

Alcohol Consumption Before and After Breast Cancer Diagnosis: Associations With Survival From Breast Cancer, Cardiovascular Disease, and Other Causes

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ABSTRACT

Purpose

Alcohol intake is associated with increased risk of breast cancer. In contrast, the relation between alcohol consumption and breast cancer survival is less clear.

Patients and Methods

We assessed pre- and postdiagnostic alcohol intake in a cohort of 22,890 women with incident invasive breast cancer who were residents of Wisconsin, Massachusetts, or New Hampshire and diagnosed from 198 to 200 at ages 20 to 79 years. All women reported on prediagnostic intake; a subsample of 4,881 reported on postdiagnostic intake.

Results

During a median follow-up of 11.3 years from diagnosis, 7,780 deaths occurred, including 3,484 resulting from breast cancer. Hazard ratios (HR) and 95% CIs were estimated. Based on a quadratic analysis, moderate alcohol consumption before diagnosis was modestly associated with disease-specific survival (compared with nondrinkers, HR = 0.93 [95% CI, 0.85 to 1.02], 0.85 [95% CI, 0.75 to 0.95], 0.88 [95% CI, 0.75 to 1.02], and 0.89 [95% CI, 0.77 to 1.04] for two or more, three to six, seven to nine, and ≥ 10 drinks/wk, respectively). Alcohol consumption after diagnosis was not associated with disease-specific survival (compared with nondrinkers, HR = 0.88 [95% CI, 0.61 to 1.27], 0.80 [95% CI, 0.49 to 1.32], 1.01 [95% CI, 0.55 to 1.87], and 0.83 [95% CI, 0.45 to 1.54] for two or more, three to six, seven to nine, and ≥ 10 drinks/wk, respectively). Results did not vary by beverage type. Women consuming moderate levels of alcohol, either before or after diagnosis, experienced better cardiovascular and overall survival than nondrinkers.

Conclusion

Overall alcohol consumption before diagnosis was not associated with disease-specific survival, but we found a suggestion favoring moderate consumption. There was no evidence for an association with postdiagnosis alcohol intake and breast cancer survival. This study, however, does provide support for a benefit of limited alcohol intake for cardiovascular and overall survival in women with breast cancer.

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INTRODUCTION

Women with breast cancer may be concerned that their lifestyle choices before diagnosis will affect their prognosis and may wonder whether modifying these behaviors might improve survival.¹⁻⁴ One readily modified factor is alcohol intake. Evidence is now incontrovertible that even moderate alcohol consumption increases risk of breast cancer⁵⁻¹¹; for each drink increase in average daily alcohol consumption, the relative risk of breast cancer increases by 7%.⁸ There is, however, mixed information on whether prediagnostic alcohol consumption is related to breast cancer

survival¹²⁻³¹ and limited literature on the association between postdiagnostic alcohol intake and survival.^{17,27}

Most studies have observed no relation between prediagnostic alcohol intake and breast cancer-specific or overall survival^{12-14,17-27}; however, some have found poorer disease-specific survival,¹⁵⁻¹⁷ and others have found better overall survival among drinkers.²⁸⁻³¹ Studies of overall survival among women with breast cancer include deaths from other cancers and chronic diseases, including cardiovascular disease, the latter being consistent in its inverse association with alcohol intake.³²⁻³⁴

The health impact of alcohol consumption after a breast cancer diagnosis is salient for the 3,000,000 breast cancer survivors in the United States today.^{35,36} To more fully evaluate this association, we analyzed data from a well-characterized cohort of 22,890 women with incident invasive breast cancer who reported on alcohol history and other factors before diagnosis.³⁷ We also examined a sub-cohort of these women who completed surveys on alcohol consumption and other behaviors after diagnosis.³⁸⁻⁴¹

PATIENTS AND METHODS

Collaborative Breast Cancer Study: Prediagnosis Alcohol Consumption

The Collaborative Breast Cancer Study (CBCS) began in 1988 as a multisite population-based case-control study of risk factors for breast cancer in New Hampshire, Massachusetts, and Wisconsin.^{37,42} A total of 23,344 women with incident breast cancer were enrolled during five successive study phases. Age eligibility varied by phase: from ages 20 to 74 years (1988 to 1991), to ages 50 to 79 years (1992 to 1995), and, more recently, ages 20 to 69 years at diagnosis (1997 to 2008). Approximately 80% of eligible women invited to join the study agreed to participate. For these analyses, we excluded 433 women (2%) with missing information on prediagnostic alcohol consumption, and 21 women (0.1%) with unknown vital status, leaving 22,890 eligible women.

Collaborative Women's Longevity Study: Postdiagnosis Alcohol Consumption

After the completion of the CBCS, patients were invited to participate in a survivorship cohort, termed the Collaborative Women's Longevity Study (CWLS). From 1998 to 2001, we mailed a follow-up questionnaire to 14,621 women known to be alive to assess how exposures may have changed after diagnosis. In total, 5,791 women (40%) returned the follow-up questionnaire. We excluded 34 women (0.6%) who had been diagnosed with metastatic disease at baseline, 617 women (11%) who reported a breast cancer recurrence, 155 women (3%) who reported that breast cancer treatment significantly interfered with diet, and 104 women (2%) missing data from the postdiagnosis alcohol questions. After these exclusions, 4,881 women were included in postdiagnosis analyses. All study activities were approved by the respective study sites' institutional review boards.

