

**Methods**

The data in this study is from an imputed version of the NHANES II<sup>1</sup>. The cross-sectional survey collected demographic, socioeconomic, and biomarker variables. Death occurrence during the follow-up was administered. The original impute dataset contains 11,258 observations. After excluding observations with missing values (2036 observations) and unreasonable age information (32 observations has age at baseline greater or equal to the age at last check up), a total of 9190 observations were included in this study.

The exposure is alcohol consumption (drinks/week) measured at baseline. The original exposure ranged from 0 to 77 drinks per week. During exploratory analysis, we found about 43.7% of people didn't take alcohol per week. After excluding people with 0 alcohol consumption, the minimum, median, and maximum alcohol consumption were 0.5, 2.0, and 77.0 per week. Thus, we divided people into four groups: 0 per week, 0-0.5 drinks per week, 0.5-2 drinks per week, and >2 drinks per week. Categorical and continuous versions of the exposure were both modeled to check the robustness of the findings. Another aim to utilize the categorical version was to mitigate the influence of leverage values of alcohol consumption.

We explored the distribution of following variables at baseline: sex, age (continuous), race (White, Black, and others), marital status (categorical), average smoking cigarettes per day (continuous), hypertension status at baseline (yes vs. no), average red blood cells at baseline (continuous), diagnosed myocardial infarction at baseline (yes vs. no), diabetes at baseline (continuous), size of residence place (categorical), and urban region (yes vs. no). Descriptive statistics were conducted. The unbalanced distribution indicated potential confounding and would be considered when modeling the outcome.

The outcome in this study is the incidence of death during the follow-up. The event time is recorded as time to death of cancer, or time to censoring, or time to death from other causes, whichever comes first. In our analysis, death from other causes served as competing risks and we treated them as censoring. This simplified procedure to deal with competing risks yields valid cause-specific hazard in Cox models, but its unbiasedness in Poisson and logistic models is not clear. Thus, we decided to use Cox models as the main analysis and to conduct Poisson and logistic models as sensitivity analysis. We considered two settings for time scale (The conceptual framework is shown in Figure S1 in Appendix):

1. Alcohol consumption can be perceived as a prevalent intake, which could induce the "prevalent user" bias. To acknowledge that the alcohol consumption might happen before the baseline, we chose age as the time scale and set the age of 21 to be the time origin. Following this approach, we conducted a crude model and a multivariate-adjusted (MV-adjusted) model. The MV-adjusted model only adjusted for sex and covariates related to socio-economic status. Baseline age was not adjusted since age was set as the time scale. Biomarkers and disease status at baseline were not adjusted for either because they might be the consequence of the prior alcohol consumption.
2. The second approach is setting the survey baseline as the time origin, and time since entry is the time scale. The study would be a simple cross-sectional study without further consideration in causal inference. We conducted a crude model, a model adjusting for baseline age, and a MV-adjusted model. In the MV-adjusted model, we adjusted for age, sex, and biomarkers and disease status at baseline. Confounders were chosen based on two criteria: 1) reasonable common causes, and 2) distribution across alcohol consumptions were unbalanced.

In the sensitivity analyses, Poisson and logistic regressions were conducted with the same exposure configurations and confounder adjustments as the Cox model following the second approach (setting year as the time scale).

We explored the potential effect modifications by sex through three approaches: (1) including a product term by sex and alcohol consumption in the MV-adjusted Cox model without stratification; (2) conducting stratified Cox regressions by sex and including an interaction term by sex and alcohol consumption; and (3) performing Cox regressions in males and females separately (as subgroup analysis).

We checked the proportional hazard assumption using Schofield residuals. Test results for the MV-adjusted models were reported. We also explored the nonlinear dose-response relationship between alcohol consumption and death from cancer. We first compared the category-specific hazard ratio. Based on the results from the main analysis, we replaced the linear term of alcohol consumption by a natural cubic spline term in the MV-adjusted model setting year as the time scale.

The statistical significance level was 0.05. R version 4.1.0 was used to clean data and conduct model analysis.

**Table 1.** Baseline characteristics of study population by alcohol consumption (N=9190)<sup>a</sup>.

	Alcohol consumption				p-value
	0/week	0-0.5/week	0.5-2/week	>2/week	

<sup>1</sup> <https://wwwn.cdc.gov/nchs/nhanes/nhanes2/default.aspx>

	N=4022 (43.76%)	N=935 (10.17%)	N=1720 (18.72%)	N=2513 (27.34%)	
Sex, Male	1430 (35.55%)	365 (39.04%)	851 (49.48%)	1668 (66.37%)	<0.001
Mean Age at entry (SD)	57.93 (12.80)	54.26 (13.37)	51.54 (13.53)	51.66 (13.17)	<0.001
Race					0.008
White	3469 (86.25%)	821 (87.81%)	1509 (87.73%)	2239 (89.10%)	
Black	474 (11.79%)	93 (9.95%)	191 (11.10%)	233 (9.27%)	
Other	79 (1.96%)	21 (2.24%)	20 (1.16%)	41 (1.63%)	
Mean year of schooling (SD)	9.98 (3.59)	11.03 (3.30)	11.40 (3.41)	12.06 (3.30)	<0.001
Marital status					<0.001
Married	2865 (71.23%)	679 (72.62%)	1284 (74.65%)	1961 (78.03%)	
Widowed	664 (16.51%)	125 (13.37%)	169 (9.83%)	168 (6.69%)	
Divorced	190 (4.72%)	67 (7.17%)	100 (5.81%)	168 (6.69%)	
Separated	94 (2.34%)	20 (2.14%)	59 (3.43%)	70 (2.79%)	
Never married	200 (4.97%)	40 (4.28%)	103 (5.99%)	139 (5.53%)	
Unknown	9 (0.22%)	4 (0.43%)	5 (0.29%)	7 (0.28%)	
Mean cigarettes per day (SD)	4.81 (10.85)	6.75 (12.65)	8.27 (13.78)	9.10 (13.92)	<0.001
Hypertension at baseline, Yes	1630 (40.53%)	307 (32.83%)	508 (29.53%)	718 (28.57%)	<0.001
Mean RBC (SD)	4.72 (0.72)	4.76 (0.72)	4.74 (0.70)	4.78 (0.70)	0.712
Diagnosed MI at baseline, Yes	280 (6.96%)	55 (5.88%)	82 (4.77%)	116 (4.62%)	<0.001
Diabetes at baseline, Yes	368 (9.15%)	53 (5.67%)	57 (3.31%)	62 (2.47%)	<0.001

a. Counts and proportions for the categorical variable, and mean and standard deviation for the continuous variables were reported. Chi-squared test and analysis of variance were conducted for the categorical variable and continuous variable respectively.

## Results

The baseline characteristics were reported in the *Table 1*. The proportion of males monotonically increased from the group with 0 drinks per week (35.55%) to the group with >2 drinks per week (66.37%). Additionally, we observed a positive correlation between average smoking cigarettes and alcohol consumption. Contrary to our expectation, the educational years monotonically increased from the group with 0 drinks per week (9.98 years) to the group with >2 drinks per week (12.06 years). Hypertension, myocardial infarction, and diabetes prevalence at baseline decreased with alcohol consumption level. Overall, in the study population, alcohol consumption showed strong correlation with sex, education years, smoking habit, and baseline disease status. Participants with basic morbidities tend to consume less alcohol at baseline. Residence features for the participants were shown in *Table S1 (appendix)*.

In the main analysis, we conducted Cox proportional hazard models for the risk of death from cancer with a homogeneity effect assumption<sup>2</sup>. *Table 2* presents results of five Cox regression models through two settings. Considering alcohol consumption as a categorical variable, we observed that there were no significant associations for alcohol consumption of 0-0.5 drinks per week and 0.5-2 drinks per week compared to 0 drinks per week. For the category >2 drinks per week, the first approach yielded an HR of 1.57 (95% CI, 1.29, 1.91) in the crude model and 1.25 (95% CI, 1.00, 1.54) in the MV-adjusted model. Following the second approach, the estimated HR was 1.15 (95% CI, 0.94, 1.39) in the crude model and was 1.24 (95% CI, 1.00, 1.55) in the MV-adjusted model. Consuming >2 drinks per week showed detrimental effect on the cancer death than consuming no drink. All the five models yielded similar results for the association between continuous alcohol consumption and the hazard of cancer death: the point estimates were around 1.03 and were of marginal significance.

To test the sensitivity of the findings to the model specification, we conducted logistic and Poisson regression with time since baseline as the time scale (*Table S2* in appendix). The results were consistent with the findings obtained using Cox models. Only the group with >2 drinks per week has a statistically significant association with death from cancer. The odds ratio from the MV-adjusted logistic regression was 1.29 (95% CI, 1.02, 1.63), and the incidence rate ratio from the MV-adjusted Poisson regression is 1.24 (95% CI 1.00, 1.55). Consistent with the beforementioned Cox regressions, the continuous alcohol consumption demonstrated statistically significant but weak association with cancer death in the MV-

<sup>2</sup> We also assumed additivity and linearity in our models.

adjusted logistic regression (OR = 1.03, 95% CI, 1.01, 1.04) and MV-adjusted Poisson regression (IRR = 1.02, 95% CI, 1.01, 1.09). To sum up, alcohol consumption showed a detrimental effect for death from cancer only with >2 drinks per week as a categorical variable, and a weak but significant harmful effect as a continuous variable.

With Schofield's residuals, we checked the proportional hazard assumption in the MV-adjusted Cox models (*Table S3* in appendix). Based on the corresponding chi-squared statistics and p-values for the exposure and for the whole model, we concluded that the assumption satisfied for the alcohol consumption in all MV-adjusted Cox models.

**Table 2.** Association between alcohol intake and hazard of death from cancer in overall NHANES II (N=9190).

	0/week	0-0.5/week	0.5-2/week	>2/week	Continuous	P <sub>trend</sub>
First approach, defining the exposure as alcohol intake age 21-entry, time scale as age						
Crude model	Ref	1.10 (0.82, 1.48)	1.13 (0.88, 1.44)	1.57 (1.29, 1.91)	1.04 (1.03, 1.05)	<0.001
Age-adjusted	Ref	-	-	-	-	-
MV-adjusted <sup>a</sup>	Ref	1.06 (0.78, 1.43)	0.98 (0.76, 1.27)	1.25 (1.00, 1.55)	1.02 (1.01, 1.04)	0.084
Second approach, defining the exposure as prevalent alcohol intake at baseline, time scale as years since entry						
Crude model	Ref	0.95 (0.70, 1.28)	0.83 (0.65, 1.06)	1.15 (0.94, 1.39)	1.03 (1.02, 1.04)	0.335
Age-adjusted	Ref	1.11 (0.82, 1.45)	1.13 (0.88, 1.45)	1.59 (1.30, 1.94)	1.04 (1.03, 1.05)	<0.001
MV-adjusted <sup>b</sup>	Ref	1.06 (0.79, 1.44)	0.98 (0.76, 1.26)	1.24 (1.00, 1.55)	1.03 (1.01, 1.04)	0.092

a. We adjusted for sex, race, education years, marital status, size of place, average cigarettes per day, standard metropolitan statistical area, and residence in urban region.

b. In addition to a., we adjusted for hypertension at baseline, RBC, diagnosed myocardial infarction, and diabetes.

**Table 3.** Associations between alcohol intake and hazard of death from cancer by sex from NHANES II (N=9190)<sup>a</sup>.

