Analysis of Alcohol Consumption on the Risk of Breast Cancer Among U.S. Women

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## Abstract

*Objective:* Researchers have identified hormonal, lifestyle, and environmental factors that may increase the risk of breast cancer. This study aims to investigate the differential effects of alcohol consumption on the risk of breast cancer during adulthood.

*Approach and Results:* A cross sectional study was conducted to determine the effects of alcohol consumption at three different levels – low/none, medium, or high – on the risk of breast cancer among U.S. women. The data was collected via the Center for Disease Control’s National Health and Nutrition Examination Survey (NHANES 2015-2016). Participants in the study were 1,560 women, aged 20-80 years. Odds ratios were calculated and then adjusted for smoking, body mass index (BMI), history of pregnancy, menopausal status, use of birth control pills, and use of female hormones. Using this adjusted model, the relationship between alcohol consumption and invasive breast cancer was assessed. No level of alcohol consumption was found to be related to risk of breast cancer in a significant manner.

*Conclusions:* The fact that the findings of this study were insignificant in all categories emphasizes the need for a larger sample size and a better survey design for any future studies.

## Introduction

While breast cancer can occur in both men and women, it's far more common in women with approximately 1 in 8 women being diagnosed with breast cancer during their lifetime vs 1 in 1,000 men. After skin cancer, breast cancer is the most commonly diagnosed cancer among women in the United States and the cancer with the second highest death rate13. In in recent years there have been higher prevention rates, and the number of deaths associated with this disease have decreased, largely due to factors such as earlier detection, a new personalized approach to treatment, and a better understanding of the disease as researchers have begun to identify hormonal, lifestyle, and environmental factors that may increase the risk of breast cancer. The most significant [risk factors](https://www.breastcancer.org/risk/factors) for breast cancer are that have been identified are gender (being a woman) and age (growing older), however other known risk factors may include family history, radiation exposure, obesity, and types of hormone therapy8, 10.

It has been shown previously that people who drink excessively have a greater risk of cancers of the oral cavity, esophagus, larynx, pharynx, liver, colon, and rectum2, 5-6. Following this line of thought, alcohol consumption was first identified as a potential risk factor of breast cancer in analyses of the Third National Cancer Survey data more than 30 years ago14. However, with this being said ongoing research is still being done to confirm the strength of this association as well as identify the biological mechanisms behind it. One possible mechanism that was suggested is alcohol's interaction and effect on oestrogen secretion1. Many lines of breast cancer cells depend on oestrogen and progesterone in growth. Higher levels of alcohol consumption trigger higher levels of oestrogen which may in turn trigger oestrogen sensitive breast tissue cells to become cancerous. It has also been suggested that alcohol may inhibit the absorption of folate, which may influence hormone receptor expression in tumors3, or that alcohol may cause natural damage to cells by acting as a carcinogen or making cells more susceptible to carcinogens9.

Past studies have been conducted to further analyze the relationship between alcohol consumption and breast cancer. In a 2004 study by McDonald et. al, it was shown that among the 4,575 women in the study population, recent consumption of 7 or more drinks per week was associated with a greater risk of breast cancer. This study also analyzed many potential confounders related to hormones as a possible biological mechanism behind this association, including number of full-term pregnancies, menopausal status, ever use of oral contraceptives, ever use of contraceptive shots and implants, and ever use of hormone replacement therapy. The results of this study seemed to indicated the importance of recent alcohol exposure and exposure later in life which leans to supporting the possibility that alcohol acts as a breast cancer promoter rather than as an initiator7.

Similarly, in a pooled analysis of 6 prospective cohort studies done by Smith-Warner et. al (1998), it was shown that for alcohol intakes of less than 60 g/d or 6 drinks per day which were reported by >99% of participants in the study, risk of breast cancer increased linearly with increasing consumption11. It is for this reason that we chose to analyze alcohol consumption at three different levels

Yet, while some studies indicate that alcohol consumption is linked with a higher risk of breast cancer, others show no association10. For this reason, our study was conducted to assess the differential effects of three levels of alcohol consumption on the risk of breast cancer. We predicted a positive association between levels of alcohol use and a higher risk of breast cancer and that higher levels of consumption would be associated with a higher risk of breast cancer. Our null hypothesis isthat there is no association between alcohol consumption and breast cancer. Our alternative hypothesis is that there is an association between alcohol consumption and breast cancer.

## Methodology

*Study Population*

The data for the participants in this study were collected from the Center for Disease Control’s 2015-2016 National Health and Nutrition Examination Survey (NHANES) questionnaire data set8. The population includes 1,560 female subjects, aged 20-80, who responded in some manner (yes/no) to both consuming alcohol and having cancer. All study participants provided informed consent to be included in the NHANES study prior to sharing health information.