Ascertainment of Alcohol Use and Other Risk Factors

At study enrollment, all women completed a structured baseline telephone interview that included information on lifetime alcohol consumption up to diagnosis, including separate questions on the amount and frequency of beer, wine, and spirits intake. Typical serving sizes were defined as a 12 oz. can/bottle of beer, a 5 oz. glass of wine, or a 1.5 oz. serving of spirits.⁴³

The questionnaire also elicited information on other breast cancer risk factors, including reproductive and menstrual history, physical activity, height, weight, use of oral contraceptives and postmenopausal hormones, and personal and family history of cancer. Selected clinical information was obtained from state cancer registries, including date and stage at diagnosis, and histology.⁴⁴ The postdiagnosis questionnaire was administered a median of 5.7 years (25th to 75th percentile: 2.7 to 8.8 years) after diagnosis and was similar to the baseline questionnaire.

Identification of Deaths

Vital status was ascertained through December 31, 2009, using the National Death Index (NDI).^{45,46} Cause of death was assigned according to the International Classification of Diseases (ICD).^{47,48} We conducted separate analyses considering deaths attributable to breast cancer (ICD-9: 174 to 174.9; ICD-10: C50.0 to C50.9), cardiovascular disease (ICD-9: 390 to 398.9 and 401 to 448.9; ICD-10: I00 to I99), and any cause.

Statistical Analysis

Survival time was calculated from the date of diagnosis to death or the end of follow-up (December 31, 2009). We assessed the frequency and type of alcohol consumption in the year before diagnosis and in the year before the

postdiagnostic questionnaire. We considered the dose response for alcohol consumption in categories of drinks per week and, separately, by including linear and quadratic terms for drinks per week. Proportional hazards regression was used to estimate adjusted hazard ratios (HR) and 95% CIs for associations with survival across categories of alcohol consumption.⁴⁹ All regression models stratified the baseline hazard on study phase, age at diagnosis, state of residence, and stage at diagnosis. For analyses involving prediagnostic alcohol consumption, several correlates measured during the baseline questionnaire were identified a priori as adjustment variables and categorized as in Table 1: first-degree family history of breast cancer, age at first birth, menopausal status, postmenopausal hormone use, recent body mass index (BMI, in kilograms per square meter), smoking status, education, and mammography screening 1 to 5 years before diagnosis. Models also included the duration of the interval between diagnosis and completion of baseline interview. Women were classified as postmenopausal if they (1) experienced a natural menopause, (2) had a hysterectomy with bilateral oophorectomy, (3) were aged ≥ 55 without bilateral oophorectomy, or (4) were using hormone therapy without bilateral oophorectomy.

For analyses involving postdiagnostic alcohol consumption, follow-up time was calculated from the date of return of the CWLS questionnaire until the date of death or December 31, 2009. Models included the same variables as in prediagnostic analyses. In addition to prediagnostic BMI, we adjusted for the change between pre- and postdiagnosis BMI (five categories of loss/gain) and for prediagnostic alcohol consumption.

We performed several secondary analyses. For both pre- and postdiagnostic alcohol intake, we considered separate models according to breast cancer histology (ductal or lobular) and menopausal status at diagnosis. To evaluate the possibility that severity of illness affected alcohol intake, we conducted analyses excluding women who died within 2 years of completing the postdiagnosis survey ($n = 95$), those who did not report a mammogram or physician breast exam any time after their diagnosis ($n = 153$), and those who reported being in poor health ($n = 44$). We also calculated HRs for postdiagnostic intake that were not adjusted for prediagnostic consumption and not stratified by stage. Finally, we considered associations according to changes in consumption before and after diagnosis. All P values are two-sided, with $P \leq .05$ considered statistically significant without consideration of multiple comparisons. Analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Prediagnostic Alcohol Consumption

The median duration of follow-up after diagnosis was 11.3 years. During this time, 7,780 deaths occurred, including 3,484 resulting from breast cancer, 1,531 resulting from cardiovascular disease, and 2,765 resulting from other causes. Of the 22,890 women who completed the baseline questionnaire, 4,396 (19%) reported never drinking, 11,497 (50%) consumed one to two drinks/wk, 3,583 (16%) consumed three to six drinks/wk, 1,647 (7%) consumed seven to nine drinks/wk, and 1,767 (8%) consumed ≥ 10 drinks/wk. Compared with those who abstained from alcohol before diagnosis, drinkers were younger, of lower BMI, higher education, and were more likely to have smoked and used hormones (Table 1).

Associations between increasing prediagnostic alcohol consumption and disease-specific survival were not linear. Relative to nondrinkers, improved survival was observed for moderate prediagnostic consumption (three to six drinks/wk), and no association was observed for heavy consumption (≥ 10 drinks/wk; Table 2). These estimates were similar to minimally adjusted HRs (not shown) indicating minimal confounding by measured covariates. To further explore the dose-response pattern for alcohol consumption and mortality, we included quadratic terms to account for a U-shaped

Table 1. Characteristics at Breast Cancer Diagnosis According to Prediagnostic Alcohol Consumption