Alcohol consumption				
>2/week vs 0/week			Continuous	
First approach, defining the exposure as alcohol intake age 21-entry, time scale as age				
Adding interaction term				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.06 (0.82, 1.36)	0.053	1.02 (1.01, 1.04)	0.712
Male	0.69 (0.38, 1.27)		1.02 (0.97, 1.06)	
Stratified Cox				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.52 (1.06, 2.18)	0.122	1.03 (0.99, 1.07)	0.868
Male	1.08 (0.84, 1.40)		1.02 (1.01, 1.04)	
Subgroup analysis				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.35 (0.92-1.96)	0.231	1.02 (0.97-1.06)	0.293
Male	1.13 (0.87-1.48)		1.03 (1.01-1.04)	
Second approach, defining the exposure as prevalent alcohol intake at baseline, time scale as years since entry				
Adding interaction term				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.59 (1.11-2.28)	0.063	1.03 (0.99-1.07)	0.758
Male	1.06 (0.82-1.37)		1.02 (1.01-1.04)	
Stratified Cox				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.58 (1.10-2.27)	0.067	1.03 (0.99-1.07)	0.772
Male	1.06 (0.82-1.38)		1.02 (1.01-1.04)	
Subgroup analysis				
	MV-adjusted	p-value <sup>Heterogeneity</sup>	MV-adjusted	p-value <sup>Heterogeneity</sup>
Female	1.35 (0.93-1.98)	0.240	1.01 (0.97-1.06)	0.717
Male	1.15 (0.88-1.49)		1.03 (1.01-1.04)	

a. Wald tests were used to test the Heterogeneity in the effect of alcohol consumption in male and females.

We examined the potential modification of sex in MV-adjusted Cox models (*Table 3*). First, we compared the estimated hazard rate (HR) comparing >2 drinks per week to 0 drinks per week across males and females. We chose this comparison because this is the only one showing statistical significance with alcohol consumption as a categorical variable. The HRs estimated in the females were greater than in the males in all the models, indicating that alcohol consumption's harmful effects were more pronounced in the females than in the males. However, none of these differences was statistically significant across all the six models. Then we treated alcohol consumption as a continuous variable. All the six models yielded similar HR for males and females, very close to the estimates in the overall sample analysis in *Table 2*. The differences in HR by sex were of no statistical significance. Overall, no matter focusing on categorical or continuous alcohol consumption and no matter which model we conducted, we detected no statistically significant effect modification by sex.

In the primary analysis, we found that high dose of alcohol consumption showed significant harmful effect compared to low dose consumptions, indicating potential nonlinear dose-response relationship. Also, the findings following the first approach and those following the second approach was very close, and thus, we would explore the nonlinear only in the MV-adjusted model following the second approach. We fit a natural cubic spline with 3 degrees of freedom, and we found no clear curvature pattern (*Figure S2 appendix*). It indicated that the dose-response relationship between alcohol consumption and log hazards ratio was linear. The estimated 95% CI in the curve covered 1 before alcohol consumption of 5 drinks per week. This finding could partially explain why we found non-significance for the results from groups 0-0.5 and 0.5-2 drinks per week, but the significant association for the group >2 drinks per week.

## Discussion

In this study, we found a weak but significantly harmful effect for alcohol consumption on the cause-specific hazard of death from cancer. Taking alcohol less than 2 drinks per week does not significantly increase the hazard for death. The exploratory non-linear analysis shows that such a relationship is close to linear with a significant harmful effect only after 5 drinks per week. No significant sex difference is found in the relationship.

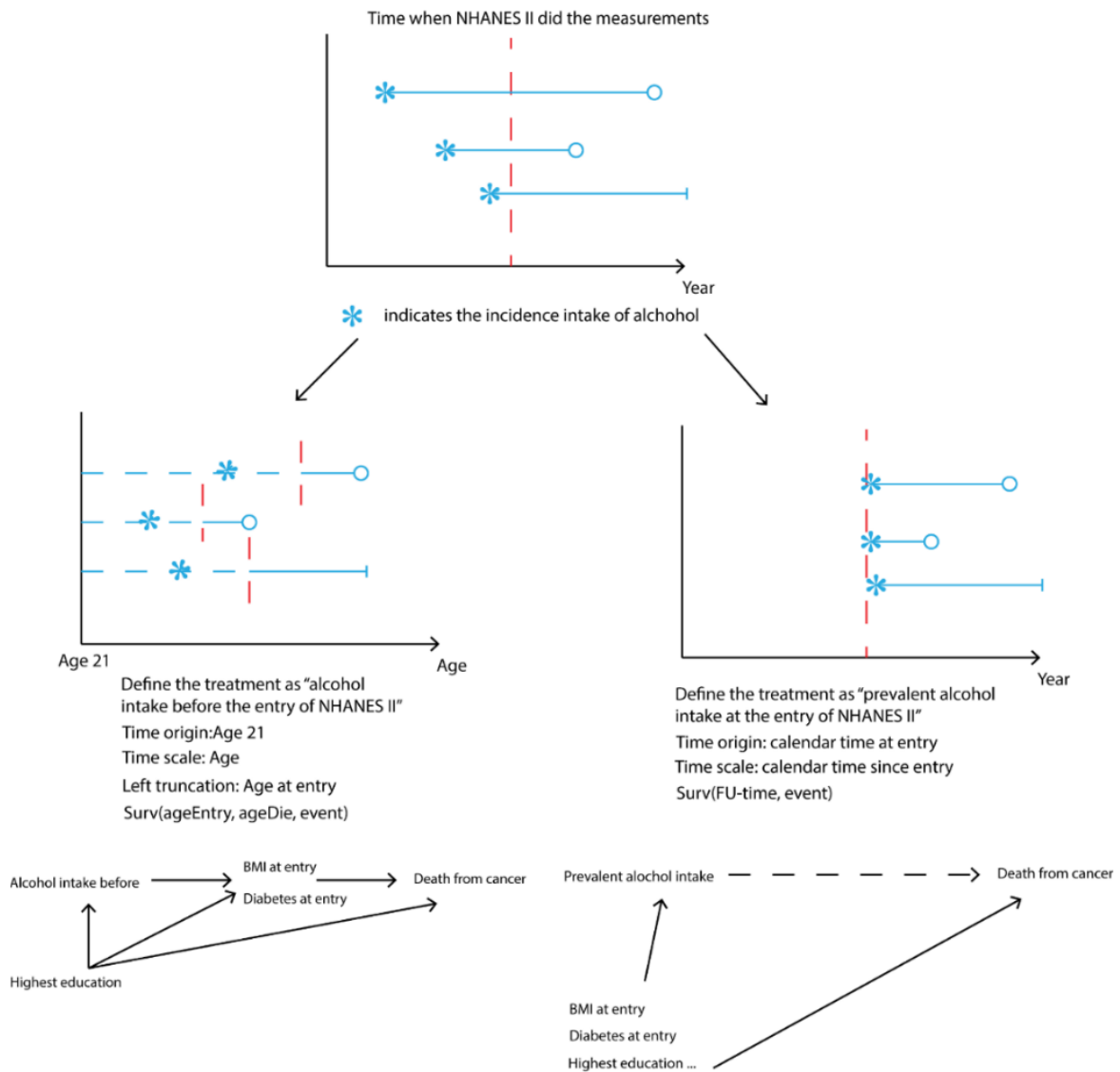
At baseline, the distribution of sex, education years, average cigarettes per day, hypertension, myocardial infarction, and diabetes are unbalanced across alcohol consumption groups. The unbalance suggests potential confounding. A reasonable explanation for the unbalance is that people with extent comorbidities tend to change their reduce alcohol consumption. The healthier population without comorbidities tend to attain the high level of alcohol consumption. Considering the pattern in the educational years, the population consuming high level of alcohol may not be the conventional low socio-economic status (SES) people but possibly be population with high SES.

In the primary analysis, we employed two different approaches to assess the association of alcohol consumption on hazard of cancer death. The first approach takes the age as the time scale and takes the temptation into account, which has a more reasonable causal structure. The second approach takes the whole dataset singly as a cross-sectional study and utilizes the time from entry as the time scale. The two approaches yield similar results in the MV-adjusted model. Given the data at hand, there are some explanations for the very similar findings in the two approaches. First, the estimated association for alcohol intake and cancer-specific death (about 1.03 HR per 1 drink/week increment) is very small. It is possible both two approaches, even including the logistic and Poisson regression, don't adjust for enough confounding. There could be residual confounding or other unknown confounders. Another explanation is that the additional adjustment (mainly diseases indicators) in the second approach had negligible influences given the prior adjustments in the first model. Lastly, it also could be the case that the true association is weak, and both approaches output the correct estimand.

In this study, we didn't detect significant effect modification by sex, though the point estimates for the >2 drinks per week group showed a more harmful effect among women than men. However, we cannot totally exclude the presence of potential effect modification since the model is of low power to detect such differences. We also explored some potential non-linear dose-response relationship, and we found the curve was pretty linear. This analysis also tells that no significant harmful effects manifest with a low dose of alcohol consumption (no greater than 5 drinks per week).

There are several limitations to our analysis. First, the original data is in the cross-sectional form, which limits the survival analysis. It is hard to tell which exposure or confounder happens first, making the model adjustment difficult and obscure. Second, we did not consider selection bias in the study. If censoring is dependent to cancer death, then there will be an open non-causal path between alcohol intake and cancer death, and causal methods will be needed to account for this selection bias. Last, we must notify that the event of interest in this study is the death from cancer. Deaths by other causes are competing risks but were treated as censored in this study. Although the Cox model is still valid, the logistic and Poisson regression are invalid, and their estimations are biased. Also, the interpretation for the findings from Cox models needs to be very careful, and the harmful effects on the hazards cannot translate to the effects on risks directly.