*Exposure and Outcomes*

Both exposure and outcome information were self-reported by participants through the NHANES questionnaire. The primary predictor (exposure) in this study was alcohol consumption. Frequency, quantity, and age at consumption were ascertained through the question “Average number of alcoholic drinks/day in the past 12 months” 8. One drink was classified as a 12-ounce glass of beer, a 5-ounce glass of wine, or 1.5 ounces of liquor. Women were classified based on drinking levels as defined by the National Institute for Alcohol Abuse and Alcoholism. 0-1 drinks per day indicated light/no drinking, 2-3 drinks per day indicated moderate drinking, and 4-15 drinks per day indicated heavy drinking4.

The primary outcome in this study was the diagnosis of breast cancer; this was determined by two questions from this NHANES questionnaire. Firstly, if the participant had ever been told by a doctor or other health professional that he/she had cancer or a malignancy of any kind, and secondly what kind of cancer(s) the participant had8. This was classified as a yes/no binary variable.

Other variables taken into account for confounding were age, race, sex, smoking, body mass index (BMI), history of pregnancy, menopausal status, and different types of hormonal therapy including use of birth control pills, use of female hormones, and use of estrogen/progestin combination pills. All data for covariates were obtained from the NHANES questionnaire with the exception of menopausal status, which was not asked in the questionnaire, and as such this was determined by creating a binary variable divided at the average age of menopause observed for most women, between 45-55.

*Statistical analysis*

All of the data was analyzed using SAS 9.3 programming. Prior to analyzing data, any participants who had missing data for either the exposure or outcome variable were excluded. The exposure status was reported as a continuous variable from 1-15 which reflected the average number of alcoholic drinks per day over the past 12 months. This was divided into three categories. The outcome status reflected a binary variable of a yes/no answer reflecting if the participant had been told that they had a cancer or malignancy by a health professional followed by a subsequent question about that type of cancer it was. A univariate analysis was conducted on the average number alcoholic beverages consumed per day and breast cancer. A covariate analysis was done after using logistic regression in order assess for confounding using variables that had been previously studied and found to have a relationship with breast cancer. A crude odds ratio was compared to the adjusted odds ratio for each potential confounder and linear regression models were made in order to assess for any effect measure modifiers. Lastly, a final model was made to assess a total adjusted odds ratio compared to the original crude. An alpha value of 0.05 was used for all models.

## Results

After exclusion, our study population consisted of 1,560 U.S. women, aged 20 to 80 years old (Table 1). Prior to adjusting for potential covariates, there were no significant associations between alcohol consumption and breast cancer at any level. The low/no drinking group was used as this reference group in these analysis. A crude odds ratio of 0.784 for moderate alcohol consumption was observed which indicates that there are 0.78 times the odds of breast cancer among those who drank a moderate amount of alcohol compared to those who drank little to no alcohol over the study period. A crude odds ratio of 0.784 for moderate alcohol consumption was observed which indicates that there are 0.275 times the odds of developing breast cancer among women who drank a high amount of alcohol compared to those who drank little to no alcohol over the study period. It was determined by the fact that the 95% confidence intervals for both of these crude odds ratios both include the value of 1 that this association is insignificant (Table 3).

When considering the variables that entered the final model, no variables were shown to be statistically significant (Table 2), however six variables (BMI, smoking, history of pregnancy, use of birth control, use of female hormones, and menopausal status) were still used in the model as they are were significant in previous literature. There was no indication that any of the covariates used were effect measure modifiers when examining beta values as all p-values were greater than the a-priori alpha (p<0.05).

Following adjustment for potential confounders, there were still no significant associations between alcohol consumption and breast cancer at any level. An adjusted odds ratio of 1.388 with a 95% CI of 0.564-3.419 was determined for moderate alcohol drinkers and an adjusted odds ratio of 0.640 with a 95% CI of 0.133-3.070 among heavy alcohol drinkers (Table 3). As both of these confidence intervals included 1, it was concluded that this data is insignificant.

## Discussion

Alcohol has been identified and implicated by many research studies as a potential risk of breast cancer1,7,11,13, however there have also been some studies that dispute this association10. Moreover, it is not clear the dose-effect that alcohol may have on the risk of breast cancer. For this reason, it is still important to study the association, especially as the biological mechanism behind it is not completely understood. The purpose of this cross-sectional study was to determine whether alcohol consumption increases the risk of breast cancer among women in the U.S at different levels of consumption. As there were no significant associations found in this study we concluded based on this data that there is no association between alcohol consumption and breast cancer.

