the breast, and details of histopathology. Pathology reports were available for 97.6 percent of breast cancer cases in the Original Cohort and 100 percent in the Offspring Cohort. The remainders were confirmed by records from the cancer registry. Six cases (two from the Original Cohort and four from the Offspring Cohort) that could not be confirmed were not included in this analysis. All cases were coded according to the *International Classification of Diseases for Oncology* (topography code 174) (27).

Other variables

Information on other breast cancer risk factors, including age, height, weight, number of cigarettes per day at the baseline examination, number of years of education, age at menarche (Offspring Cohort only), age at first pregnancy (Original Cohort only), parity, and age at menopause, was obtained from each subject. For the women whose menstrual period stopped because of hysterectomy without bilateral oophorectomy, the median ages of the menopause for the Original

Cohort and the Offspring Cohort were calculated separately, and these values were assigned to those women. Postmenopausal estrogen use was assessed at each biennial examination of the Original Cohort since 1960 and at all examinations of the Offspring Cohort. Physical activity was ascertained by asking each woman how many hours a day she usually spent at sleep and rest and, during work and leisure time, at sedentary (e.g., standing), slight (e.g., walking), moderate (e.g., greater than walking but less than running), and heavy (e.g., running) activities. The hours at each level of activity, weighted by the relative oxygen consumption for that activity, were summed to create a physical activity index (28). The total number of years of postmenopausal estrogen use for each woman was summed from the time the data were available to either the time of breast cancer diagnosis or the time of censoring.

Statistical analysis

We divided subjects into four groups according to their average amount of alcoholic beverage consumption over the follow-up period: nondrinkers, <5.0 g/day, 5.0–<15.0 g/day, and ≥15.0 g/day (5 g of alcohol approximate the amount contained in one half of an average "drink," while 15 g represent the amount in 1–1.5 typical "drinks"). The average alcohol consumption for each subject was weighted, with weights equal to the number of years since the subject's last report on alcohol consumption. We compared the characteristics of women according to their average alcohol consumption level using analysis of variance for continuous variables and a chi-square test for categorical variables for each cohort separately. Person-years of follow-up for each woman were computed as the amount of time from the date of initial assessment of alcohol consumption (examination 2 for 96.3 percent of subjects in the Original Cohort and examination 1 for 98.7 percent of subjects in the Offspring Cohort) to the date of the first of the following events: 1) breast cancer diagnosis; 2) for those lost to follow-up, the last contact date; and 3) the study closing date of December 31, 1993. The incidence rates of breast cancer for each category were calculated by dividing the number of events by the person-years of follow-up.

Since age is an important determinant of breast cancer, and older women tended to drink less alcohol, we matched each breast cancer case to all available noncases on age. Specifically, for each breast cancer case, we created a risk set that included all women who were within 2 years of age of the breast cancer case at the time of entry into the study and who were alive and free of breast cancer when the case was diagnosed (29). A woman could be included in more than one risk set, and those who developed breast cancer could be included as noncases up to the age at which cancer was diagnosed. Alcohol consumption for noncases within each risk set was averaged up to the age when the case was diagnosed. We applied a Cox proportional hazards model to assess the relation of average alcohol consumption to the risk of breast cancer, using age as the time variable. In the multivariate Cox proportional hazards model, we adjusted for education, height, body mass index, physical activity index, age at first pregnancy (Original Cohort only), parity, age at menarche (Offspring Cohort only), age at menopause, average number of cigarettes smoked, and postmenopausal estrogen use.