## Appendix



**Figure S1.** Conceptual framework for Cox proportional hazard models in the primary analysis

**Table S1.** Baseline characteristics for residence (N=9190)

	Alcohol consumption				p-value
	0/week	0-0.5/week	0.5-2/week	>2/week	
Size of residence place					<0.001
Urbanized are with 3, 000, 000 or more	310 (7.71%)	110 (11.76%)	282 (16.40%)	444 (17.67%)	
Urbanized area with 1,000,000 to 2,999,999	358 (8.90%)	134 (14.33%)	252 (14.65%)	439 (17.47%)	
Urbanized area with 250,000 to 999,999	428 (10.64%)	102 (10.91%)	218 (12.67%)	349 (13.89%)	
Urbanized area under 250,000	303 (7.53%)	83 (8.88%)	165 (9.59%)	234 (9.31%)	
Urban place 25,000 or more outside urbanized area	148 (3.68%)	39 (4.17%)	79 (4.59%)	108 (4.30%)	
Urban place 10,000 to 24,999 outside urbanized area	172 (4.28%)	43 (4.60%)	59 (3.43%)	96 (3.82%)	
Urban place 2,500 to 9,999 outside urbanized area	395 (9.82%)	73 (7.81%)	145 (8.43%)	164 (6.53%)	
Rural	1908 (47.44%)	351 (37.54%)	520 (30.23%)	679 (27.02%)	
Standard metropolitan statistical area					<0.001
In central city	915 (22.75%)	259 (27.70%)	524 (30.47%)	754 (30.00%)	
Not in central	741 (18.42%)	244 (26.10%)	570 (33.13%)	979 (38.96%)	
Not in SMSA	2366 (58.83%)	432 (46.20%)	626 (36.40%)	780 (31.04%)	
Resides in urban area, Yes	2118 (52.66%)	584 (62.55%)	1202 (69.88%)	1836 (73.06%)	<0.001

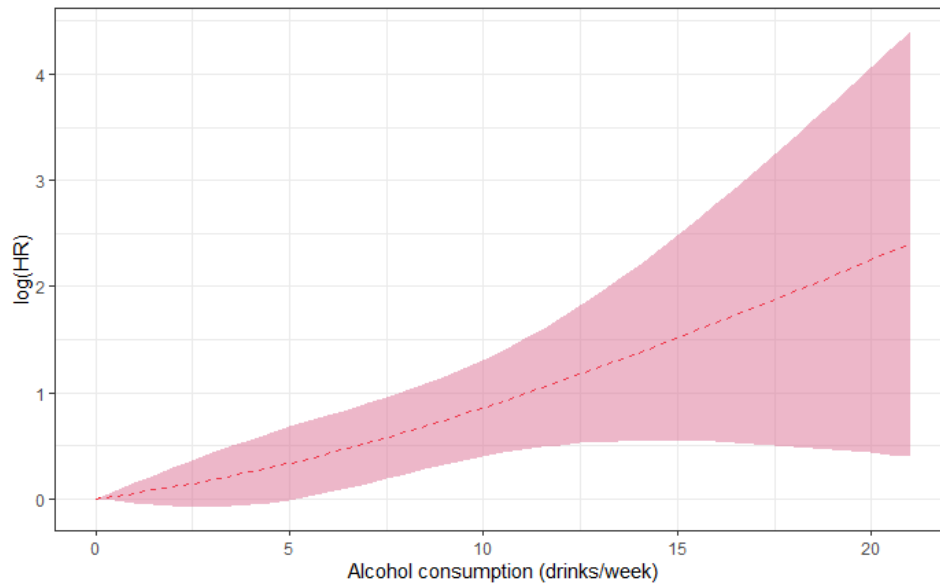
**Table S2.** Association between alcohol intake and hazard of death from cancer in overall NHANES II (N=9190).

		0/week	0-0.5/week	0.5-2/week	>2/week	Continuous	P <sub>trend</sub>
Logistics regression <sup>a</sup>							
Crude model	Ref		0.97 (0.72, 1.32)	0.87 (0.68, 1.12)	1.23 (1.00, 1.50)	1.03 (1.01, 1.05)	0.127
Age-adjusted	Ref		1.12 (0.82, 1.53)	1.17 (0.90, 1.51)	1.67 (1.36, 2.06)	1.04 (1.03, 1.06)	<0.001
MV-adjusted	Ref		1.06 (0.77, 1.45)	1.00 (0.77, 1.31)	1.29 (1.02, 1.63)	1.03 (1.01, 1.04)	0.054
Poisson regression <sup>a</sup>							
Crude model	Ref		0.95 (0.70, 1.27)	0.84 (0.66, 1.07)	1.16 (0.95, 1.41)	1.03 (1.02, 1.04)	0.309
Age-adjusted	Ref		1.11 (0.83, 1.50)	1.14 (0.89, 1.45)	1.60 (1.31, 1.95)	1.04 (1.03, 1.05)	<0.001
MV-adjusted	Ref		1.06 (0.79, 1.44)	0.98 (0.76, 1.27)	1.24 (1.00, 1.55)	1.02 (1.01, 1.09)	0.088

- a. Odds ratios are reported for logistic regressions and incidence rate ratios are reported for Poisson regressions.  
Log of follow-up years are set as the offset in Poisson regressions.

**Tables S3.** Tests for the proportional hazard assumption throughout the Cox models in the primary analysis (N=9190).

	Chi-squared statistic	p-value for alcohol consumption	Global p-value
First approach, defining the exposure as alcohol intake age 21-entry, time scale as age			
MV-adjusted categorical model	6.93	0.074	0.178
MV-adjusted continuous model	0.15	0.697	0.2326
Second approach, defining the exposure as prevalent alcohol intake at baseline, time scale as years since entry			
MV-adjusted categorical model	2.92	0.404	0.653
MV-adjusted continuous model	0.53	0.465	0.672

**Figure S2.** Dose-response relationship between alcohol consumption and log hazard ratio for death from cancer (N= 9190).



# Cox model

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This RMD file is corresponding to the Cox models in the main analysis following the second conceptual framework (the study is simplified as a cross-sectional study and time scale is time since entry)

## Load data and packages

```
library(tidyverse)

## -- Attaching packages ----- tidyverse 1.3.1 --
## v ggplot2 3.3.5      v purrr  0.3.4
## v tibble  3.1.6      v dplyr  1.0.8
## v tidyr   1.2.0      v stringr 1.4.0
## v readr   2.1.2      v forcats 0.5.1

## -- Conflicts ----- tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()

library(survival)
dta <- readRDS("clean_data_0425.rds")

dta$fu_time <- ifelse(!is.na(dta$DIE_YR), dta$DIE_YR - dta$EXAM_YR,
                     dta$LAST_YR-dta$EXAM_YR)
# exclude people whose follow-up time is 0
dta <- dta %>% filter(fu_time > 0)
```

## Main analysis

### Model 1: Crude analysis

```
dta$B00ZE_ord <- dta$B00ZE_q %>% as.numeric()
# categorical version
fit1_q <- coxph(Surv(fu_time, cancer_death) ~ B00ZE_q, data = dta)
fit1_q %>% summary()

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ B00ZE_q, data = dta)
##
##      n= 9190, number of events= 552
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
```

```
## B00ZE_q(0,0.5] -0.05525  0.94625  0.15213 -0.363  0.716
## B00ZE_q(0.5,2] -0.17802  0.83693  0.12506 -1.423  0.155
## B00ZE_q(2,77]  0.14322  1.15398  0.09963  1.437  0.151
##
##               exp(coef) exp(-coef) lower .95 upper .95
## B00ZE_q(0,0.5]  0.9462  1.0568  0.7023  1.275
## B00ZE_q(0.5,2]  0.8369  1.1948  0.6550  1.069
## B00ZE_q(2,77]  1.1540  0.8666  0.9493  1.403
##
## Concordance= 0.532 (se = 0.012 )
## Likelihood ratio test= 6.57 on 3 df,  p=0.09
## Wald test              = 6.5 on 3 df,  p=0.09
## Score (logrank) test = 6.53 on 3 df,  p=0.09

# continuous version
fit1_con <- coxph(Surv(fu_time, cancer_death) ~ B00ZE, data = dta)
fit1_con %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ B00ZE, data = dta)
##
## n= 9190, number of events= 552
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## B00ZE 0.029295  1.029728 0.006454 4.539 5.66e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##           exp(coef) exp(-coef) lower .95 upper .95
## B00ZE      1.03      0.9711      1.017      1.043
##
## Concordance= 0.515 (se = 0.013 )
## Likelihood ratio test= 15.91 on 1 df,  p=7e-05
## Wald test              = 20.6 on 1 df,  p=6e-06
## Score (logrank) test = 20.32 on 1 df,  p=7e-06
```

```
# ordinal version for p-value for trend
fit1_ord <- coxph(Surv(fu_time, cancer_death) ~ B00ZE_ord, data = dta)
fit1_ord %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ B00ZE_ord, data = dta)
##
## n= 9190, number of events= 552
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## B00ZE_ord 0.03206  1.03258 0.03323 0.965  0.335
##
##           exp(coef) exp(-coef) lower .95 upper .95
## B00ZE_ord      1.033      0.9684      0.9675      1.102
##
## Concordance= 0.509 (se = 0.012 )
## Likelihood ratio test= 0.93 on 1 df,  p=0.3
## Wald test              = 0.93 on 1 df,  p=0.3
## Score (logrank) test = 0.93 on 1 df,  p=0.3
```

## Model 2: Adjusting for age

```
# categorical version
fit2_q <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS, data = dta)
fit2_q %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS,
##       data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5] 0.105880  1.111688 0.152333  0.695    0.487
## BOOZE_q(0.5,2] 0.123222  1.131135 0.125812  0.979    0.327
## BOOZE_q(2,77]  0.472044  1.603267 0.101003  4.674 2.96e-06 ***
## AGEYRS          0.070455  1.072996 0.004475 15.744 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_q(0,0.5]      1.112      0.8995    0.8247    1.498
## BOOZE_q(0.5,2]      1.131      0.8841    0.8839    1.447
## BOOZE_q(2,77]      1.603      0.6237    1.3153    1.954
## AGEYRS              1.073      0.9320    1.0636    1.082
##
## Concordance= 0.715 (se = 0.01 )
## Likelihood ratio test= 332.5 on 4 df,  p=<2e-16
## Wald test               = 255.1 on 4 df,  p=<2e-16
## Score (logrank) test = 291.1 on 4 df,  p=<2e-16
```

```
# continuous version
fit2_con <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS, data = dta)
fit2_con %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS,
##       data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE  0.038740  1.039500 0.006129  6.321 2.6e-10 ***
## AGEYRS 0.069202  1.071653 0.004416 15.671 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE      1.040      0.9620    1.027    1.052
## AGEYRS      1.072      0.9331    1.062    1.081
##
## Concordance= 0.719 (se = 0.01 )
## Likelihood ratio test= 339.9 on 2 df,  p=<2e-16
## Wald test               = 269.9 on 2 df,  p=<2e-16
## Score (logrank) test = 306.5 on 2 df,  p=<2e-16
```

```
# ordinal version for p-value for trend
fit2_ord <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_ord + AGEYRS, data = dta)
fit2_ord %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_ord + AGEYRS,
##       data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_ord 0.14660   1.15789  0.03342  4.386 1.15e-05 ***
## AGEYRS    0.07063   1.07319  0.00447 15.800 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_ord      1.158      0.8636      1.084      1.236
## AGEYRS          1.073      0.9318      1.064      1.083
##
## Concordance= 0.715 (se = 0.01 )
## Likelihood ratio test= 329.9 on 2 df,  p=<2e-16
## Wald test               = 252.7 on 2 df,  p=<2e-16
## Score (logrank) test = 288.9 on 2 df,  p=<2e-16
```