| Characteristic | Prediagnostic Alcohol Consumption (drinks/wk)* (N = 22,890) | | | | | | | | | |
|--|---|----|------------------|----|-----------------|----|-----------------|----|------------------|----|
| | 0 (n = 4,396) | | ≤ 2 (n = 11,497) | | 3-6 (n = 3,583) | | 7-9 (n = 1,647) | | ≥ 10 (n = 1,767) | |
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| Age, years | | | | | | | | | | |
| < 50 | 695 | 16 | 3,039 | 26 | 990 | 28 | 323 | 20 | 357 | 20 |
| 50-59 | 1,114 | 25 | 3,473 | 30 | 1,104 | 31 | 491 | 30 | 556 | 31 |
| 60-69 | 1,712 | 39 | 3,666 | 32 | 1,154 | 32 | 614 | 37 | 637 | 36 |
| 70-79 | 875 | 20 | 1,319 | 11 | 335 | 9 | 219 | 13 | 217 | 12 |
| State of residence | | | | | | | | | | |
| MA | 1,075 | 24 | 2,578 | 22 | 782 | 22 | 454 | 28 | 450 | 25 |
| NH | 435 | 10 | 737 | 6 | 215 | 6 | 182 | 11 | 172 | 10 |
| WI | 2,886 | 66 | 8,182 | 71 | 2,586 | 72 | 1011 | 61 | 1,145 | 65 |
| First-degree family history of breast cancer | | | | | | | | | | |
| No | 3,373 | 77 | 9,019 | 78 | 2,800 | 78 | 1,266 | 77 | 1,317 | 78 |
| Yes | 909 | 21 | 2,278 | 20 | 729 | 20 | 350 | 21 | 360 | 20 |
| Unknown | 114 | 3 | 200 | 2 | 54 | 2 | 31 | 2 | 36 | 2 |
| Age at first birth, years | | | | | | | | | | |
| < 20 | 745 | 17 | 1,544 | 13 | 445 | 12 | 144 | 9 | 227 | 13 |
| 20-24 | 1,718 | 39 | 4,607 | 40 | 1,406 | 39 | 676 | 41 | 655 | 37 |
| 25-29 | 881 | 20 | 2,678 | 23 | 836 | 23 | 383 | 23 | 397 | 22 |
| ≥ 30 | 404 | 9 | 1,234 | 12 | 380 | 11 | 166 | 10 | 164 | 9 |
| Nulliparous | 620 | 14 | 1,389 | 12 | 505 | 14 | 267 | 16 | 317 | 18 |
| Unknown | 28 | 1 | 45 | 0 | 11 | 0 | 11 | 1 | 7 | 0 |
| Menopausal status | | | | | | | | | | |
| Premenopausal | 787 | 18 | 3,295 | 29 | 1,078 | 30 | 365 | 22 | 429 | 24 |
| Postmenopausal | 3,419 | 78 | 7,554 | 66 | 2,297 | 64 | 1,198 | 78 | 1258 | 71 |
| Unknown | 190 | 4 | 648 | 6 | 208 | 6 | 84 | 5 | 80 | 5 |
| Postmenopausal hormone use† | | | | | | | | | | |
| Never | 2,099 | 61 | 3,976 | 53 | 1,136 | 49 | 620 | 52 | 693 | 55 |
| Former | 319 | 9 | 802 | 11 | 268 | 12 | 121 | 10 | 117 | 9 |
| Current‡ | 591 | 17 | 1,928 | 26 | 656 | 29 | 333 | 28 | 311 | 25 |
| Unknown | 410 | 12 | 848 | 11 | 237 | 10 | 124 | 10 | 137 | 11 |
| Body mass index, kg/m ² | | | | | | | | | | |
| < 18.5 | 77 | 2 | 177 | 2 | 56 | 2 | 41 | 2 | 48 | 3 |
| 18.5-24.9 | 1,646 | 37 | 5,128 | 45 | 2,026 | 57 | 975 | 59 | 977 | 55 |
| 25.0-29.9 | 1,376 | 31 | 3,628 | 32 | 1,022 | 29 | 448 | 27 | 520 | 29 |
| ≥ 30 | 1,205 | 27 | 2,458 | 21 | 452 | 13 | 174 | 11 | 204 | 12 |
| Unknown | 92 | 2 | 106 | 1 | 27 | 1 | 9 | 1 | 18 | 1 |
| Smoking status | | | | | | | | | | |
| Never | 2,559 | 58 | 6,308 | 55 | 1,499 | 42 | 551 | 33 | 422 | 24 |
| Former | 1,120 | 25 | 3,215 | 28 | 1,307 | 36 | 678 | 41 | 680 | 38 |
| Current‡ | 706 | 16 | 1,945 | 17 | 770 | 21 | 413 | 25 | 658 | 37 |
| Unknown | 11 | 0 | 29 | 0 | 7 | 0 | 5 | 0 | 7 | 0 |
| Education | | | | | | | | | | |
| Less than high school diploma | 795 | 18 | 1,171 | 10 | 274 | 8 | 114 | 7 | 170 | 10 |
| High school diploma | 1,939 | 44 | 4,903 | 43 | 1,401 | 39 | 645 | 39 | 749 | 42 |
| Some college | 923 | 21 | 2,837 | 25 | 905 | 25 | 432 | 26 | 417 | 24 |
| College degree | 716 | 16 | 2,552 | 22 | 996 | 28 | 453 | 28 | 421 | 24 |
| Unknown | 23 | 1 | 34 | 0 | 7 | 0 | 3 | 0 | 10 | 1 |
| Mammography | | | | | | | | | | |
| Never | 966 | 22 | 2,216 | 19 | 669 | 19 | 278 | 17 | 322 | 19 |
| Ever | 2,777 | 63 | 7781 | 68 | 2,468 | 69 | 1,137 | 69 | 1,145 | 65 |
| Unknown | 653 | 15 | 1,500 | 13 | 446 | 12 | 232 | 14 | 290 | 16 |
| Stage of disease | | | | | | | | | | |
| Localized | 2,621 | 60 | 7,061 | 61 | 2,217 | 62 | 1,054 | 64 | 1,099 | 62 |
| Regional | 1,290 | 29 | 3,422 | 30 | 1,035 | 29 | 425 | 26 | 484 | 27 |
| Distant | 126 | 3 | 212 | 2 | 60 | 2 | 32 | 2 | 36 | 2 |
| Unknown | 359 | 8 | 802 | 7 | 271 | 8 | 136 | 8 | 148 | 8 |

*Alcohol consumption as reported on baseline questionnaire.

†Premenopausal women are not included.

‡Current as of year before diagnosis.