To examine the effect of each type of alcoholic beverage on the occurrence of breast cancer, we believed it appropriate to categorize consumption in terms of number of drinks, rather than grams of alcohol, since nonalcoholic components of different beverages may relate to breast cancer risk. We classified women into four groups according to their average weekly number of drinks of beer, wine, or spirits: 0, <1, 1–2, and ≥3 drinks per week, adjusting data collected in examinations 2 and 7 of the Original Cohort to reflect current drinks, as described. Thus, one drink of wine, beer, and spirits in examination 2 or 7 is equivalent to 1.68 drinks of wine, 0.91 drink of beer, and 1.75 drinks of spirits, respectively, in subsequent examinations. The incidence rate of breast cancer was calculated for each category of specific type of alcoholic beverage consumption. The association between breast cancer and the specific type of alcoholic beverage was then assessed using a Cox proportional hazards model adjusting for other potential confounding factors, including the intake of other alcoholic beverages.

Initial analyses were conducted separately for each cohort, the Original and the Offspring. Since the results from the Original Cohort and the Offspring Cohort were similar, we combined subjects of both cohorts and assessed alcohol consumption as well as the different types of alcoholic beverage intakes in relation to the risk of breast cancer.

RESULTS

Of the 2,873 women in the Original Cohort, 11 had a history of breast cancer prior to examination 2, and 98 did not have alcohol information; these subjects were excluded from the analysis. During the follow-up period (median, 34.3 years; range, 0.2–42.5 years), 221 women in the Original Cohort developed breast cancer. The median age at the time of diagnosis was 68.4 years, and 95.5 percent of cases occurred after the menopause. Of the 2,641 women in the Offspring Cohort, 357 subjects were excluded from the analysis

because of a history of breast cancer before examination 1 ($n = 7$), incomplete follow-up for subjects who came only for examination 1 ($n = 255$), being younger than 20 years at examination 1 ($n = 94$) (none of them developed breast cancer), and lack of alcohol consumption information ($n = 1$). Of the remaining 2,284 subjects, 66 developed breast cancer during the follow-up period (median follow-up of 19.3 years with the range being 0.2–22.6 years). The median age at the time of diagnosis for women in the Offspring Cohort was 54.2 years, and 81.8 percent of cases occurred after the menopause.

Table 1 shows the characteristics of the women with breast cancer and those without breast cancer in the Original and the Offspring cohorts, respectively. Among the Original Cohort, women with breast cancer were significantly older at menopause ($p = 0.03$), older at first pregnancy ($p = 0.01$), more educated ($p = 0.02$), and more likely to be nulliparous ($p = 0.06$). However, there were no statistically significant differences between the two groups of women in terms of age at entry into the study, height, body mass index, years of postmenopausal estrogen use, cigarette smoking, or level of physical activity. Characteristics of breast cancer cases and noncases in the Offspring Cohort were similar to those observed among the Original Cohort, except that breast cancer cases were older at entry to the study ($p < 0.01$) and the years of education were not statistically significant between breast cancer cases and noncases.

Table 2 displays the distribution of potential confounding factors for breast cancer according to the average alcohol consumption over the follow-up period among subjects in the Original Cohort. As compared with nondrinkers, alcohol drinkers tended to be younger, taller, and leaner and to have a later age at their first pregnancy. Alcohol consumers also had more years of education, used postmenopausal hormonal therapy for a longer period, smoked more cigarettes, and were at a higher level of physical activity. Similar differences, except parity and physical activity level, were also found among the Offspring Cohort (table 3).

The incidence of breast cancer was slightly higher among nondrinkers than drinkers in both the Original and Offspring cohorts (table 4). The incidence rate decreased from 3.60 per 1,000 person-years among nondrinkers to 2.47, 2.30, and 2.33 per 1,000 person-years in each increased category of alcohol consumption among the Original Cohort. The corresponding incidence rates were 3.07, 1.26, 1.24, and 2.22 per 1,000 person-years, respectively, among the Offspring Cohort. When the two cohorts were combined, the multivariate-adjusted rate ratios of breast cancer for women in each increased category of alcohol consumption were 0.8 (95 percent confidence interval (CI) 0.6–1.1), 0.7 (95 percent CI 0.5–1.1), and 0.7 (95 percent CI 0.5–1.1), respectively.