### Model 3: MV-adjusted analysis

```
# categorical version
fit3_q <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS +
               SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) + AVGSMK + as
               HTN_REP + RBC + DRMI + DIAB, data = dta)
fit3_q %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS +
##       SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5]    0.062381  1.064368  0.153886  0.405  0.6852
## BOOZE_q(0.5,2]   -0.022538  0.977714  0.130281 -0.173  0.8627
## BOOZE_q(2,77]    0.216482  1.241701  0.111603  1.940  0.0524 .
## AGEYRS            0.078181  1.081318  0.004890 15.988 < 2e-16 ***
## SEX              -0.533047  0.586814  0.101146 -5.270 1.36e-07 ***
## as.factor(RACE)2  -0.065050  0.937021  0.154848 -0.420  0.6744
## as.factor(RACE)3  -0.466283  0.627330  0.416720 -1.119  0.2632
## GRADES            -0.014233  0.985868  0.012522 -1.137  0.2557
## as.factor(SIZE)2   0.163250  1.177331  0.168056  0.971  0.3313
## as.factor(SIZE)3   0.353475  1.424007  0.166891  2.118  0.0342 *
## as.factor(SIZE)4   0.006977  1.007001  0.194056  0.036  0.9713
## as.factor(SIZE)5  -0.095880  0.908573  0.322831 -0.297  0.7665
```

```

## as.factor(SIZE)6    0.048661  1.049864  0.306838  0.159    0.8740
## as.factor(SIZE)7   -0.049226  0.951966  0.261103 -0.189    0.8505
## as.factor(SIZE)8    1.769602  5.868518  0.738832  2.395    0.0166 *
## as.factor(MARRY)3   0.024005  1.024296  0.129198  0.186    0.8526
## as.factor(MARRY)4   0.231038  1.259907  0.182961  1.263    0.2067
## as.factor(MARRY)5  -0.131390  0.876875  0.328963 -0.399    0.6896
## as.factor(MARRY)6  -0.157045  0.854666  0.216598 -0.725    0.4684
## as.factor(MARRY)8   0.086953  1.090846  0.712647  0.122    0.9029
## AVGSMK              0.025014  1.025329  0.002750  9.097    < 2e-16 ***
## as.factor(SMSA)2    -0.198918  0.819617  0.134333 -1.481    0.1387
## as.factor(SMSA)4    -0.077507  0.925421  0.226029 -0.343    0.7317
## URBAN               -1.775186  0.169452  0.745544 -2.381    0.0173 *
## HTN_REP             -0.053813  0.947609  0.091773 -0.586    0.5576
## RBC                 0.004711  1.004723  0.061802  0.076    0.9392
## DRMI                -0.095295  0.909104  0.171634 -0.555    0.5787
## DIAB                -0.118480  0.888269  0.185637 -0.638    0.5233
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_q(0,0.5]      1.0644      0.9395      0.7872      1.4391
## BOOZE_q(0.5,2]      0.9777      1.0228      0.7574      1.2621
## BOOZE_q(2,77]       1.2417      0.8053      0.9977      1.5453
## AGEYRS              1.0813      0.9248      1.0710      1.0917
## SEX                 0.5868      1.7041      0.4813      0.7155
## as.factor(RACE)2     0.9370      1.0672      0.6917      1.2693
## as.factor(RACE)3     0.6273      1.5941      0.2772      1.4197
## GRADES              0.9859      1.0143      0.9620      1.0104
## as.factor(SIZE)2     1.1773      0.8494      0.8469      1.6366
## as.factor(SIZE)3     1.4240      0.7022      1.0267      1.9750
## as.factor(SIZE)4     1.0070      0.9930      0.6884      1.4730
## as.factor(SIZE)5     0.9086      1.1006      0.4826      1.7106
## as.factor(SIZE)6     1.0499      0.9525      0.5754      1.9156
## as.factor(SIZE)7     0.9520      1.0505      0.5707      1.5881
## as.factor(SIZE)8     5.8685      0.1704      1.3792     24.9703
## as.factor(MARRY)3    1.0243      0.9763      0.7952      1.3195
## as.factor(MARRY)4    1.2599      0.7937      0.8802      1.8033
## as.factor(MARRY)5    0.8769      1.1404      0.4602      1.6709
## as.factor(MARRY)6    0.8547      1.1700      0.5590      1.3067
## as.factor(MARRY)8    1.0908      0.9167      0.2699      4.4093
## AVGSMK              1.0253      0.9753      1.0198      1.0309
## as.factor(SMSA)2     0.8196      1.2201      0.6299      1.0665
## as.factor(SMSA)4     0.9254      1.0806      0.5942      1.4412
## URBAN               0.1695      5.9014      0.0393      0.7306
## HTN_REP             0.9476      1.0553      0.7916      1.1343
## RBC                 1.0047      0.9953      0.8901      1.1341
## DRMI                0.9091      1.1000      0.6494      1.2726
## DIAB                0.8883      1.1258      0.6173      1.2781
##
## Concordance= 0.753 (se = 0.01 )
## Likelihood ratio test= 471.8 on 28 df,  p=<2e-16
## Wald test              = 402.1 on 28 df,  p=<2e-16
## Score (logrank) test = 428.7 on 28 df,  p=<2e-16

```

```

# continuous version
fit3_con <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS +
                  SEX + as.factor(RACE) + GRADES + as.factor(SIZE)+ as.factor(MARRY) + AVGSMK + as.
                  HTN_REP + RBC + DRMI + DIAB, data = dta)
fit3_con %>% summary()

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS +
##       SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta)
##
## n= 9190, number of events= 552
##
##              coef exp(coef)  se(coef)      z Pr(>|z|)
## BOOZE          0.025297  1.025620  0.007071   3.578 0.000347 ***
## AGEYRS          0.078123  1.081255  0.004866  16.056 < 2e-16 ***
## SEX           -0.509585  0.600745  0.100083  -5.092 3.55e-07 ***
## as.factor(RACE)2 -0.058130  0.943527  0.154639  -0.376 0.706985
## as.factor(RACE)3 -0.450551  0.637277  0.416578  -1.082 0.279451
## GRADES         -0.013815  0.986280  0.012375  -1.116 0.264277
## as.factor(SIZE)2  0.149436  1.161180  0.168014   0.889 0.373773
## as.factor(SIZE)3  0.343525  1.409909  0.166630   2.062 0.039245 *
## as.factor(SIZE)4  0.004909  1.004921  0.193847   0.025 0.979797
## as.factor(SIZE)5 -0.112964  0.893183  0.322738  -0.350 0.726326
## as.factor(SIZE)6  0.040942  1.041791  0.306999   0.133 0.893908
## as.factor(SIZE)7 -0.068461  0.933830  0.260874  -0.262 0.792990
## as.factor(SIZE)8  1.823447  6.193169  0.737773   2.472 0.013453 *
## as.factor(MARRY)3 0.016787  1.016929  0.129056   0.130 0.896505
## as.factor(MARRY)4 0.234022  1.263673  0.182686   1.281 0.200191
## as.factor(MARRY)5 -0.128498  0.879415  0.328669  -0.391 0.695822
## as.factor(MARRY)6 -0.159279  0.852758  0.216308  -0.736 0.461514
## as.factor(MARRY)8 0.095722  1.100453  0.712576   0.134 0.893140
## AVGSMK          0.024881  1.025193  0.002741   9.077 < 2e-16 ***
## as.factor(SMSA)2 -0.196148  0.821890  0.134305  -1.460 0.144162
## as.factor(SMSA)4 -0.059435  0.942297  0.225652  -0.263 0.792250
## URBAN          -1.844398  0.158121  0.744804  -2.476 0.013273 *
## HTN_REP        -0.057840  0.943801  0.091702  -0.631 0.528210
## RBC             0.009358  1.009401  0.061458   0.152 0.878984
## DRMI           -0.086226  0.917387  0.171515  -0.503 0.615154
## DIAB           -0.111931  0.894106  0.185001  -0.605 0.545160
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## BOOZE          1.0256    0.9750    1.01150    1.0399
## AGEYRS          1.0813    0.9249    1.07099    1.0916
## SEX             0.6007    1.6646    0.49374    0.7309
## as.factor(RACE)2  0.9435    1.0599    0.69683    1.2776
## as.factor(RACE)3  0.6373    1.5692    0.28167    1.4418
## GRADES          0.9863    1.0139    0.96265    1.0105
## as.factor(SIZE)2  1.1612    0.8612    0.83538    1.6140
## as.factor(SIZE)3  1.4099    0.7093    1.01708    1.9545
## as.factor(SIZE)4  1.0049    0.9951    0.68727    1.4694

```

```
## as.factor(SIZE)5      0.8932      1.1196      0.47449      1.6813
## as.factor(SIZE)6      1.0418      0.9599      0.57077      1.9015
## as.factor(SIZE)7      0.9338      1.0709      0.56003      1.5571
## as.factor(SIZE)8      6.1932      0.1615      1.45854     26.2970
## as.factor(MARRY)3     1.0169      0.9834      0.78966      1.3096
## as.factor(MARRY)4     1.2637      0.7913      0.88335      1.8077
## as.factor(MARRY)5     0.8794      1.1371      0.46178      1.6748
## as.factor(MARRY)6     0.8528      1.1727      0.55809      1.3030
## as.factor(MARRY)8     1.1005      0.9087      0.27229      4.4475
## AVGSMK                1.0252      0.9754      1.01970      1.0307
## as.factor(SMSA)2      0.8219      1.2167      0.63167      1.0694
## as.factor(SMSA)4      0.9423      1.0612      0.60550      1.4664
## URBAN                 0.1581      6.3243      0.03673      0.6807
## HTN_REP               0.9438      1.0595      0.78854      1.1296
## RBC                   1.0094      0.9907      0.89485      1.1386
## DRMI                  0.9174      1.0901      0.65548      1.2839
## DIAB                  0.8941      1.1184      0.62218      1.2849
```

```
##
## Concordance= 0.755 (se = 0.01 )
## Likelihood ratio test= 477.7 on 26 df, p=<2e-16
## Wald test              = 411.4 on 26 df, p=<2e-16
## Score (logrank) test = 438.2 on 26 df, p=<2e-16
```

```
# ordinal version for p-value for trend
```

```
fit3_ord <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_ord + AGEYRS +
                  SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) + AVGSMK + as
                  HTN_REP + RBC + DRMI + DIAB, data = dta)
fit3_ord %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_ord + AGEYRS +
##       SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta)
##
## n= 9190, number of events= 552
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_ord      0.062151  1.064122  0.036847  1.687  0.0917 .
## AGEYRS          0.078365  1.081517  0.004886 16.039 < 2e-16 ***
## SEX            -0.538485  0.583632  0.100911 -5.336 9.49e-08 ***
## as.factor(RACE)2 -0.066634  0.935537  0.154802 -0.430  0.6669
## as.factor(RACE)3 -0.457329  0.632972  0.416624 -1.098  0.2723
## GRADES          -0.013534  0.986557  0.012497 -1.083  0.2788
## as.factor(SIZE)2  0.167929  1.182852  0.168016  0.999  0.3176
## as.factor(SIZE)3  0.360193  1.433606  0.166776  2.160  0.0308 *
## as.factor(SIZE)4  0.014382  1.014486  0.193901  0.074  0.9409
## as.factor(SIZE)5 -0.105015  0.900311  0.322890 -0.325  0.7450
## as.factor(SIZE)6  0.042319  1.043227  0.307031  0.138  0.8904
## as.factor(SIZE)7 -0.050068  0.951165  0.261082 -0.192  0.8479
## as.factor(SIZE)8  1.793805  6.012284  0.738198  2.430  0.0151 *
## as.factor(MARRY)3  0.025838  1.026174  0.129184  0.200  0.8415
## as.factor(MARRY)4  0.238907  1.269860  0.182786  1.307  0.1912
## as.factor(MARRY)5 -0.127184  0.880572  0.328802 -0.387  0.6989
## as.factor(MARRY)6 -0.159988  0.852154  0.216474 -0.739  0.4599
```

```

## as.factor(MARRY)8  0.086470  1.090319  0.712627  0.121  0.9034
## AVGSMK             0.024900  1.025212  0.002740  9.087  < 2e-16 ***
## as.factor(SMSA)2   -0.192976  0.824501  0.134187 -1.438  0.1504
## as.factor(SMSA)4   -0.064359  0.937668  0.225840 -0.285  0.7757
## URBAN              -1.800171  0.165271  0.744872 -2.417  0.0157 *
## HTN_REP            -0.051133  0.950153  0.091712 -0.558  0.5772
## RBC                 0.005406  1.005421  0.061781  0.088  0.9303
## DRMI               -0.105163  0.900178  0.171519 -0.613  0.5398
## DIAB               -0.111261  0.894706  0.185551 -0.600  0.5488
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_ord      1.0641      0.9397   0.98998   1.1438
## AGEYRS         1.0815      0.9246   1.07121   1.0919
## SEX            0.5836      1.7134   0.47890   0.7113
## as.factor(RACE)2  0.9355      1.0689   0.69071   1.2672
## as.factor(RACE)3  0.6330      1.5798   0.27974   1.4322
## GRADES         0.9866      1.0136   0.96269   1.0110
## as.factor(SIZE)2  1.1829      0.8454   0.85097   1.6442
## as.factor(SIZE)3  1.4336      0.6975   1.03388   1.9879
## as.factor(SIZE)4  1.0145      0.9857   0.69374   1.4835
## as.factor(SIZE)5  0.9003      1.1107   0.47813   1.6953
## as.factor(SIZE)6  1.0432      0.9586   0.57152   1.9042
## as.factor(SIZE)7  0.9512      1.0513   0.57019   1.5867
## as.factor(SIZE)8  6.0123      0.1663   1.41477  25.5502
## as.factor(MARRY)3  1.0262      0.9745   0.79663   1.3219
## as.factor(MARRY)4  1.2699      0.7875   0.88750   1.8170
## as.factor(MARRY)5  0.8806      1.1356   0.46226   1.6774
## as.factor(MARRY)6  0.8522      1.1735   0.55751   1.3025
## as.factor(MARRY)8  1.0903      0.9172   0.26975   4.4070
## AVGSMK          1.0252      0.9754   1.01972   1.0307
## as.factor(SMSA)2   0.8245      1.2129   0.63383   1.0725
## as.factor(SMSA)4   0.9377      1.0665   0.60230   1.4598
## URBAN            0.1653      6.0507   0.03838   0.7116
## HTN_REP          0.9502      1.0525   0.79383   1.1373
## RBC              1.0054      0.9946   0.89076   1.1348
## DRMI             0.9002      1.1109   0.64318   1.2599
## DIAB             0.8947      1.1177   0.62193   1.2871
##
## Concordance= 0.753 (se = 0.01 )
## Likelihood ratio test= 469.8 on 26 df,  p=<2e-16
## Wald test              = 401.1 on 26 df,  p=<2e-16
## Score (logrank) test = 427.2 on 26 df,  p=<2e-16