Table 2. Association Between Prediagnostic Alcohol Consumption and Death From Breast Cancer, Cardiovascular Disease, or Any Cause

| Prediagnostic Alcohol Consumption (drinks/wk) | At Risk No. % | | Cause of Death | | | | | | | | |
|--|------------------|----|------------------|------|--------------|------------------------|------|--------------|------------------|------|--------------|
| | | | Breast Cancer | | | Cardiovascular Disease | | | Any Cause | | |
| | | | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI |
| Total | | | | | | | | | | | |
| 0 | 4,396 | 19 | 726 | 1 | Reference | 454 | 1 | Reference | 1,851 | 1 | Reference |
| 1-2 | 11,497 | 50 | 1,769 | 0.93 | 0.85 to 1.02 | 622 | 0.70 | 0.61 to 0.79 | 3,609 | 0.84 | 0.80 to 0.90 |
| 3-6 | 3,583 | 16 | 487 | 0.85 | 0.75 to 0.95 | 201 | 0.75 | 0.63 to 0.90 | 1,052 | 0.80 | 0.74 to 0.86 |
| 7-9 | 1,647 | 7 | 228 | 0.88 | 0.75 to 1.02 | 107 | 0.73 | 0.58 to 0.91 | 559 | 0.85 | 0.77 to 0.93 |
| ≥ 10 | 1,767 | 8 | 274 | 0.89 | 0.77 to 1.04 | 147 | 0.98 | 0.80 to 1.20 | 709 | 0.96 | 0.88 to 1.05 |
| Wine | | | | | | | | | | | |
| 0 | 8,914 | 39 | 1,474 | 1 | Reference | 816 | 1 | Reference | 3,655 | 1 | Reference |
| 1-2 | 11,469 | 50 | 1,692 | 0.98 | 0.91 to 1.06 | 607 | 0.77 | 0.68 to 0.86 | 3,466 | 0.88 | 0.84 to 0.93 |
| 3-6 | 1,521 | 7 | 176 | 0.85 | 0.72 to 1.01 | 55 | 0.65 | 0.49 to 0.86 | 348 | 0.75 | 0.67 to 0.84 |
| ≥ 7 | 986 | 4 | 142 | 1.11 | 0.93 to 1.34 | 53 | 0.81 | 0.61 to 1.08 | 311 | 0.97 | 0.85 to 1.09 |
| Beer | | | | | | | | | | | |
| 0 | 13,065 | 57 | 2,076 | 1 | Reference | 1,003 | 1 | Reference | 4,900 | 1 | Reference |
| 1-2 | 7,811 | 34 | 1,092 | 0.94 | 0.87 to 1.02 | 378 | 0.98 | 0.86 to 1.12 | 2,150 | 0.92 | 0.87 to 0.97 |
| 3-6 | 1,137 | 5 | 163 | 0.90 | 0.76 to 1.06 | 82 | 1.30 | 1.02 to 1.65 | 363 | 0.99 | 0.89 to 1.11 |
| ≥ 7 | 877 | 4 | 153 | 0.96 | 0.81 to 1.14 | 68 | 1.35 | 1.04 to 1.75 | 367 | 1.13 | 1.01 to 1.26 |
| Spirits | | | | | | | | | | | |
| 0 | 8,702 | 38 | 1,358 | 1 | Reference | 668 | 1 | Reference | 3,156 | 1 | Reference |
| 1-2 | 11,583 | 51 | 1,740 | 0.92 | 0.85 to 1.00 | 629 | 0.87 | 0.77 to 0.99 | 3,578 | 0.91 | 0.87 to 0.96 |
| 3-6 | 1,364 | 6 | 207 | 0.91 | 0.78 to 1.06 | 94 | 0.81 | 0.64 to 1.02 | 478 | 0.88 | 0.80 to 0.97 |
| ≥ 7 | 1,241 | 5 | 179 | 0.86 | 0.73 to 1.02 | 140 | 1.24 | 1.02 to 1.52 | 568 | 1.05 | 0.95 to 1.15 |

NOTE. HR adjusted for age at diagnosis, stage of disease at diagnosis, state of residence at diagnosis, study phase, family history of breast cancer, age at first birth, menopausal status, hormone therapy use, body mass index, smoking status, education, and mammography.
Abbreviation: HR, hazard ratio.

relation. When we did so, with 28 drinks/wk as the maximum allowable value, this quadratic term was statistically significantly associated with breast cancer-specific survival ($P = .03$). In general, our results were similar according to breast cancer histology (Appendix Table A1, online only).

HRs for the association between alcohol consumption and cardiovascular disease survival also suggested a U-shaped pattern with increasing alcohol consumption. A quadratic term for alcohol intake was associated with cardiovascular disease ($P = .01$) and all-cause mortality ($P = .001$). Trends for disease-specific and overall survival did not vary much by beverage type. Consumption of wine was associated with increased cardiovascular disease survival, whereas beer and spirit intake appeared to be associated with decreased cardiovascular disease survival, but these estimates are based on limited sample sizes and should be interpreted with caution.

Postdiagnostic Alcohol Consumption

In total, 1,140 women (23%) reported never drinking alcohol after their breast cancer diagnosis, 2,232 (46%) consumed one to two drinks/wk, 790 (1%) consumed three to six drinks/wk, 305 (%) consumed seven to nine drinks/wk, and 414 (9%) consumed ≥ 10 drinks/wk (Table 3). Compared with those who abstained from alcohol after diagnosis, drinkers were younger at diagnosis, more educated, and more likely to have had a mammogram before study enrollment (Appendix Table A2, online only). As was the case for prediagnostic alcohol consumption, heavy drinkers were more likely to smoke. Postdiagnostic drinkers were also more likely to have gained weight after diagnosis compared with postdiagnostic nondrinkers.