We further examined the separate effects of wine, beer, and spirits on the risk of breast cancer (table 5). In both cohorts, there were no clear patterns of either a protective or adverse effect for wine, beer, or spirits consumption. When the two cohorts were combined, the risk of breast cancer for spirits drinkers tended to decrease with increasing number of drinks, but the trend was of borderline statistical significance ($p = 0.067$).

To permit comparisons between these data and data from other studies in which only baseline alcohol consumption data are available, we also assessed the effect of alcohol consumption at the baseline examination on the risk of breast cancer. For total alcohol consumption, multivariate-adjusted rate ratios for each increased category of alcohol consumption were 1.0 (nondrinkers), 0.8 (95 percent CI 0.6–1.1), 0.8 (95 percent CI 0.5–1.2), and 0.7 (95 percent CI 0.5–1.1), respectively. In comparison with nondrinkers, the rate ratios for wine drinkers who consumed <1, 1–2, and ≥3 drinks per week were 0.9, 0.7, and 0.7, respectively; for beer drinkers, 1.4, 1.3, and 1.0, respectively; and for spirits drinkers, 0.7, 0.7, and 0.6, respectively. Except for the highest category of spirits intake, all of these point estimates included 1.0 in their 95 percent confidence intervals.

DISCUSSION

The results from this prospective cohort study, based on two generations of women, suggest that neither a light-to-moderate level of alcohol consumption nor consumption of any particular type of alcoholic beverage increases the risk of breast cancer. Although the majority of epidemiologic studies have found that moderate-to-heavy alcohol consumption is associated with an increased risk of breast cancer (1, 25), the percentage of women drinkers who average two or more alcoholic beverage drinks per day is relatively small. According to a 1990 national survey of drinking by American adults, about 10 percent of female drinkers consumed two or more alcoholic beverages daily (30). In the present study, 12.1 percent of women in the Original Cohort and 7.8 percent of women in the Offspring Cohort consumed more than 26 g of alcohol (the equivalent of about two drinks) per day. Considering that the majority of female drinkers consumed less than one drink of an alcoholic beverage per day, a level consistent with current US Department of Agriculture dietary guidelines (an average of no more than one drink per day), our study provides valuable data on the effect of light

TABLE 1. Characteristics of women according to the status of incident breast cancer in the Framingham Original Cohort (1948–1993) and Offspring Cohort (1971–1993), Framingham, Massachusetts

	Mean age at baseline examination (years)	Mean height at baseline examination (cm)	Mean BMI† at baseline examination (kg/m²)	Mean age at menarche (years)	Mean age at menopause (years)	Mean age at first pregnancy (years)
Original Cohort						
Cases (n = 221)	45.8 (8.4)‡	160 (5.8)	24.9 (4.3)		48.8 (4.3)	26.8 (5.2)
Noncases (n = 2,543)	46.7 (8.5)	159 (6.3)	25.4 (4.6)		48.0 (4.9)*	25.8 (5.1)**
Offspring Cohort						
Cases (n = 66)	42.1 (7.3)	161 (5.6)	24.3 (3.8)	13.0 (1.6)	48.1 (6.1)	
Noncases (n = 2,218)	36.7 (9.4)*	161 (6.1)	24.3 (4.6)	12.9 (1.6)	46.0 (6.6)*	

	% of women													
	Education			Parity			Years of estrogen use			No. of cigarettes smoked per day at baseline examination			Physical activity index at baseline examination		
	<12 years	12 years	>12 years	0	1	2	None	<5	≥5	None	<10	≥10	26–29	30–32	≥33
Original Cohort															
Cases (n = 221)	31.5	36.1	32.4	29.9	12.2	57.9	89.1	7.2	3.6	58.4	15.8	25.8	30.6	42.1	27.3
Noncases (n = 2,543)	41.4*	31.0	27.5	22.8	13.7	63.6	87.7	7.8	4.5	59.0	14.7	26.3	36.4	38.8	24.8
Offspring Cohort															
Cases (n = 66)	14.3	42.9	42.9	19.7	9.1	71.2	84.9	12.1	3.0	43.8	9.4	46.9	6.1	27.3	66.7
Noncases (n = 2,218)	6.9	38.5	54.6	12.4	10.4	77.2	81.7	12.0	6.2	40.4	12.0	47.6	10.3	35.5	54.3

* $p < 0.05$; ** $p < 0.01$.
† BMI, body mass index.
‡ Numbers in parentheses, standard deviation.