```

## Exploring effect modification by sex

### Sex interaction terms in the Cox model

```

dta$SEX <- if_else(dta$SEX == 1, "Male", "Female")

# categorical version
fit4_q <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + BOOZE_q:SEX + AGEYRS +

```



```

SEX + as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) + AVGSMK + as
HTN_REP + RBC + DRMI + DIAB, data = dta)
fit4_q %>% summary()

```

```

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + BOOZE_q:SEX +
## AGEYRS + SEX + as.factor(RACE) + GRADES + as.factor(MARRY) +
## as.factor(SIZE) + AVGSMK + as.factor(SMSA) + URBAN + HTN_REP +
## RBC + DRMI + DIAB, data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5]    0.302619  1.353399  0.207658  1.457   0.1450
## BOOZE_q(0.5,2]    0.286139  1.331278  0.190068  1.505   0.1322
## BOOZE_q(2,77]     0.463128  1.589037  0.183904  2.518   0.0118 *
## AGEYRS            0.078086  1.081215  0.004893 15.959 < 2e-16 ***
## SEXMale           0.783906  2.190009  0.139428  5.622 1.88e-08 ***
## as.factor(RACE)2  -0.066640  0.935532  0.154850 -0.430   0.6669
## as.factor(RACE)3  -0.467228  0.626737  0.416778 -1.121   0.2623
## GRADES            -0.014812  0.985297  0.012532 -1.182   0.2372
## as.factor(MARRY)3  0.030567  1.031039  0.129223  0.237   0.8130
## as.factor(MARRY)4  0.225202  1.252575  0.183173  1.229   0.2189
## as.factor(MARRY)5 -0.134948  0.873761  0.328997 -0.410   0.6817
## as.factor(MARRY)6 -0.156478  0.855150  0.216471 -0.723   0.4698
## as.factor(MARRY)8  0.023324  1.023598  0.713275  0.033   0.9739
## as.factor(SIZE)2   0.167515  1.182363  0.168075  0.997   0.3189
## as.factor(SIZE)3   0.361694  1.435759  0.166878  2.167   0.0302 *
## as.factor(SIZE)4   0.014946  1.015058  0.194024  0.077   0.9386
## as.factor(SIZE)5  -0.105367  0.899994  0.323012 -0.326   0.7443
## as.factor(SIZE)6   0.071535  1.074155  0.307017  0.233   0.8158
## as.factor(SIZE)7  -0.056982  0.944611  0.260965 -0.218   0.8272
## as.factor(SIZE)8   1.756008  5.789279  0.738936  2.376   0.0175 *
## AVGSMK            0.025052  1.025369  0.002761  9.073 < 2e-16 ***
## as.factor(SMSA)2  -0.198166  0.820234  0.134216 -1.476   0.1398
## as.factor(SMSA)4  -0.067451  0.934773  0.225930 -0.299   0.7653
## URBAN             -1.766685  0.170899  0.745551 -2.370   0.0178 *
## HTN_REP           -0.043962  0.956990  0.091853 -0.479   0.6322
## RBC                0.009946  1.009996  0.061852  0.161   0.8722
## DRMI              -0.090652  0.913335  0.171547 -0.528   0.5972
## DIAB              -0.112334  0.893746  0.185810 -0.605   0.5455
## BOOZE_q(0,0.5]:SEXMale -0.493872  0.610259  0.307189 -1.608   0.1079
## BOOZE_q(0.5,2]:SEXMale -0.555087  0.574023  0.252243 -2.201   0.0278 *
## BOOZE_q(2,77]:SEXMale -0.405682  0.666522  0.218054 -1.860   0.0628 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_q(0,0.5]    1.3534    0.7389   0.90088   2.0332
## BOOZE_q(0.5,2]    1.3313    0.7512   0.91724   1.9322
## BOOZE_q(2,77]     1.5890    0.6293   1.10814   2.2786
## AGEYRS            1.0812    0.9249   1.07090   1.0916
## SEXMale           2.1900    0.4566   1.66634   2.8782
## as.factor(RACE)2   0.9355    1.0689   0.69064   1.2673

```

```
## as.factor(RACE)3      0.6267      1.5956      0.27690      1.4186
## GRADES                0.9853      1.0149      0.96139      1.0098
## as.factor(MARRY)3     1.0310      0.9699      0.80035      1.3282
## as.factor(MARRY)4     1.2526      0.7984      0.87476      1.7936
## as.factor(MARRY)5     0.8738      1.1445      0.45851      1.6651
## as.factor(MARRY)6     0.8551      1.1694      0.55948      1.3071
## as.factor(MARRY)8     1.0236      0.9769      0.25292      4.1426
## as.factor(SIZE)2      1.1824      0.8458      0.85052      1.6437
## as.factor(SIZE)3      1.4358      0.6965      1.03522      1.9913
## as.factor(SIZE)4      1.0151      0.9852      0.69396      1.4847
## as.factor(SIZE)5      0.9000      1.1111      0.47785      1.6951
## as.factor(SIZE)6      1.0742      0.9310      0.58848      1.9607
## as.factor(SIZE)7      0.9446      1.0586      0.56640      1.5754
## as.factor(SIZE)8      5.7893      0.1727      1.36032      24.6381
## AVGSMD                1.0254      0.9753      1.01983      1.0309
## as.factor(SMSA)2      0.8202      1.2192      0.63051      1.0670
## as.factor(SMSA)4      0.9348      1.0698      0.60034      1.4555
## URBAN                 0.1709      5.8514      0.03964      0.7368
## HTN_REP               0.9570      1.0449      0.79932      1.1458
## RBC                   1.0100      0.9901      0.89469      1.1402
## DRMI                  0.9133      1.0949      0.65254      1.2784
## DIAB                  0.8937      1.1189      0.62094      1.2864
## BOOZE_q(0,0.5]:SEXMale 0.6103      1.6386      0.33422      1.1143
## BOOZE_q(0.5,2]:SEXMale 0.5740      1.7421      0.35012      0.9411
## BOOZE_q(2,77]:SEXMale  0.6665      1.5003      0.43472      1.0219
```

```
##
## Concordance= 0.754 (se = 0.01 )
## Likelihood ratio test= 478.9 on 31 df, p=<2e-16
## Wald test              = 408.7 on 31 df, p=<2e-16
## Score (logrank) test = 437.8 on 31 df, p=<2e-16
```

```
coef <- coef(fit4_q)[c(3, 31)] %>% as.matrix(ncol = 1)
vcov <- vcov(fit4_q)[c(3, 31), c(3, 31)]
var <- t(c(1, 1)) %*% vcov %*% c(1, 1)
sd <- sqrt(var)
mean_male <- coef[2,] + coef[1,]
exp(mean_male)
```

```
## BOOZE_q(2,77]:SEXMale
## 1.059128
```

```
c(mean_male - 1.96*sd, mean_male+ 1.96*sd) %>% exp()
```

```
## [1] 0.8187146 1.3701391
```

```
# Continuous version
```

```
fit4_con <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + BOOZE:SEX + AGEYRS +
                  SEX + as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) + AVGSMD + as
                  HTN_REP + RBC + DRMI + DIAB, data = dta)
fit4_con %>% summary()
```

```
## Call:
```

```
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + BOOZE:SEX +
## AGEYRS + SEX + as.factor(RACE) + GRADES + as.factor(MARRY) +
## as.factor(SIZE) + AVGSMD + as.factor(SMSA) + URBAN + HTN_REP +
## RBC + DRMI + DIAB, data = dta)
```

```

##
##   n= 9190, number of events= 552
##
##               coef exp(coef)   se(coef)      z Pr(>|z|)
## BOOZE          0.030800  1.031279  0.019053  1.617  0.1060
## AGEYRS          0.078126  1.081259  0.004866 16.054 < 2e-16 ***
## SEXMale         0.522100  1.685564  0.108219  4.825  1.4e-06 ***
## as.factor(RACE)2 -0.058404  0.943269  0.154645 -0.378  0.7057
## as.factor(RACE)3 -0.449974  0.637645  0.416591 -1.080  0.2801
## GRADES          -0.014027  0.986071  0.012392 -1.132  0.2577
## as.factor(MARRY)3  0.018414  1.018584  0.129168  0.143  0.8866
## as.factor(MARRY)4  0.234040  1.263695  0.182684  1.281  0.2002
## as.factor(MARRY)5 -0.127087  0.880657  0.328696 -0.387  0.6990
## as.factor(MARRY)6 -0.159358  0.852691  0.216306 -0.737  0.4613
## as.factor(MARRY)8  0.094250  1.098834  0.712587  0.132  0.8948
## as.factor(SIZE)2   0.150162  1.162023  0.168022  0.894  0.3715
## as.factor(SIZE)3   0.345427  1.412592  0.166742  2.072  0.0383 *
## as.factor(SIZE)4   0.007147  1.007173  0.193984  0.037  0.9706
## as.factor(SIZE)5  -0.113895  0.892352  0.322744 -0.353  0.7242
## as.factor(SIZE)6   0.041269  1.042133  0.306998  0.134  0.8931
## as.factor(SIZE)7  -0.069331  0.933017  0.260922 -0.266  0.7905
## as.factor(SIZE)8   1.825465  6.205679  0.737802  2.474  0.0134 *
## AVGSMK          0.024850  1.025161  0.002744  9.057 < 2e-16 ***
## as.factor(SMSA)2  -0.196562  0.821551  0.134291 -1.464  0.1433
## as.factor(SMSA)4  -0.056827  0.944757  0.225800 -0.252  0.8013
## URBAN           -1.846863  0.157731  0.744872 -2.479  0.0132 *
## HTN_REP          -0.056597  0.944975  0.091777 -0.617  0.5374
## RBC              0.009765  1.009813  0.061460  0.159  0.8738
## DRMI             -0.086738  0.916918  0.171529 -0.506  0.6131
## DIAB             -0.110376  0.895497  0.185070 -0.596  0.5509
## BOOZE:SEXMale    -0.006266  0.993753  0.020302 -0.309  0.7576
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE          1.0313      0.9697  0.99348  1.0705
## AGEYRS          1.0813      0.9248  1.07099  1.0916
## SEXMale         1.6856      0.5933  1.36342  2.0838
## as.factor(RACE)2  0.9433      1.0601  0.69663  1.2772
## as.factor(RACE)3  0.6376      1.5683  0.28182  1.4427
## GRADES          0.9861      1.0141  0.96241  1.0103
## as.factor(MARRY)3  1.0186      0.9818  0.79077  1.3120
## as.factor(MARRY)4  1.2637      0.7913  0.88337  1.8078
## as.factor(MARRY)5  0.8807      1.1355  0.46240  1.6772
## as.factor(MARRY)6  0.8527      1.1728  0.55805  1.3029
## as.factor(MARRY)8  1.0988      0.9101  0.27188  4.4411
## as.factor(SIZE)2   1.1620      0.8606  0.83598  1.6152
## as.factor(SIZE)3   1.4126      0.7079  1.01879  1.9586
## as.factor(SIZE)4   1.0072      0.9929  0.68863  1.4731
## as.factor(SIZE)5   0.8924      1.1206  0.47404  1.6798
## as.factor(SIZE)6   1.0421      0.9596  0.57096  1.9021
## as.factor(SIZE)7   0.9330      1.0718  0.55949  1.5559
## as.factor(SIZE)8   6.2057      0.1611  1.46141 26.3516
## AVGSMK          1.0252      0.9755  1.01966  1.0307