A limitation of the study is with the data itself as it was pre-existing data. The participants were given a long questionnaire to fill out in which it is very possible that may have not completed all of the questions, and if a question was left unanswered or the participant refused to answer the question, there was no way to rectify this. Moreover, it is a concern that there may be information bias in this study due to self-reporting and recall bias of answers regarding the exposure and potential covariates. Self-reporting could also potentially lead to misclassification as if the participants reported their information incorrectly then they would be classified incorrectly.

The study also had a relatively small sample size, as at first the sample population included 9,971 participants8 however after filtering the sample size decreased to only 1,560 female participants. Of these women, only 86 had breast cancer, and among these 86 only 48 also responded in some manner to the alcohol consumption question. It is possible that the prevalence of breast cancer in our study population may not be representative of the prevalence of breast cancer in the entire U.S. population as it is predicted that 1 in 8 women will develop breast cancer over her lifetime13 yet only 1/16th of the women in this study population reported having breast cancer. Additionally, as both the exposure and outcome were analyzed at the same time a temporal relationship cannot be established through this study design. However, advantages of this cross-sectional study design include the ability to test the prevalence of all factors under investigation and to obtain results quickly.

Another limitation of this study was the inability to assess all potential confounders. It has been shown that a woman’s risk of breast cancer nearly doubles if she has a first-degree relative (mother, sister, or daughter) who has been diagnosed with breast cancer **12**. Unfortunately, family history data was not available in the NHANES data set and as a result we were unable to account for this. Additionally, while a strength of this study was its consideration of many different hormonal factors that could potentially affect the development of breast cancer (history of pregnancy, menopausal status, use of birth control pills, use of female hormones), we were able to analyze estrogen/progestin combination pill usage. This served was a limitation because only a small percentage of the total women answered the question asked in the NHANES questionnaire regarding estrogen/progestin pill usage, and among our study population there were 1,415 missing answers for the 1,560 observations. Due to the small number of responses it was determined that it would not be statistically accurate to use this question variable in our study. Future studies would do well to include both of these variables, family history and estrogen/progestin combination pill usage, as potential confounders, as other studies have shown the importance of them1,7. Additionally, it would be interesting to also assess diet and folate intake as this has been shown to be a potential risk factor for breast cancer3.

It would also be important to increase the sample size, which would in turn increase the study power. If this study were to be repeated using the same source of data, adding more data from the same questions from a previous year of the NHANES questionnaire would be a good way to do this. With more resources and time, it would also be possible to conduct a prospective cohort study. This would allow for us to study the temporal relationship between alcohol consumption and breast cancer. Also, through a prospective study it might be possible eliminate some information bias as data would be from current records instead of from pre-existing records which would allow us to try to resolve any missing questions.

Unfortunately, breast cancer is a disease that is very prevalent among women in the United States, and for this reason it is crucial try to understand every facet of this disease. Given that alcohol use is very common in the United States with 78.3 percent of females age 18 or older reporting that they drank alcohol at some point in their lifetime and 62.9 percent of females reporting that they drank in the past year12 it is important to be aware of possible effects of this consumption. Hopefully, through future research we will be able to discover more about the effect of alcohol consumption on the risk of breast cancer which could prove to be very helpful in the prevention of the disease.

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## Tables

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No Breast Cancer**  N=1,474 | **History of Breast Cancer**  N=86 | |
| **Median Age, years** |  |  | |
|  | 45±17.5 | | 45±17.5 |
| **Alcohol Consumption, n (%)** |  |  | |
| Low/none  Medium  Heavy | 654, (42.0%)  642 (41.2%)  178 (11.4%) | 26 (1.67%)  20 (1.28%)  2 (0.128%) | |
| **Race, n (%)** |  |  | |
| White  Non-White | 558 (35.8%)  243 (15.6%) | 40 (2.56%)  11 (0.705%) | |
| **History of Pregnancy, n (%)** |  |  | |
| Yes  No | 1,198 (76.8%)  276 (17.7%) | 74 (4.74%)  12 (0.769%) | |
| **Menopausal Status, n (%)** |  |  | |
| Pre  Current/post | 745 (47.8%)  729 (46.7%) | 2 (0.128%)  84 (5.38%) | |
| **BMI, n (%)** |  |  | |
| Underweight  Normal  Overweight  Obese | 35 (2.24%)  408 (26.2%)  386 (24.7%)  645 (41.4%) | 5 (0.321%)  20 (1.28%)  26 (1.67%)  35 (2.24%) | |
| **Smoking Status, n (%)** |  |  | |
| Non-smoker  Smoker | 22 (1.41%)  552 (35.4%) | 0 (0.00%)  40 (2.56%) | |
| **Birth Control Usage, n (%)** |  |  | |
| Yes  No | 1,085 (69.6%)  389 (24.9%) | 53 (3.40%)  33 (2.12%) | |
| **Female Hormone Usage, n (%)** |  |  | |
| Yes  No | 231 (14.8%)  1,243 (79.7%) | 23 (1.47%)  63 (4.04%) | |