TABLE 2. Characteristics of women in the Framingham Original Cohort according to average alcohol consumption during the follow-up period, Framingham, Massachusetts, 1948–1993

Average alcohol consumption (g/day)	Mean age at baseline examination (years)	Mean height at baseline examination (cm)	Mean BMI† at baseline examination (kg/m²)	Mean age at menopause (years)	Mean age at first pregnancy (years)
Nondrinker (n = 633)	51.1 (8.1)‡	158 (5.8)	27.0 (5.6)	48.0 (4.6)	25.3 (5.0)
0.1–<5.0 (n = 1,121)	46.1 (8.2)	159 (6.1)	25.5 (4.4)	48.0 (5.0)	25.9 (5.2)
5.0–<15 (n = 518)	44.7 (8.1)	160 (6.6)	24.5 (4.0)	48.1 (5.0)	26.4 (5.1)
≥15 (n = 492)	44.3 (8.1)**	161 (6.1)**	23.7 (3.6)**	48.3 (5.0)	26.0 (4.8)**

	% of women													
	Education			Parity			Years of estrogen use			No. of cigarettes smoked per day at baseline examination			Physical activity index at baseline examination		
	<12 years	12 years	>12 years	0	1	≥2	None	<5	≥5	None	<10	≥10	26–29	30–32	≥33
Nondrinker (n = 633)	53.1	24.4	22.5	26.4	13.0	60.6	94.5	4.4	1.1	77.9	8.9	13.3	43.3	37.2	19.5
0.1–<5.0 (n = 1,121)	43.5	33.0	23.5	22.9	14.5	62.6	87.2	8.2	4.6	63.3	14.7	22.0	34.9	39.2	25.9
5.0–<15 (n = 518)	32.7	35.1	32.2	22.4	12.7	64.9	85.3	8.9	5.8	50.0	19.1	30.9	32.7	40.0	27.3
≥15 (n = 492)	26.5	32.8	40.6*	21.3	13.0	65.6	83.5	9.8	6.7*	34.4	17.9	47.8*	33.3	40.0	26.8*

* $p < 0.05$; ** $p < 0.01$.
† BMI, body mass index.
‡ Numbers in parentheses, standard deviation.

TABLE 3. Characteristics of women in the Framingham Offspring Cohort according to average alcohol consumption during the follow-up period, Framingham, Massachusetts, 1971–1993

Average alcohol consumption (g/day)	Mean age at baseline examination (years)	Mean height at baseline examination (cm)	Mean BMI† at baseline examination (kg/m²)	Mean age at menarche (years)	Mean age at menopause (years)
Nondrinker (n = 202)	38.0 (9.8)‡	160 (6.1)	25.1 (5.9)	12.9 (1.7)	45.7 (6.8)
0.1–<5.0 (n = 954)	36.7 (9.4)	160 (6.4)	24.9 (5.1)	12.8 (1.5)	46.4 (6.5)
5.0–<15 (n = 701)	36.4 (9.6)	161 (6.1)	23.5 (3.7)	13.0 (1.6)	45.8 (6.7)
≥15 (n = 427)	37.7 (8.8)*	161 (5.6)**	23.7 (3.9)**	12.9 (1.6)	46.3 (6.6)