```

```
## as.factor(SMSA)2      0.8216      1.2172      0.63143      1.0689
## as.factor(SMSA)4      0.9448      1.0585      0.60690      1.4707
## URBAN                 0.1577      6.3399      0.03663      0.6791
## HTN_REP               0.9450      1.0582      0.78940      1.1312
## RBC                   1.0098      0.9903      0.89521      1.1391
## DRMI                  0.9169      1.0906      0.65513      1.2833
## DIAB                  0.8955      1.1167      0.62306      1.2871
## BOOZE:SEXMale        0.9938      1.0063      0.95499      1.0341
```

```
##
## Concordance= 0.755 (se = 0.01 )
## Likelihood ratio test= 477.8 on 27 df, p=<2e-16
## Wald test              = 411 on 27 df, p=<2e-16
## Score (logrank) test = 438.4 on 27 df, p=<2e-16
```

```
coef <- coef(fit4_con)[c(1, 27)] %>% as.matrix(ncol = 1)
vcov <- vcov(fit4_con)[c(1, 27), c(1, 27)]
var <- t(c(1, 1)) %*% vcov %*% c(1, 1)
sd <- sqrt(var)
mean_male <- coef[2,] + coef[1,]
exp(mean_male)
```

```
## BOOZE:SEXMale
##      1.024837
```

```
c(mean_male - 1.96*sd, mean_male+ 1.96*sd) %>% exp()
```

```
## [1] 1.009782 1.040117
```

## Stratified Cox model by sex, and adding an interaction term by SEX and alcohol consumption

```
# Categorical version
fit5_q <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + strata(SEX) + BOOZE_q:strata(SEX) + AGEYRS + as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) + AVGSMD + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI + DIAB, data = dta)
fit5_q %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + strata(SEX) + BOOZE_q:strata(SEX) + AGEYRS + as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) + AVGSMD + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI + DIAB, data = dta)
##
##      n= 9190, number of events= 552
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5]      0.300374  1.350364  0.207677  1.446  0.1481
## BOOZE_q(0.5,2]      0.280642  1.323980  0.190103  1.476  0.1399
## BOOZE_q(2,77]       0.460000  1.584074  0.183936  2.501  0.0124
## AGEYRS              0.077855  1.080966  0.004891 15.918 <2e-16
## as.factor(RACE)2     -0.066293  0.935857  0.154866 -0.428  0.6686
## as.factor(RACE)3     -0.466262  0.627343  0.416794 -1.119  0.2633
## GRADES              -0.014681  0.985426  0.012538 -1.171  0.2416
## as.factor(MARRY)3     0.032210  1.032734  0.129181  0.249  0.8031
## as.factor(MARRY)4     0.223209  1.250082  0.183193  1.218  0.2231
## as.factor(MARRY)5    -0.133737  0.874820  0.328993 -0.407  0.6844
```

```

## as.factor(MARRY)6      -0.158490  0.853432  0.216451 -0.732  0.4640
## as.factor(MARRY)8      0.028605  1.029018  0.713344  0.040  0.9680
## as.factor(SIZE)2       0.166094  1.180684  0.168084  0.988  0.3231
## as.factor(SIZE)3       0.362502  1.436921  0.166874  2.172  0.0298
## as.factor(SIZE)4       0.016400  1.016535  0.194023  0.085  0.9326
## as.factor(SIZE)5      -0.104615  0.900671  0.323020 -0.324  0.7460
## as.factor(SIZE)6       0.072781  1.075495  0.307076  0.237  0.8126
## as.factor(SIZE)7      -0.056924  0.944666  0.260976 -0.218  0.8273
## as.factor(SIZE)8       1.724272  5.608434  0.739043  2.333  0.0196
## AVGSMK                 0.024968  1.025282  0.002762  9.039  <2e-16
## as.factor(SMSA)2      -0.196934  0.821245  0.134203 -1.467  0.1423
## as.factor(SMSA)4      -0.069065  0.933266  0.225912 -0.306  0.7598
## URBAN                  -1.733064  0.176742  0.745653 -2.324  0.0201
## HTN_REP                -0.044148  0.956812  0.091822 -0.481  0.6307
## RBC                    0.012230  1.012305  0.061772  0.198  0.8431
## DRMI                   -0.094820  0.909537  0.171556 -0.553  0.5805
## DIAB                   -0.113823  0.892416  0.185809 -0.613  0.5402
## BOOZE_q(0,0.5]:strata(SEX)Male -0.491957  0.611428  0.307200 -1.601  0.1093
## BOOZE_q(0.5,2]:strata(SEX)Male -0.546088  0.579211  0.252285 -2.165  0.0304
## BOOZE_q(2,77]:strata(SEX)Male -0.398870  0.671078  0.218088 -1.829  0.0674
##
## BOOZE_q(0,0.5]
## BOOZE_q(0.5,2]
## BOOZE_q(2,77]          *
## AGEYRS                 ***
## as.factor(RACE)2
## as.factor(RACE)3
## GRADES
## as.factor(MARRY)3
## as.factor(MARRY)4
## as.factor(MARRY)5
## as.factor(MARRY)6
## as.factor(MARRY)8
## as.factor(SIZE)2
## as.factor(SIZE)3          *
## as.factor(SIZE)4
## as.factor(SIZE)5
## as.factor(SIZE)6
## as.factor(SIZE)7
## as.factor(SIZE)8          *
## AVGSMK                 ***
## as.factor(SMSA)2
## as.factor(SMSA)4
## URBAN                  *
## HTN_REP
## RBC
## DRMI
## DIAB
## BOOZE_q(0,0.5]:strata(SEX)Male
## BOOZE_q(0.5,2]:strata(SEX)Male *
## BOOZE_q(2,77]:strata(SEX)Male .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##