**Table 1.** Summary of Demographics (N=1,560).

|  |  |  |  |
| --- | --- | --- | --- |
| Covariate | **Estimate** | **P-Value** | **R2** |
| Age | 0.0552 (± 0.2456) | 0.822 | 0.0376 |
| Race | -0.4271 (± 0.2379) | 0.0727 | 0.0022 |
| Smoking | -0.2876 (± 0.3041) | 0.3443 | 0.0046 |
| BMI | -0.4185 (± 0.2372) | 0.0776 | 0.0027 |
| History of Pregnancy | -0.3959 (± 0.2363) | 0.0938 | 0.0036 |
| Menopausal Status | -0.0986 (± 0.2403) | 0.6814 | 0.0322 |
| Birth Control Pill Usage | -0.4109 (± 0.2359) | 0.0815 | 0.0028 |
| Female Hormone Usage | -0.3623 (± 0.2388) | 0.1291 | 0.0042 |
| Estrogen/Progestin Combination Pills | -0.3400 (± 0.5442) | 0.5321 | 0.0028 |

**Table 2.** Risk factors contributing to the relation between alcohol consumption and breast cancer.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Odds Ratio** | **95% Confidence Interval** | **P-Value** | **R2** |
| **Moderate Alcohol Consumption** |  |  |  |  |
| Crude                    Adjusted  \*models adjusted for smoking, BMI, history of pregnancy, menopausal status, birth control usage, and female hormone usage. | 0.784  1.388 | 0.433-1.418  0.564-3.419 | 0.3709  0.2769 | 0.0028  0.0421 |
| **Heavy Alcohol Consumption** |  |  |  |  |
| Crude                    Adjusted  \*models adjusted for smoking, BMI, history of pregnancy, menopausal status, birth control usage, and female hormone usage. | 0.283  0.640 | 0.066-1.202  0.133-3.070 | 0.1163  0.4221 | 0.0028  0.0421 |

**Table 3.** Relation between alcohol consumption and odds of breast cancer. Low/no alcohol consumption was used as the reference group.

Syntax

**data** epigroup5;

set epigroup4 (where=(RIAGENDR=**2**));

run;

**data** epigroup5;

set epigroup5;

if MCQ220 = **1** and MCQ230a = **14** or MCQ230b = **14** then breastcancer=**1**;

else breastcancer=**0**;

if MCQ220 = **.** or MCQ230a = **99** then breastcancer = **.**;

run;

**proc** **freq** data = epigroup5;

table breastcancer;

run;

**data** epigroup5;

set epigroup5;

if ALQ130 = **1** then alcohol = **0**;

else if **1** < ALQ130 <= **3** then alcohol = **1**;

else if **3** < ALQ130 <= **15** then alcohol = **2**;

if ALQ130 = **.** or ALQ130 = **999** then alcohol = **.**;

run;

**proc** **freq** data = epigroup5;

table alcohol;

run;

**proc** **freq** data = epigroup5;

table alcohol\*breastcancer;

run;

**proc** **freq** data = epigroup5;

where alcohol=**0** or alcohol=**1**;

table alcohol\*breastcancer / OR;

run;

**proc** **freq** data = epigroup5;

where alcohol=**0** or alcohol=**2**;

table alcohol\*breastcancer / OR;

run;

**data** epigroup6;

set epigroup5 (where=(alcohol=**0** or alcohol=**1** or alcohol=**2** and breastcancer=**0** or breastcancer=**1**));

run;

**proc** **contents** data = epigroup6;

run;

**proc** **univariate** data = epigroup6;

var RIDAGEYR;

run;

**proc** **univariate** data=epigroup6;

var RIDAGEYR;

histogram;

run;

proc freq;

table RIDAGEYR;

run;

**data** epigroup6;

set epigroup6;

if RIDAGEYR <= **35** then agegroup = **0**;

else if **35** < RIDAGEYR <= **54** then agegroup = **1**;

else if **55** < RIDAGEYR <= **80** then agegroup = **2**;

run;