	% of women														
	Education			Parity			Years of estrogen use			No. of cigarettes smoked per day at baseline examination			Physical activity index at baseline examination		
	<12 years	12 years	>12 years	0	1	≥2	0	<5	≥5	0	<10	≥10	26–29	30–32	≥33
Nondrinker (n = 202)	12.7	44.0	43.0	8.4	9.4	82.2	82.7	14.1	3.0	60.4	4.5	35.2	8.8	32.0	59.2
0.1–<5.0 (n = 954)	6.5	42.9	50.6	10.2	11.7	78.1	81.9	11.7	6.4	46.5	11.1	42.4	9.6	39.3	51.1
5.0–<15 (n = 701)	6.0	34.8	59.2	14.8	9.1	76.0	81.0	12.1	6.9	38.0	14.6	47.4	10.2	32.2	57.7
≥15 (n = 427)	7.8	33.2	59.0**	16.4	9.6	74.0**	82.7	11.5	5.9	21.8	12.8	65.5**	12.1	33.2	54.7

* $p < 0.05$; ** $p < 0.01$.
† BMI, body mass index.
‡ Numbers in parentheses, standard deviation.

TABLE 4. Relation of average alcohol consumption to the risk of breast cancer in the Framingham Original Cohort (1948–1993) and Offspring Cohort (1971–1993), Framingham, Massachusetts

Average alcohol consumption (g/day)	No. of women with breast cancer	Incidence rate (per 1,000 person-years)	Age-adjusted rate ratio	Multivariate-adjusted rate ratio*
Original Cohort				
Nondrinker	58	3.60	1.0	1.0
0.1–<5.0	88	2.47	0.9	0.9 (0.6–1.2)†
5.0–<15	39	2.30	0.8	0.7 (0.5–1.1)
≥15.0	36	2.33	0.8	0.7 (0.5–1.1)
Offspring Cohort				
Nondrinker	11	3.07	1.0	1.0
0.1–<5.0	22	1.26	0.6	0.7 (0.3–1.4)
5.0–<15	16	1.24	0.7	0.7 (0.3–1.6)
≥15.0	17	2.22	0.9	1.0 (0.4–2.2)
Both cohorts combined				
Nondrinker	69	3.50	1.0	1.0
0.1–<5.0	110	2.07	0.8	0.8 (0.6–1.1)
5.0–<15	55	1.85	0.8	0.7 (0.5–1.1)
≥15.0	53	2.30	0.8	0.7 (0.5–1.1)

* The rate ratios were adjusted for education, height, body mass index, physical activity index, age at first pregnancy (Original Cohort only), parity, age at menarche (Offspring Cohort only), age at menopause, average number of cigarettes smoked, and postmenopausal estrogen use.

† Numbers in parentheses, 95% confidence interval.

drinking on the risk of breast cancer, where some controversy remains. While no increase in breast cancer was observed among the women in the highest category of alcohol consumption in the present study, it should be noted that there were very few heavy drinkers in this study. Of the women who reported the intake of ≥15 g of alcohol per day, the median intake was 24 g (about two drinks per day). Our study does not have adequate power to examine the relation of heavy alcohol consumption to the risk of breast cancer.

Many studies have also evaluated the effects of different types of alcoholic beverages on the risk of breast cancer. Several investigators have hypothesized that the relation of different types of alcoholic beverages to the risk of breast cancer may differ because of various chemical compounds contained in different beverages, such as phenolic compounds, including antioxidants, in wine and estrogenic substances in beer and spirits (31–33). To date, no particular alcoholic beverage has been implicated consistently (1, 25). In the present study, we did not find that light-to-moderate intakes of any particular type of alcoholic beverage were associated with an increased risk of breast cancer.