```

	exp(coef)	exp(-coef)	lower .95	upper .95
##				
## BOOZE_q(0,0.5]	1.3504	0.7405	0.89883	2.0287
## BOOZE_q(0.5,2]	1.3240	0.7553	0.91215	1.9218
## BOOZE_q(2,77]	1.5841	0.6313	1.10461	2.2717
## AGEYRS	1.0810	0.9251	1.07065	1.0914
## as.factor(RACE)2	0.9359	1.0685	0.69086	1.2677
## as.factor(RACE)3	0.6273	1.5940	0.27716	1.4200
## GRADES	0.9854	1.0148	0.96151	1.0099
## as.factor(MARRY)3	1.0327	0.9683	0.80173	1.3303
## as.factor(MARRY)4	1.2501	0.7999	0.87298	1.7901
## as.factor(MARRY)5	0.8748	1.1431	0.45907	1.6671
## as.factor(MARRY)6	0.8534	1.1717	0.55837	1.3044
## as.factor(MARRY)8	1.0290	0.9718	0.25423	4.1651
## as.factor(SIZE)2	1.1807	0.8470	0.84930	1.6414
## as.factor(SIZE)3	1.4369	0.6959	1.03607	1.9929
## as.factor(SIZE)4	1.0165	0.9837	0.69498	1.4869
## as.factor(SIZE)5	0.9007	1.1103	0.47820	1.6964
## as.factor(SIZE)6	1.0755	0.9298	0.58915	1.9633
## as.factor(SIZE)7	0.9447	1.0586	0.56642	1.5755
## as.factor(SIZE)8	5.6084	0.1783	1.31755	23.8735
## AVGSMK	1.0253	0.9753	1.01975	1.0308
## as.factor(SMSA)2	0.8212	1.2177	0.63130	1.0683
## as.factor(SMSA)4	0.9333	1.0715	0.59939	1.4531
## URBAN	0.1767	5.6580	0.04099	0.7622
## HTN_REP	0.9568	1.0451	0.79922	1.1455
## RBC	1.0123	0.9878	0.89687	1.1426
## DRMI	0.9095	1.0995	0.64982	1.2731
## DIAB	0.8924	1.1206	0.62002	1.2845
## BOOZE_q(0,0.5]:strata(SEX)Male	0.6114	1.6355	0.33485	1.1164
## BOOZE_q(0.5,2]:strata(SEX)Male	0.5792	1.7265	0.35326	0.9497
## BOOZE_q(2,77]:strata(SEX)Male	0.6711	1.4901	0.43766	1.0290
##				

```
## Concordance= 0.738 (se = 0.01 )
## Likelihood ratio test= 429.9 on 30 df, p=<2e-16
## Wald test = 353.9 on 30 df, p=<2e-16
## Score (logrank) test = 383.4 on 30 df, p=<2e-16
```

```
coef <- coef(fit5_q)[c(3, 30)] %>% as.matrix(ncol = 1)
vcov <- vcov(fit5_q)[c(3, 30), c(3, 30)]
var <- t(c(1, 1)) %*% vcov %*% c(1, 1)
sd <- sqrt(var)
mean_male <- coef[2,] + coef[1,]
exp(mean_male)
```

```
## BOOZE_q(2,77]:strata(SEX)Male
## 1.063037
```

```
c(mean_male - 1.96*sd, mean_male+ 1.96*sd) %>% exp()
```

```
## [1] 0.8217616 1.3751522
```

```
# Continuous version
```

```
fit5_cont <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + strata(SEX) + BOOZE:strata(SEX) + AGEYRS + as
HTN_REP + RBC + DRMI + DIAB, data = dta)
fit5_cont %>% summary()
```

```
## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + strata(SEX) +
##       BOOZE:strata(SEX) + AGEYRS + as.factor(RACE) + GRADES + as.factor(MARRY) +
##       as.factor(SIZE) + AVGSMK + as.factor(SMSA) + URBAN + HTN_REP +
##       RBC + DRMI + DIAB, data = dta)
##
## n= 9190, number of events= 552
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE           0.030383  1.030849  0.019053  1.595  0.1108
## AGEYRS           0.077876  1.080989  0.004865 16.009 <2e-16 ***
## as.factor(RACE)2 -0.058446  0.943229  0.154663 -0.378  0.7055
## as.factor(RACE)3 -0.449498  0.637948  0.416599 -1.079  0.2806
## GRADES          -0.013846  0.986249  0.012398 -1.117  0.2641
## as.factor(MARRY)3  0.020074  1.020277  0.129126  0.155  0.8765
## as.factor(MARRY)4  0.231805  1.260874  0.182702  1.269  0.2045
## as.factor(MARRY)5 -0.125861  0.881738  0.328694 -0.383  0.7018
## as.factor(MARRY)6 -0.161532  0.850839  0.216294 -0.747  0.4552
## as.factor(MARRY)8  0.099779  1.104927  0.712624  0.140  0.8886
## as.factor(SIZE)2   0.148899  1.160556  0.168026  0.886  0.3755
## as.factor(SIZE)3   0.345704  1.412985  0.166733  2.073  0.0381 *
## as.factor(SIZE)4   0.008757  1.008795  0.193967  0.045  0.9640
## as.factor(SIZE)5  -0.113205  0.892968  0.322759 -0.351  0.7258
## as.factor(SIZE)6   0.042694  1.043619  0.307055  0.139  0.8894
## as.factor(SIZE)7  -0.069086  0.933246  0.260948 -0.265  0.7912
## as.factor(SIZE)8   1.794065  6.013851  0.737925  2.431  0.0150 *
## AVGSMK           0.024763  1.025072  0.002745  9.020 <2e-16 ***
## as.factor(SMSA)2  -0.195066  0.822781  0.134280 -1.453  0.1463
## as.factor(SMSA)4  -0.058536  0.943144  0.225792 -0.259  0.7954
## URBAN            -1.813968  0.163006  0.744990 -2.435  0.0149 *
## HTN_REP          -0.056634  0.944940  0.091743 -0.617  0.5370
## RBC              0.012133  1.012207  0.061377  0.198  0.8433
## DRMI             -0.090597  0.913386  0.171533 -0.528  0.5974
## DIAB             -0.111247  0.894718  0.185062 -0.601  0.5478
## BOOZE:strata(SEX)Male -0.005884  0.994133  0.020297 -0.290  0.7719
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE           1.0308      0.9701   0.99306   1.070
## AGEYRS           1.0810      0.9251   1.07073   1.091
## as.factor(RACE)2  0.9432      1.0602   0.69658   1.277
## as.factor(RACE)3  0.6379      1.5675   0.28195   1.443
## GRADES           0.9862      1.0139   0.96257   1.011
## as.factor(MARRY)3  1.0203      0.9801   0.79215   1.314
## as.factor(MARRY)4  1.2609      0.7931   0.88136   1.804
## as.factor(MARRY)5  0.8817      1.1341   0.46297   1.679
## as.factor(MARRY)6  0.8508      1.1753   0.55685   1.300
## as.factor(MARRY)8  1.1049      0.9050   0.27337   4.466
## as.factor(SIZE)2   1.1606      0.8617   0.83491   1.613
## as.factor(SIZE)3   1.4130      0.7077   1.01909   1.959
## as.factor(SIZE)4   1.0088      0.9913   0.68976   1.475
## as.factor(SIZE)5   0.8930      1.1199   0.47435   1.681
## as.factor(SIZE)6   1.0436      0.9582   0.57171   1.905
```

```
## as.factor(SIZE)7      0.9332      1.0715      0.55960      1.556
## as.factor(SIZE)8      6.0139      0.1663      1.41589      25.543
## AVGSMK                1.0251      0.9755      1.01957      1.031
## as.factor(SMSA)2      0.8228      1.2154      0.63239      1.070
## as.factor(SMSA)4      0.9431      1.0603      0.60588      1.468
## URBAN                 0.1630      6.1347      0.03785      0.702
## HTN_REP               0.9449      1.0583      0.78943      1.131
## RBC                   1.0122      0.9879      0.89748      1.142
## DRMI                  0.9134      1.0948      0.65260      1.278
## DIAB                  0.8947      1.1177      0.62253      1.286
## BOOZE:strata(SEX)Male 0.9941      1.0059      0.95536      1.034
##
## Concordance= 0.739 (se = 0.01 )
## Likelihood ratio test= 428.9 on 26 df, p=<2e-16
## Wald test              = 355.5 on 26 df, p=<2e-16
## Score (logrank) test = 384.2 on 26 df, p=<2e-16

coef <- coef(fit5_cont)[c(1, 26)] %>% as.matrix(ncol = 1)
vcov <- vcov(fit5_cont)[c(1, 26), c(1, 26)]
var <- t(c(1, 1)) %*% vcov %*% c(1, 1)
sd <- sqrt(var)
mean_male <- coef[2,] + coef[1,]
exp(mean_male)
```

```
## BOOZE:strata(SEX)Male
##                1.024801
c(mean_male - 1.96*sd, mean_male+ 1.96*sd) %>% exp()

## [1] 1.009775 1.040050
```

## Subgroup analysis

```
# categorical version
fit6_q_m <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS + as.factor(RACE) + GRADES + as.factor(
  HTN_REP + RBC + DRMI + DIAB, data = dta[dta$SEX == "Male",])
fit6_q_m %>% summary()

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS +
##       as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta[dta$SEX == "Male", ])
##
##      n= 4314, number of events= 329
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5] -0.119329  0.887516  0.229390 -0.520  0.6029
## BOOZE_q(0.5,2] -0.219839  0.802648  0.174367 -1.261  0.2074
## BOOZE_q(2,77]  0.136033  1.145720  0.135379  1.005  0.3150
## AGEYRS         0.088349  1.092370  0.006724 13.140 < 2e-16 ***
## as.factor(RACE)2  0.014507  1.014613  0.190425  0.076  0.9393
## as.factor(RACE)3 -0.752925  0.470987  0.589271 -1.278  0.2013
## GRADES         -0.033238  0.967308  0.015547 -2.138  0.0325 *
## as.factor(MARRY)3 -0.040408  0.960397  0.227778 -0.177  0.8592
```



```

## as.factor(MARRY)4  0.114662  1.121494  0.271474  0.422  0.6728
## as.factor(MARRY)5 -0.269597  0.763687  0.424699 -0.635  0.5256
## as.factor(MARRY)6  0.083859  1.087475  0.264647  0.317  0.7513
## as.factor(MARRY)8 -0.065804  0.936315  1.015043 -0.065  0.9483
## as.factor(SIZE)2   0.219714  1.245721  0.223155  0.985  0.3248
## as.factor(SIZE)3   0.471345  1.602148  0.214932  2.193  0.0283 *
## as.factor(SIZE)4  -0.008270  0.991764  0.256648 -0.032  0.9743
## as.factor(SIZE)5  -0.032918  0.967618  0.417673 -0.079  0.9372
## as.factor(SIZE)6  -0.582896  0.558279  0.493430 -1.181  0.2375
## as.factor(SIZE)7  -0.066800  0.935382  0.356182 -0.188  0.8512
## as.factor(SIZE)8   1.639899  5.154651  0.768539  2.134  0.0329 *
## AVGSMDK           0.024089  1.024381  0.003367  7.155 8.35e-13 ***
## as.factor(SMSA)2  -0.173825  0.840444  0.176303 -0.986  0.3242
## as.factor(SMSA)4   0.213062  1.237462  0.318649  0.669  0.5037
## URBAN              -1.956302  0.141380  0.789058 -2.479  0.0132 *
## HTN_REP            -0.110896  0.895032  0.122633 -0.904  0.3658
## RBC                -0.118771  0.888011  0.094023 -1.263  0.2065
## DRMI               -0.049896  0.951328  0.193459 -0.258  0.7965
## DIAB               -0.044193  0.956769  0.238210 -0.186  0.8528
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_q(0,0.5]      0.8875      1.1267   0.56613   1.3913
## BOOZE_q(0.5,2]      0.8026      1.2459   0.57030   1.1297
## BOOZE_q(2,77]       1.1457      0.8728   0.87871   1.4939
## AGEYRS              1.0924      0.9154   1.07807   1.1069
## as.factor(RACE)2     1.0146      0.9856   0.69857   1.4736
## as.factor(RACE)3     0.4710      2.1232   0.14840   1.4949
## GRADES              0.9673      1.0338   0.93828   0.9972
## as.factor(MARRY)3    0.9604      1.0412   0.61456   1.5008
## as.factor(MARRY)4    1.1215      0.8917   0.65875   1.9093
## as.factor(MARRY)5    0.7637      1.3094   0.33221   1.7556
## as.factor(MARRY)6    1.0875      0.9196   0.64737   1.8268
## as.factor(MARRY)8    0.9363      1.0680   0.12806   6.8459
## as.factor(SIZE)2     1.2457      0.8027   0.80440   1.9292
## as.factor(SIZE)3     1.6021      0.6242   1.05136   2.4415
## as.factor(SIZE)4     0.9918      1.0083   0.59972   1.6401
## as.factor(SIZE)5     0.9676      1.0335   0.42676   2.1940
## as.factor(SIZE)6     0.5583      1.7912   0.21225   1.4685
## as.factor(SIZE)7     0.9354      1.0691   0.46538   1.8801
## as.factor(SIZE)8     5.1547      0.1940   1.14292  23.2478
## AVGSMDK             1.0244      0.9762   1.01764   1.0312
## as.factor(SMSA)2     0.8404      1.1898   0.59489   1.1873
## as.factor(SMSA)4     1.2375      0.8081   0.66267   2.3108
## URBAN                0.1414      7.0731   0.03011   0.6638
## HTN_REP              0.8950      1.1173   0.70381   1.1382
## RBC                  0.8880      1.1261   0.73856   1.0677
## DRMI                 0.9513      1.0512   0.65112   1.3900
## DIAB                 0.9568      1.0452   0.59985   1.5261
##
## Concordance= 0.772 (se = 0.012 )
## Likelihood ratio test= 333 on 27 df,  p=<2e-16
## Wald test              = 262.3 on 27 df,  p=<2e-16