**proc** **freq** data = epigroup6;

table agegroup;

run;

\*////////Crude analysis/////////;

proc logistic;

class alcohol (ref='0');

model breastcancer(event='1')= alcohol/rsquare;

run;

proc logistic;

model breastcancer(event='1')= alcohol agegroup/rsquare;

run;

**data** epigroup6;

set epigroup6;

if RIDRETH3 = **1** and **2** and **4** and **6** and **7** then race = **0**;

else if RIDRETH3 = **3** then race = **1**;

run;

**proc** **freq** data = epigroup6;

table race;

run;

proc logistic;

model breastcancer(event='1')= alcohol race/rsquare;

run;

**data** epigroup6;

set epigroup6;

if SMD030 = **0** then smoke = **0**;

else if SMD030 = **.** and **999** and **777** then smoke = **.**;

else smoke = **1**;

Run;

**proc** **freq** data = epigroup6;

table smoke;

Run;

proc logistic;

model breastcancer(event='1')= alcohol smoke/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if BMXBMI < **18.5** then BMI = **0**;

else if **18.5** <= BMXBMI <= **24.9** then BMI = **1**;

else if **25** <= BMXBMI <= **29.9** then BMI = **2**;

else if BMXBMI >= **30** then BMI = **3**;

run;

**proc** **freq** data = epigroup6;

table BMI;

Run;

proc logistic;

model breastcancer(event='1')= alcohol BMI/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if RIDAGEYR < **45** then menopause = **0**;

else menopause = **1**;

run;

**proc** **freq** data = epigroup6;

table menopause;

Run;

proc logistic;

model breastcancer(event='1')= alcohol menopause/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if RHQ131 = **1** then pregnancy = **0**;

else if RHQ131 = **7** or **9** and **.** then pregnancy = **.**;

else pregnancy = **1**;

Run;

**proc** **freq** data = epigroup6;

table pregnancy;

Run;

proc logistic;

model breastcancer(event='1')= alcohol pregnancy/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if RHQ420 = **2** then bc = **0**;

else if RHQ420 = **7** and **9** and **.** then bc = **.**;

else bc = **1**;

Run;

**proc** **freq** data = epigroup6;

table bc;

Run;

proc logistic;

model breastcancer(event='1')= alcohol bc/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if RHQ540 = **2** then fhormone = **0**;

else if RHQ540 = **7** and **9** and **.** then fhormone = **.**;

else fhormone = **1**;

Run;

**proc** **freq** data = epigroup6;

table fhormone;

Run;

proc logistic;

model breastcancer(event='1')= alcohol fhormone/rsquare;

Run;

**data** epigroup6;

set epigroup6;

if RHQ570 = **1** then ep\_pills = **1**;

else if RHQ570 = **2** then ep\_pills = **0**;

if RHQ570 = **.** then ep\_pills = **.**;

Run;

**proc** **freq** data = epigroup6;

table ep\_pills;

Run;

\*/////////FINAL MODEL////////;

**proc** **logistic** data=epigroup6;

class alcohol (ref='0');

model breastcancer(event='1')= alcohol BMI smoke pregnancy bc fhormone menopause/rsquare;

run;

**data** epigroup6;

set epigroup6;

inter1 = alcohol\*BMI;

Run;

proc logistic;

model breastcancer(event='1')= alcohol BMI inter1;

Run;

**data** epigroup6;

set epigroup6;

inter2 = alcohol\*smoke;

Run;

proc logistic;

model breastcancer(event='1')= alcohol smoke inter2;

Run;

**data** epigroup6;

set epigroup6;

inter3 = alcohol\*pregnancy;

Run;

proc logistic;

model breastcancer(event='1')= alcohol pregnancy inter3;

Run;

**data** epigroup6;

set epigroup6;

inter4 = alcohol\*bc;

Run;

proc logistic;

model breastcancer(event='1')= alcohol bc inter4;

Run;

**data** epigroup6;

set epigroup6;

inter5 = alcohol\*fhormone;

Run;

proc logistic;

model breastcancer(event='1')= alcohol fhormone inter5;

Run;

**data** epigroup6;

set epigroup6;

inter7 = alcohol\*menopause;

Run;

proc logistic;

model breastcancer(event='1')= alcohol menopause inter7;

Run;

**proc** **freq** data = epigroup6;

table breastcancer;

run;

**proc** **freq** data = epigroup6;

table alcohol\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table race\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table smoke\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table BMI\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table menopause\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table pregnancy\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table bc\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table fhormone\*breastcancer;

run;

**proc** **freq** data = epigroup6;

table RIDAGEYR\*breastcancer;

run;