Disease-specific survival was similar in women who drank alcohol after diagnosis as compared with nondrinkers (Table 3). There was no association for a nonlinear term for weekly alcohol intake and breast cancer mortality ($P = .78$). No beverage-specific associations were observed. Trends in postdiagnostic consumption by histology were not considered because very few women with lobular disease were included in the survival cohort.

Women who consumed higher levels of alcohol after diagnosis were less likely than nondrinkers to die from cardiovascular disease. There was a similar association between increasing alcohol consumption and more favorable overall survival. The quadratic terms for cardiovascular disease-specific ($P = .07$) and all-cause mortality ($P = .04$) suggested that the relation with alcohol intake was nonlinear.

There remained no association between postdiagnostic alcohol consumption in models that did not adjust for prediagnostic alcohol intake and stage at diagnosis (data not shown). Results were essentially unchanged after excluding women who died within 2 years of completing the survey, did not report having a mammogram or physician breast exam after their diagnosis, or reported they were in poor health at the time of the questionnaire.

Change in Alcohol Consumption Before Versus After Diagnosis

Among women who reported both pre- and postdiagnostic alcohol consumption, the average weekly alcohol intake was not substantially different before and after diagnosis (mean drinks/wk: 3.4, standard deviation [SD] 5.6, prediagnostic; mean drinks/wk 3.2, SD

Table 3. Association Between Postdiagnostic Alcohol Consumption and Death From Breast Cancer, Cardiovascular Disease, or Any Cause

| Postdiagnostic Alcohol Consumption (drinks/wk) | At Risk No. % | | Cause of Death | | | | | | | | |
|---|------------------|----|------------------|------|--------------|------------------------|------|--------------|------------------|------|--------------|
| | | | Breast Cancer | | | Cardiovascular Disease | | | Any Cause | | |
| | | | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI |
| Total | | | | | | | | | | | |
| 0 | 1,140 | 23 | 69 | 1 | Reference | 97 | 1 | Reference | 326 | 1 | Reference |
| 1-2 | 2,232 | 46 | 122 | 0.88 | 0.61 to 1.27 | 125 | 1.00 | 0.72 to 1.40 | 467 | 0.89 | 0.75 to 1.06 |
| 3-6 | 790 | 16 | 39 | 0.80 | 0.49 to 1.32 | 28 | 0.61 | 0.37 to 1.03 | 141 | 0.77 | 0.60 to 0.98 |
| 7-9 | 305 | 6 | 21 | 1.01 | 0.55 to 1.87 | 11 | 0.50 | 0.24 to 1.03 | 57 | 0.63 | 0.45 to 0.88 |
| ≥ 10 | 414 | 9 | 25 | 0.83 | 0.45 to 1.54 | 15 | 0.47 | 0.24 to 0.91 | 78 | 0.64 | 0.47 to 0.88 |
| Wine | | | | | | | | | | | |
| 0 | 1,614 | 33 | 100 | 1 | Reference | 125 | 1 | Reference | 452 | 1 | Reference |
| 1-2 | 2,451 | 50 | 128 | 1.00 | 0.70 to 1.42 | 118 | 1.07 | 0.77 to 1.49 | 483 | 0.90 | 0.76 to 1.07 |
| 3-6 | 534 | 11 | 27 | 1.00 | 0.58 to 1.72 | 23 | 1.22 | 0.67 to 2.20 | 84 | 0.76 | 0.57 to 1.03 |
| ≥ 7 | 282 | 6 | 21 | 1.45 | 0.77 to 2.73 | 10 | 0.81 | 0.36 to 1.82 | 50 | 0.73 | 0.51 to 1.05 |
| Beer | | | | | | | | | | | |
| 0 | 2,830 | 58 | 157 | 1 | Reference | 195 | 1 | Reference | 696 | 1 | Reference |
| 1-2 | 1,731 | 36 | 102 | 1.26 | 0.88 to 1.79 | 74 | 0.85 | 0.58 to 1.24 | 322 | 1.02 | 0.85 to 1.23 |
| 3-6 | 215 | 4 | 10 | 1.04 | 0.49 to 2.22 | 5 | 0.68 | 0.25 to 1.82 | 32 | 1.04 | 0.69 to 1.57 |
| ≥ 7 | 105 | 2 | 7 | 0.94 | 0.37 to 2.39 | 2 | 0.44 | 0.10 to 2.06 | 19 | 0.91 | 0.53 to 1.57 |
| Spirits | | | | | | | | | | | |
| 0 | 2,406 | 49 | 146 | 1 | Reference | 168 | 1 | Reference | 604 | 1 | Reference |
| 1-2 | 1,826 | 37 | 94 | 0.74 | 0.53 to 1.03 | 78 | 0.78 | 0.54 to 1.11 | 327 | 0.84 | 0.70 to 1.00 |
| 3-6 | 394 | 8 | 20 | 0.78 | 0.45 to 1.36 | 17 | 0.65 | 0.35 to 1.21 | 79 | 0.86 | 0.65 to 1.14 |
| ≥ 7 | 255 | 5 | 16 | 0.83 | 0.43 to 1.62 | 13 | 0.51 | 0.25 to 1.05 | 59 | 0.69 | 0.49 to 0.98 |

NOTE. HR adjusted for prediagnostic alcohol consumption, age at diagnosis, stage of disease at diagnosis, state of residence at diagnosis, study phase, family history of breast cancer, age at first birth, menopausal status, hormone therapy use, body mass index, weight change, smoking status, education, and mammography.

Abbreviation: HR, hazard ratio.