While the number of breast cancer cases in our study is not large, several characteristics of this study are

TABLE 5. Relation of wine, beer, and spirits consumption to the risk of breast cancer among women in the Framingham Original Cohort (1948-1993) and Offspring Cohort (1971-1993), Framingham, Massachusetts

Type of beverage (drinks/week)	No. of women with breast cancer	Incidence rate (per 1,000 person-years)	Multivariate-adjusted rate ratio*
Original Cohort			
Wine			
None	105	3.38	1.0
0.1–<1.0	78	2.24	0.9 (0.6–1.4)†
1.0–<3.0	15	1.54	0.7 (0.3–1.7)
≥3	23	2.73	1.0 (0.7–1.5)
Beer			
None	150	2.85	1.0
0.1–<1.0	55	2.28	1.0 (0.7–1.4)
1.0–<3.0	9	2.47	0.7 (0.3–1.6)
≥3	7	1.93	1.0 (0.4–2.6)
Spirits			
None	76	3.41	1.0
0.1–<1.0	73	2.32	0.8 (0.5–1.4)
1.0–<3.0	27	2.17	0.9 (0.4–1.9)
≥3	45	2.52	0.7 (0.5–1.0)
Offspring Cohort			
Wine			
None	27	2.57	1.0
0.1–<1.0	13	1.00	1.0 (0.5–2.1)
1.0–<3.0	16	1.52	0.7 (0.4–1.4)
≥3	10	1.38	0.7 (0.3–1.5)
Beer			
None	45	1.68	1.0
0.1–<1.0	9	1.07	1.6 (0.7–3.6)
1.0–<3.0	9	2.03	1.2 (0.6–2.6)
≥3	3	1.58	0.9 (0.3–3.1)
Spirits			
None	16	2.05	1.0
0.1–<1.0	13	0.75	0.9 (0.4–2.0)
1.0–<3.0	19	2.03	0.8 (0.4–1.7)
≥3	18	2.51	1.1 (0.5–2.4)
Both cohorts combined			
Wine			
None	132	3.20	1.0
0.1–<1.0	91	1.90	0.9 (0.6–1.3)
1.0–<3.0	31	1.53	0.7 (0.4–1.3)
≥3	33	2.02	1.0 (0.7–1.3)
Beer			
None	195	2.47	1.0
0.1–<1.0	64	1.97	1.1 (0.8–1.5)
1.0–<3.0	18	2.23	1.0 (0.5–1.7)
≥3	10	1.63	1.0 (0.5–2.2)
Spirits			
None	92	3.06	1.0
0.1–<1.0	86	1.76	0.8 (0.5–1.2)
1.0–<3.0	46	2.11	0.7 (0.5–1.3)
≥3	63	2.52	0.7 (0.5–1.0)

* The rate ratios were adjusted for education, height, body mass index, physical activity index, age at first pregnancy (Original Cohort only), parity, age at menarche (Offspring Cohort only), age at menopause, average number of cigarettes smoked, postmenopausal estrogen use, and intake of other alcoholic beverages.

† Numbers in parentheses, 95% confidence interval.

noteworthy. The data are from population-based cohorts of women followed over a long period of time, permitting an assessment of potential alcohol effects that may require many years to appear. The estimates of average alcohol consumption were derived from multiple examinations for the large majority of women. It should be pointed out that the questions used to assess alcohol consumption in the Original Cohort after examination 7 were changed from number of drinks per month to number of drinks per week; this may have led to some underreporting of the absolute number of drinks consumed in the two early examinations. However, we found that the repeated assessments of alcohol consumption over the follow-up period were quite stable, and the risk estimates based on alcohol consumption at the baseline examination were very similar to those obtained when the average intake over the follow-up was considered, suggesting reasonable accuracy of the exposure assessment. Almost all cases of breast cancer were confirmed by histologic reports, and the rate of breast cancer occurrence in the Framingham Study is similar to that in the Surveillance, Epidemiology, and End Results Program (26). Thus, we believe that virtually all clinically detected incident cases of breast cancer were ascertained. Information on age at menarche in the Original Cohort, on age at first pregnancy in the Offspring Cohort, and on family history of breast cancer in both cohorts was not collected in the study, and we were unable to assess the potential confounding effects for these variables. However, the relation of alcohol intake and type of alcoholic beverage consumed to the risk of breast cancer was not changed in either cohort when age at first pregnancy in the Original Cohort or age at menarche in the Offspring Cohort was added in the analyses. Nevertheless, a potential residual confounding effect due to unadjusted confounders is still a possibility, and this must be considered in interpreting these findings.