5.8, postdiagnostic). At the extremes, 19% of prediagnostic regular (three or more drinks/wk) drinkers became nondrinkers after diagnosis, whereas 20% of prediagnostic nondrinkers reported regular (three or more drinks/wk) alcohol consumption after diagnosis. Compared with women who never consumed alcohol (before or after diagnosis), women who reported drinking more frequently after their breast cancer diagnosis were less likely to die from cardiovascular disease, although there was no association with breast cancer-specific survival (Table 4).

DISCUSSION

In this large population-based cohort of women with breast cancer, we found there was no linear association between prediagnostic alcohol consumption and disease-specific survival, but did find an inverse association for moderate levels of intake using a quadratic model. We evaluated whether postdiagnostic alcohol consumption was associated with survival in a subgroup of this population, independent of

Table 4. Association Between the Change in Alcohol Consumption Before and After Breast Cancer Diagnosis and Death From Breast Cancer, Cardiovascular Disease, or Any Cause

| Change in Alcohol Consumption Before and After Diagnosis | At Risk No. % | | Cause of Death | | | | | | | | |
|---|------------------|----|------------------|------|--------------|------------------------|------|--------------|------------------|------|--------------|
| | | | Breast Cancer | | | Cardiovascular Disease | | | Any Cause | | |
| | | | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI | No. of Deaths | HR | 95% CI |
| Total | | | | | | | | | | | |
| Never drinker* | 631 | 13 | 31 | 1 | Reference | 58 | 1 | Reference | 167 | 1 | Reference |
| < 1 drink/wk change | 2,096 | 43 | 110 | 0.96 | 0.63 to 1.46 | 101 | 0.64 | 0.45 to 0.90 | 418 | 0.86 | 0.71 to 1.03 |
| ≥ 1 drink/wk decrease | 1,241 | 25 | 82 | 1.33 | 0.87 to 2.05 | 95 | 0.87 | 0.61 to 1.23 | 336 | 1.03 | 0.85 to 1.25 |
| ≥ 1 drink/wk increase | 913 | 18 | 53 | 1.13 | 0.70 to 1.80 | 22 | 0.39 | 0.22 to 0.66 | 148 | 0.76 | 0.60 to 0.97 |
| HR per 1 drink/wk change | | | | 0.99 | 0.97 to 1.01 | | 0.96 | 0.93 to 0.98 | | 0.98 | 0.97 to 0.99 |

NOTE. HR adjusted for age at diagnosis, stage of disease at diagnosis, state of residence at diagnosis, study phase, family history of breast cancer, age at first birth, menopausal status, hormone therapy use, body mass index, weight change, smoking status, education, and mammography.

Abbreviation: HR, hazard ratio.

*Zero drinks/week reported on both the prediagnostic and postdiagnostic questionnaire.

prediagnostic consumption, and found no relation with disease-specific survival. We also observed that cardiovascular disease survival and overall survival were improved in women who consumed moderate levels of alcohol prediagnostically or postdiagnostically, consistent with prior literature.^{32,34,50,51} Furthermore, women who increased their level of alcohol consumption after breast cancer diagnosis had better survival from cardiovascular disease and other causes.

Population-based estimates suggest that approximately 65% of US women consume alcohol.⁵² Although women may alter their habits after breast cancer diagnosis,⁵³ our results do not support a meaningful effect of changing consumption patterns on breast cancer survival. Alcohol consumption is believed to influence breast cancer risk through increases in endogenous estrogens in both pre- and postmenopausal women.⁵⁴⁻⁵⁶ Limiting estrogen exposure is important in controlling breast cancer progression,⁵⁷ given evidence that oophorectomy in premenopausal women,⁵⁸ antiestrogens,⁵⁹ and aromatase inhibitors⁶⁰ are effective treatments for breast cancer. Reductions in alcohol intake might, therefore, be plausibly expected to improve breast cancer survival through similar mechanisms. Such parallel relationships with incidence and survival, though, have not always been observed for breast cancer. For example, some exposures known to increase risk of disease, such as hormone therapy or late age at first birth, do not appear to be positively associated with mortality in women with breast cancer.^{18,61-64} If alcohol use is an important promoting factor, then terminating alcohol use shortly after diagnosis might result in tumors that would be particularly responsive to treatment. We did not, however, observe differences in breast cancer–specific survival in women who continued alcohol intake postdiagnosis.

There is limited evidence relating postdiagnostic alcohol intake to clinical outcomes in women with breast cancer. Kwan et al¹⁷ observed that disease-specific mortality ($n = 154$ deaths) was increased in women consuming ≥ 6 versus 0 g/d at 2 years postdiagnosis (HR, 1.51; 95% CI, 1.00 to 2.29). Li et al⁶⁵ reported on a population-based case-control study of contralateral breast cancer where a statistically significant doubling of risk of second primary breast cancer was observed in women consuming seven or more drinks per week. Unlike our study, this design may also reflect the positive effect of alcohol on breast cancer incidence.⁵⁻¹¹ In contrast to Li et al,⁶⁵ the Women's Healthy Eating and Living study found the occurrence of new breast cancer events ($n = 518$) in breast cancer survivors did not differ according to baseline alcohol consumption (≥ 10 g/month v < 10 g/month) after a mean follow-up of 7.3 years.²⁷

Cardiovascular disease is increasingly recognized as an important contributor to mortality among breast cancer survivors.⁶⁶⁻⁶⁸ Deaths owing to cardiovascular causes may be related to the cardiotoxic and metabolic effects of some breast cancer treatments.⁶⁹ Our findings suggest that alcohol consumption, before and after breast cancer diagnosis, is associated with a reduced risk of death from cardiovascular disease. These results are reassuringly concordant with the previously described role for moderate levels of alcohol consumption in improved cardiovascular survival, regardless of breast cancer status.^{32,34,50,51}