The biologic mechanisms linking alcohol consumption to the risk of breast cancer are not fully understood. Investigators have proposed that alcohol consumption increases the risk of breast cancer among women by influencing estrogen metabolism. Recently, Ginsburg et al. (34) reported that alcohol ingestion led to a threefold increase in circulating estradiol in women on estrogen replacement therapy but that it had no effect in women who did not take postmenopausal estrogen. However, the amount of alcohol given in that study was large, the equivalent of approximately four drinks, and it was consumed in a fasting state. Data are not available on the effects of blood estrogen levels of women on hormone replacement therapy who consume smaller amounts of alcohol (i.e., up to one drink per day) in a more normal drinking pattern. To examine if women who drank alcohol and also took postmenopausal estrogens were at an increased risk, we stratified the women into two groups according to their estrogen use during the study period and found no differences between estrogen users and nonusers in the relation of alcohol to the risk of breast cancer. When drinkers were compared with nondrinkers, the rate ratios of breast cancer for each increased category of alcohol consumption were 0.6, 0.7, and 0.4 among estrogen users and 0.8, 0.7, and 0.8 among nonusers, respectively.

In summary, this prospective, population-based study among two generations of Framingham women shows that the light consumption of alcohol or of any type of alcoholic beverage is not associated with an increase in the risk of breast cancer.

ACKNOWLEDGMENTS

This work was supported by NIH/NHLBI contract N01–HC-38038 and by funds from the Institute on Lifestyle & Health, Boston University School of Medicine. The Institute on Lifestyle & Health is supported by unrestricted educational grants to Boston University from a variety of individuals, institutions, and companies, including some in the wine and alcoholic beverage industries.

REFERENCES

1. Longnecker MP. Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. Cancer Causes Control 1994;5:73–82.
2. Friedenreich CM, Howe GR, Miller AB. A cohort study of alcohol consumption and risk of breast cancer. Am J Epidemiol 1993;137:512–20.
3. Freudenheim JL, Marshall JR, Graham S, et al. Lifetime alcohol consumption and risk of breast cancer. Nutr Cancer 1995;23:1–11.
4. Ranstam J, Olsson H. Alcohol, cigarette smoking, and the risk of breast cancer. Cancer Detect Prevent 1995;19:487–93.
5. Smith SJ, Deacon JM, Chilvers CED, et al. Alcohol, smoking, passive smoking and caffeine in relation to breast cancer risk in young women. Br J Cancer 1994;70:112–19.
6. Howe G, Rohan T, Decarli A, et al. The association between alcohol and breast cancer risk: evidence from the combined analysis of six dietary case-control studies. Int J Cancer 1991;47:707–10.
7. Adami H-O, Lund E, Bergstrom R, et al. Cigarette smoking, alcohol consumption, and risk of breast cancer in young women. Br J Cancer 1988;58:832–7.
8. Rosenberg L, Palmer JR, Miller DR, et al. A case-control study of alcoholic beverage consumption and breast cancer. Am J Epidemiol 1990;131:6–14.
9. Ewertz M. Alcohol consumption and breast cancer risk in Denmark. Cancer Causes Control 1991;2:247–52.
10. Sneyd MJ, Paul C, Spears GFS, et al. Alcohol consumption and risk of breast cancer. Int J Cancer 1991;48:812–15.

11. Chu SY, Lee NC, Wingo PA, et al. Alcohol consumption and risk of breast cancer. Am J Epidemiol 1989;30:867–77.
12. Longnecker MP, Newcomb PA, Mittendorf R, et al. Risk of breast cancer in relation to lifetime alcohol consumption. J Natl Cancer Inst 1995;87:923–9.
13. van den Brandt PA, Goldbohm RA, van't Veer P. Alcohol and breast cancer: results from the Netherlands Cohort Study. Am J Epidemiol 1995;141:907–15.
14. Gapstur SM, Potter JD, Sellers TA, et al. Increased risk of breast cancer with alcohol consumption in postmenopausal women. Am J Epidemiol 1992;136:1221–31.
15. Schatzkin A, Jones DY, Hoover RN, et al. Alcohol consumption and breast cancer in the epidemiologic follow-up study of the First National Health and Nutrition Examination Survey. N Engl J Med 1987;316:1169–73.
16. Willett WG, Stampfer MJ, Colditz GA, et al. Moderate alcohol consumption and the risk of breast cancer. N Engl J Med 1987;316:1174–80.
17. Martin-Moreno JM, Boyle P, Gorgojo L, et al. Alcoholic beverage consumption and risk of breast cancer in Spain. Cancer Causes Control 1993;4:345–53.
18. Simon MS, Carman W, Wolfe R, et al. Alcohol consumption and the risk of breast cancer: a report from the Tecumseh Community Health Study. J Clin Epidemiol 1991;44:755–61.
19. Schatzkin A, Carter CL, Green SB, et al. Is alcohol consumption related to breast cancer? Results from the Framingham Heart Study. J Natl Cancer Inst 1989;81:31–5.
20. Webster LA, Layde PM, Wingo PA, et al. The Cancer and Steroid Hormone Study Group. Alcohol consumption and risk of breast cancer. Lancet 1987;2:724–7.
21. Katsouyanni K, Trichopoulou A, Stuver S, et al. Ethanol and breast cancer: an association that may be both confounded and causal. Int J Cancer 1994;58:356–61.
22. Ferraroni M, Decarli A, Willett WC, et al. Alcohol and breast cancer risk: a case-control study from northern Italy. Int J Epidemiol 1991;20:859–64.
23. Harvey EB, Schairer C, Brinton LA, et al. Alcohol consumption and breast cancer. J Natl Cancer Inst 1987;78:657–61.
24. Swanson CA, Coates RJ, Malone KE, et al. Alcohol consumption and breast cancer risk among women under age 45 years. Epidemiology 1997;8:231–7.
25. Rosenberg L, Metzger LS, Palmer JR. Alcohol consumption and risk of breast cancer: a review of the epidemiologic evidence. Epidemiol Rev 1993;15:133–44.
26. Kreger BE, Splansky GL, Schatzkin AS. The cancer experience in the Framingham Heart Study cohort. Cancer 1991;67:1–6.
27. World Health Organization. International classification of diseases for oncology. Geneva: World Health Organization, 1976.
28. Kannel WB, Sorlie P. Some health benefits of physical activity—The Framingham Study. Arch Intern Med 1979;139:857–61.
29. Breslow NE, Day NE, eds. Statistical methods in cancer research. Vol II. The design and analysis of cohort studies. Lyon: International Agency for Research on Cancer, 1987:178–229. (IARC scientific publication no. 82).
30. Wilsnack SC, Wilsnack RW, Hiller-Sturmh S. How women drink: epidemiology of women's drinking and problem drinking. Alcohol Health Res World 1994;18:173–80.
31. Frankel EN, Kanner J, German JB, et al. Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. Lancet 1993;341:454–7.
32. Gavaler JS. Alcohol and nutrition in postmenopausal women. J Am Coll Nutr 1993;12:349–56.
33. Jang M, Cai L, Udeani GO, et al. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. Science 1997;275:218–20.
34. Ginsburg ES, Mello NK, Mendelson JH, et al. Effects of alcohol ingestion on estrogens in postmenopausal women. JAMA 1996;276:1747–51.