Strengths of this study include its large sample size, long follow-up, and detailed information on both pre- and postdiagnosis alcohol intake. We used standardized and reliable instruments for exposures, including alcohol consumption.⁷⁰⁻⁷⁵ Our measurement of prediag-

nostic alcohol intake was based on recalled alcohol consumption habits from approximately 2 years before interview. We believe this retrospective interval yielded valid results, as our previous findings on alcohol and breast cancer risk in this study population⁷⁶ were consistent with the results from prospective cohort studies.^{5,8} We did not observe major changes in alcohol drinking habits after breast cancer diagnosis. Reassuringly, in another recent study of alcohol and breast cancer mortality, 92% of the subset of women with postdiagnosis alcohol intake reported the same level or adjacent category of intake as those that reported before diagnosis.¹⁴ Our confidence in these study results is enhanced by the incorporation of information on risk factors for breast cancer mortality, the minimal confounding by measured covariates, and the fact that our survival cohort reflects the spectrum of breast cancer as it occurs in the population.

Some limitations should be considered when interpreting our results. Hormone receptor status of tumors was not available. Estrogen receptor–positive tumors are the most common phenotype of breast cancer and may be associated with alcohol consumption.^{22,77,78} However, our inability to control for receptor positivity is unlikely to lead to an overestimation of the association between alcohol use and survival. That is, if alcohol use is related to survival only among those with hormone receptor–positive tumors, the heterogeneity of tumor types in our sample probably leads to conservatively biased estimates for alcohol consumption and survival. Because hormone receptor positivity increases with increasing age at diagnosis,⁷⁹ and our sample was primarily postmenopausal, we suspect that most women's tumors would have been hormone receptor positive. We did not have information on breast cancer recurrence or the occurrence of second primaries, such as ovarian cancers, which may be associated with alcohol consumption,⁸⁰ to support analyses of other end points.

Mammography is particularly important when considering survival. In our population, alcohol users were slightly more likely to have ever had a mammogram (68% of drinkers v 63% of nondrinkers). Because screening history was self-reported by each woman, residual confounding is possible. It is also conceivable that breast density confounded the association between alcohol consumption and breast cancer survival. Breast density is generally, but not always, positively associated with markers of poorer prognosis,⁸¹⁻⁸³ and women who drink are more likely to have greater breast density than those who do not.⁸⁴ Additionally, it remains unclear whether the effects of alcohol on breast cancer development and progression depend on other dietary factors, such as folate status,⁸⁵ which were not available for our analyses.

One practical concern of our postdiagnosis data is that our results may only be applicable to women who survive several years after diagnosis. Not all women with prediagnostic information were participants in our evaluation of postdiagnostic alcohol consumption. In general, women who participated in our postdiagnostic study were similar to nonresponders with respect to age, stage at diagnosis, reproductive history, and prediagnostic alcohol consumption, although there were differences in prediagnosis BMI and smoking status.³⁸ We previously found positive associations of increased alcohol intake with greater risk of developing breast cancer in our case-control analysis, consistent with previous prospective and retrospective studies,^{40,76} indicating that losses owing to death or other causes at the time of initial enrollment did not distort our evaluation.⁵⁻¹¹ In a sensitivity

analysis, we compared the results for prediagnostic alcohol consumption with the more limited CWLS and the total cohort in Table 2. Overall, the HRs were reassuringly similar (data not shown). Our observation of better overall survival for alcohol users compared with nonusers further demonstrates that any losses over follow-up may not introduce substantial bias. Finally, it is important to note that the reported level of consumption from a single follow-up questionnaire may not be fully representative of alcohol use across the entire postdiagnosis period.

In summary, this research suggests a U-shaped association between alcohol intake before breast cancer diagnosis and modestly better breast cancer survival. We did not observe this relationship with postdiagnostic alcohol consumption. This study also provides additional support for a beneficial role for moderate alcohol intake with respect to cardiovascular-specific and overall survival in women with breast cancer.

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Appendix**Table A1.** Association Between Prediagnostic Alcohol Consumption and Death From Breast Cancer, Cardiovascular Disease, or Any Cause

| Prediagnostic Alcohol Consumption (drinks/wk) | Breast Cancer Death According to Histology at Diagnosis | | | | | | | | | |
|--|---|----|------------------|------|--------------|-----------------------|----|------------------|------|--------------|
| | Ductal Breast Cancer | | | | | Lobular Breast Cancer | | | | |
| | At Risk | | No. of Deaths | HR | 95% CI | At Risk | | No. of Deaths | HR | 95% CI |
| | No. | % | | | | No. | % | | | |
| Total | | | | | | | | | | |
| 0 | 3,500 | 19 | 593 | 1 | Reference | 392 | 19 | 71 | 1 | Reference |
| 1-2 | 9,100 | 50 | 1,443 | 0.94 | 0.85 to 1.04 | 986 | 49 | 173 | 0.93 | 0.67 to 1.28 |
| 3-6 | 2,856 | 16 | 407 | 0.86 | 0.75 to 0.98 | 319 | 16 | 50 | 0.97 | 0.62 to 1.51 |
| 7-9 | 1,286 | 7 | 179 | 0.86 | 0.72 to 1.02 | 147 | 7 | 28 | 1.23 | 0.74 to 2.05 |
| ≥ 10 | 1,385 | 8 | 216 | 0.86 | 0.73 to 1.02 | 170 | 8 | 27 | 0.90 | 0.53 to 1.52 |
| Wine | | | | | | | | | | |
| 0 | 7,079 | 39 | 1,197 | 1 | Reference | 800 | 38 | 150 | 1 | Reference |
| 1-2 | 6,104 | 50 | 1,386 | 1.00 | 0.92 to 1.10 | 977 | 49 | 166 | 1.00 | 0.75 to 1.34 |
| 3-6 | 877 | 5 | 145 | 0.89 | 0.74 to 1.07 | 141 | 7 | 16 | 0.79 | 0.44 to 1.43 |
| ≥ 7 | 700 | 4 | 110 | 1.16 | 0.94 to 1.42 | 96 | 5 | 17 | 1.34 | 0.73 to 2.48 |
| Beer | | | | | | | | | | |
| 0 | 10,376 | 57 | 1,704 | 1 | Reference | 1,132 | 56 | 203 | 1 | Reference |
| 1-2 | 6,164 | 34 | 885 | 0.93 | 0.85 to 1.02 | 707 | 35 | 110 | 0.96 | 0.71 to 1.29 |
| 3-6 | 887 | 5 | 125 | 0.82 | 0.68 to 0.99 | 96 | 5 | 23 | 2.74 | 1.60 to 4.71 |
| ≥ 7 | 700 | 4 | 124 | 0.92 | 0.76 to 1.12 | 79 | 4 | 13 | 0.90 | 0.46 to 1.74 |
| Spirits | | | | | | | | | | |
| 0 | 6,913 | 38 | 1,113 | 1 | Reference | 754 | 37 | 125 | 1 | Reference |
| 1-2 | 9,151 | 50 | 1,417 | 0.91 | 0.83 to 1.00 | 1,018 | 51 | 178 | 0.89 | 0.66 to 1.20 |
| 3-6 | 1,100 | 6 | 170 | 0.90 | 0.76 to 1.06 | 125 | 6 | 25 | 0.72 | 0.41 to 1.25 |
| ≥ 7 | 963 | 5 | 138 | 0.82 | 0.68 to 0.99 | 117 | 6 | 21 | 1.08 | 0.60 to 1.96 |

NOTE. HR adjusted for age at diagnosis, stage of disease at diagnosis, state of residence at diagnosis, study phase, family history of breast cancer, age at first birth, menopausal status, hormone therapy use, body mass index, smoking status, education, and mammography.
Abbreviation: HR, hazard ratio.

Table A2. Characteristics at Breast Cancer Diagnosis and at the Follow-Up Interview According to Postdiagnostic Alcohol Consumption

| Characteristic | Postdiagnostic Alcohol Consumption (drinks/wk)* (N = 4,881) | | | | | | | | | |
|--|---|----|----------------------|----|---------------|----|---------------|----|---------------------|----|
| | 0 (n = 1,140) | | ≤ 2 (n = 2,232) | | 3-6 (n = 790) | | 7-9 (n = 305) | | ≥ 10 (n = 414) | |
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| At breast cancer diagnosis | | | | | | | | | | |
| Age, years | | | | | | | | | | |
| < 69 | | | | | | | | | | |
| -69 | | | | | | | | | | |
| -79 | | 1 | | | | | | | | |
| State of residence | | | | | | | | | | |
| MA | | | | | | | 1 | | 1 | 4 |
| NH | | | | | | | | | | |
| WI | | | 1, | | | | | | | |
| First-degree family history of breast cancer | | | | | | | | | | |
| No | | | ,7 | | | | | | | |
| Yes | | | | | | | | | | |
| Unknown | 18 | | 2 | 1 | | | | | 4 | 1 |
| Age at first birth, years | | | | | | | | | | |
| < 20 | | | | | | | 1 | | | |
| -24 | | | | | | | | | | |
| -29 | | | | 2 | | | | | | |
| ≥ 30 | | | | | | | | | | |
| Nulliparous | | | | | | | | | | |
| Unknown | | | | | | | | | | |
| Education | | | | | | | | | | |
| Less than high school diploma | | | | | | | 9 | 3 | 1 | |
| High school diploma | | | | 4 | | | | 3 | 1 | 3 |
| Some college | 2 | | | | 1 | | | | | |
| College degree | | | | | | | | | | |
| Unknown | 2 | | | | 1 | | | 0 | | |
| Mammography | | | | | | | | | | |
| Never | | | | 1 | 10 | 14 | | 1 | 5 | 12 |
| Ever | | | ,595 | | | | | | | |
| Unknown | | | | | | | | | | |
| Stage of disease | | | | | | | | | | |
| Localized | | | 1,502 | | 5 | | 2 | | | |
| Regional | 268 | 24 | 564 | 25 | 182 | 23 | 78 | 26 | 96 | 23 |
| Unknown | | | | | | | | | | |
| At follow-up | | | | | | | | | | |
| Age, years | | | | | | | | | | |
| < 50 | | | | | | | | | | 9 |
| -59 | | 2 | | | | 2 | | | 10 | 26 |
| -69 | | | | | | | | | | |
| ≥ 70 | | | | | | | 9 | 3 | | |
| Current postmenopausal hormone use†‡ | | | | | | | | | | |
| No | | | ,471 | | | | | | | |
| Yes | | | | | | | | | | |
| Unknown | | | | | | | | | | |
| Current smoking status‡ | | | | | | | | | | |
| No | ,030 | | ,035 | | | | | | | |
| Yes | | | | | | | | | | |
| Unknown | | | | 1 | 3 | | | | | 1 |
| Weight change since diagnosis, kg | | | | | | | | | | |
| < -.0 | | 2 | | | | | 5 | | | |
| -. to .0 | | | | | | | | | | |
| .1 to 6. | | | | | | | | | | |
| .1 to 10.0 | | | | | | | | | | |
| ≥ 10 | 154 | 14 | 309 | 14 | 97 | 12 | 26 | 9 | 42 | 10 |
| Unknown | 48 | 4 | 84 | 4 | 25 | 3 | 11 | 4 | 11 | 3 |

*Alcohol consumption as reported on follow-up questionnaire.

†Premenopausal women are not included.

‡Current as of year before follow-up interview.