```

```
## Score (logrank) test = 294.4 on 27 df, p=<2e-16
fit6_q_f <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS + as.factor(RACE) + GRADES + as.factor(
  HTN_REP + RBC + DRMI + DIAB, data = dta[dta$SEX == "Female",])

## Warning in coxph.fit(X, Y, istrat, offset, init, control, weights = weights, :
## Loglik converged before variable 19,23 ; coefficient may be infinite.
fit6_q_f %>% summary()

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS +
##       as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) +
##       AVGSМК + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta[dta$SEX == "Female", ])
##
## n= 4876, number of events= 223
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE_q(0,0.5]  2.346e-01  1.264e+00  2.101e-01  1.117  0.2641
## BOOZE_q(0.5,2]  1.785e-01  1.195e+00  1.959e-01  0.911  0.3621
## BOOZE_q(2,77]  3.028e-01  1.354e+00  1.940e-01  1.561  0.1186
## AGEYRS          6.231e-02  1.064e+00  7.383e-03  8.440 < 2e-16 ***
## as.factor(RACE)2 -3.387e-01  7.127e-01  2.776e-01 -1.220  0.2224
## as.factor(RACE)3 -1.188e-02  9.882e-01  5.903e-01 -0.020  0.9839
## GRADES          3.107e-02  1.032e+00  2.223e-02  1.398  0.1622
## as.factor(MARRY)3  1.736e-01  1.190e+00  1.624e-01  1.068  0.2854
## as.factor(MARRY)4  2.914e-01  1.338e+00  2.519e-01  1.157  0.2473
## as.factor(MARRY)5  1.062e-01  1.112e+00  5.257e-01  0.202  0.8400
## as.factor(MARRY)6 -5.246e-01  5.918e-01  3.937e-01 -1.332  0.1828
## as.factor(MARRY)8  5.692e-02  1.059e+00  1.010e+00  0.056  0.9551
## as.factor(SIZE)2  7.061e-02  1.073e+00  2.568e-01  0.275  0.7834
## as.factor(SIZE)3  1.723e-01  1.188e+00  2.672e-01  0.645  0.5190
## as.factor(SIZE)4  1.997e-02  1.020e+00  2.987e-01  0.067  0.9467
## as.factor(SIZE)5 -4.074e-01  6.654e-01  5.554e-01 -0.734  0.4632
## as.factor(SIZE)6  6.107e-01  1.842e+00  4.059e-01  1.505  0.1324
## as.factor(SIZE)7 -1.391e-01  8.701e-01  3.996e-01 -0.348  0.7277
## as.factor(SIZE)8 -1.101e+01  1.656e-05  1.123e+03 -0.010  0.9922
## AVGSМК          2.856e-02  1.029e+00  5.019e-03  5.691 1.27e-08 ***
## as.factor(SMSA)2 -2.101e-01  8.105e-01  2.083e-01 -1.009  0.3131
## as.factor(SMSA)4 -4.197e-01  6.572e-01  3.284e-01 -1.278  0.2012
## URBAN           1.138e+01  8.721e+04  1.123e+03  0.010  0.9919
## HTN_REP         1.116e-01  1.118e+00  1.408e-01  0.793  0.4281
## RBC             1.427e-01  1.153e+00  7.628e-02  1.871  0.0613 .
## DRMI            -3.667e-01  6.930e-01  3.878e-01 -0.946  0.3443
## DIAB            -2.153e-01  8.063e-01  3.017e-01 -0.713  0.4756
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## BOOZE_q(0,0.5]  1.264e+00  7.909e-01  0.8377  1.909
## BOOZE_q(0.5,2]  1.195e+00  8.365e-01  0.8143  1.755
## BOOZE_q(2,77]  1.354e+00  7.388e-01  0.9255  1.980
## AGEYRS          1.064e+00  9.396e-01  1.0490  1.080
## as.factor(RACE)2  7.127e-01  1.403e+00  0.4137  1.228
```

```

## as.factor(RACE)3  9.882e-01  1.012e+00  0.3107  3.143
## GRADES           1.032e+00  9.694e-01  0.9876  1.077
## as.factor(MARRY)3 1.190e+00  8.407e-01  0.8652  1.636
## as.factor(MARRY)4 1.338e+00  7.472e-01  0.8169  2.193
## as.factor(MARRY)5 1.112e+00  8.993e-01  0.3969  3.116
## as.factor(MARRY)6 5.918e-01  1.690e+00  0.2735  1.280
## as.factor(MARRY)8 1.059e+00  9.447e-01  0.1461  7.668
## as.factor(SIZE)2  1.073e+00  9.318e-01  0.6487  1.775
## as.factor(SIZE)3  1.188e+00  8.417e-01  0.7037  2.006
## as.factor(SIZE)4  1.020e+00  9.802e-01  0.5681  1.832
## as.factor(SIZE)5  6.654e-01  1.503e+00  0.2241  1.976
## as.factor(SIZE)6  1.842e+00  5.430e-01  0.8313  4.080
## as.factor(SIZE)7  8.701e-01  1.149e+00  0.3976  1.904
## as.factor(SIZE)8  1.656e-05  6.040e+04  0.0000  Inf
## AVGSMK           1.029e+00  9.718e-01  1.0189  1.039
## as.factor(SMSA)2  8.105e-01  1.234e+00  0.5388  1.219
## as.factor(SMSA)4  6.572e-01  1.522e+00  0.3453  1.251
## URBAN            8.721e+04  1.147e-05  0.0000  Inf
## HTN_REP          1.118e+00  8.944e-01  0.8484  1.473
## RBC              1.153e+00  8.670e-01  0.9932  1.339
## DRMI             6.930e-01  1.443e+00  0.3241  1.482
## DIAB            8.063e-01  1.240e+00  0.4463  1.457
##
## Concordance= 0.717 (se = 0.016 )
## Likelihood ratio test= 141.4 on 27 df, p=<2e-16
## Wald test              = 124.5 on 27 df, p=2e-14
## Score (logrank) test = 132.7 on 27 df, p=6e-16

z <- (coef(fit6_q_f)[3] - coef(fit6_q_m)[3])/sqrt(vcov(fit6_q_f)[3,3] + vcov(fit6_q_m)[3,3])
1 - pnorm(abs(z))

## BOOZE_q(2,77]
##      0.2404372

# continuous version
fit6_cont_m <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS + as.factor(RACE) + GRADES + as.factor(MARRY) +
                     HTN_REP + RBC + DRMI + DIAB, data = dta[dta$SEX == "Male",])
fit6_cont_m %>% summary()

## Call:
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS +
##       as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta[dta$SEX == "Male", ])
##
##      n= 4314, number of events= 329
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## BOOZE          0.027028  1.027396  0.007505  3.601 0.000316 ***
## AGEYRS          0.089025  1.093108  0.006717 13.254 < 2e-16 ***
## as.factor(RACE)2  0.032191  1.032715  0.190032  0.169 0.865485
## as.factor(RACE)3 -0.711462  0.490926  0.589152 -1.208 0.227200
## GRADES          -0.034877  0.965724  0.015428 -2.261 0.023780 *
## as.factor(MARRY)3 -0.071713  0.930798  0.228175 -0.314 0.753303
## as.factor(MARRY)4  0.124238  1.132285  0.270507  0.459 0.646034

```

```

## as.factor(MARRY)5 -0.253290 0.776243 0.423828 -0.598 0.550091
## as.factor(MARRY)6 0.083721 1.087326 0.264406 0.317 0.751517
## as.factor(MARRY)8 0.021485 1.021718 1.014861 0.021 0.983110
## as.factor(SIZE)2 0.200740 1.222307 0.223233 0.899 0.368525
## as.factor(SIZE)3 0.467983 1.596770 0.215059 2.176 0.029550 *
## as.factor(SIZE)4 0.002177 1.002180 0.256571 0.008 0.993229
## as.factor(SIZE)5 -0.068238 0.934038 0.417371 -0.163 0.870129
## as.factor(SIZE)6 -0.612824 0.541819 0.493718 -1.241 0.214516
## as.factor(SIZE)7 -0.081216 0.921994 0.355378 -0.229 0.819230
## as.factor(SIZE)8 1.760029 5.812603 0.767788 2.292 0.021886 *
## AVGSMK 0.023583 1.023863 0.003348 7.044 1.87e-12 ***
## as.factor(SMSA)2 -0.164745 0.848110 0.176423 -0.934 0.350402
## as.factor(SMSA)4 0.265983 1.304713 0.318330 0.836 0.403404
## URBAN -2.085212 0.124281 0.788630 -2.644 0.008191 **
## HTN_REP -0.113310 0.892873 0.122585 -0.924 0.355308
## RBC -0.105150 0.900190 0.093337 -1.127 0.259927
## DRMI -0.050182 0.951056 0.193419 -0.259 0.795288
## DIAB -0.014320 0.985783 0.237405 -0.060 0.951903
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## exp(coef) exp(-coef) lower .95 upper .95
## BOOZE 1.0274 0.9733 1.01239 1.0426
## AGEYRS 1.0931 0.9148 1.07881 1.1076
## as.factor(RACE)2 1.0327 0.9683 0.71158 1.4988
## as.factor(RACE)3 0.4909 2.0370 0.15471 1.5578
## GRADES 0.9657 1.0355 0.93696 0.9954
## as.factor(MARRY)3 0.9308 1.0743 0.59516 1.4557
## as.factor(MARRY)4 1.1323 0.8832 0.66635 1.9240
## as.factor(MARRY)5 0.7762 1.2883 0.33825 1.7814
## as.factor(MARRY)6 1.0873 0.9197 0.64759 1.8257
## as.factor(MARRY)8 1.0217 0.9787 0.13979 7.4676
## as.factor(SIZE)2 1.2223 0.8181 0.78916 1.8932
## as.factor(SIZE)3 1.5968 0.6263 1.04757 2.4339
## as.factor(SIZE)4 1.0022 0.9978 0.60611 1.6571
## as.factor(SIZE)5 0.9340 1.0706 0.41219 2.1166
## as.factor(SIZE)6 0.5418 1.8456 0.20587 1.4260
## as.factor(SIZE)7 0.9220 1.0846 0.45944 1.8502
## as.factor(SIZE)8 5.8126 0.1720 1.29071 26.1766
## AVGSMK 1.0239 0.9767 1.01717 1.0306
## as.factor(SMSA)2 0.8481 1.1791 0.60018 1.1985
## as.factor(SMSA)4 1.3047 0.7665 0.69912 2.4349
## URBAN 0.1243 8.0463 0.02649 0.5830
## HTN_REP 0.8929 1.1200 0.70218 1.1354
## RBC 0.9002 1.1109 0.74970 1.0809
## DRMI 0.9511 1.0515 0.65098 1.3895
## DIAB 0.9858 1.0144 0.61902 1.5699
##
## Concordance= 0.775 (se = 0.011 )
## Likelihood ratio test= 338.7 on 25 df, p=<2e-16
## Wald test = 269.3 on 25 df, p=<2e-16
## Score (logrank) test = 301 on 25 df, p=<2e-16

```

```
fit6_cont_f <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS + as.factor(RACE) + GRADES + as.factor(
  HTN_REP + RBC + DRMI + DIAB, data = dta[dta$SEX == "Female",])
```

```
## Warning in coxph.fit(X, Y, istrat, offset, init, control, weights = weights, :
## Loglik converged before variable 17,21 ; coefficient may be infinite.
```

```
fit6_cont_f %>% summary()
```

```
## Call:
```

```
## coxph(formula = Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS +
##       as.factor(RACE) + GRADES + as.factor(MARRY) + as.factor(SIZE) +
##       AVGSMK + as.factor(SMSA) + URBAN + HTN_REP + RBC + DRMI +
##       DIAB, data = dta[dta$SEX == "Female", ])
```

```
##
```

```
## n= 4876, number of events= 223
```

```
##
```

	coef	exp(coef)	se(coef)	z	Pr(> z )
## BOOZE	1.422e-02	1.014e+00	2.099e-02	0.677	0.4981
## AGEYRS	6.111e-02	1.063e+00	7.301e-03	8.370	< 2e-16 ***
## as.factor(RACE)2	-3.515e-01	7.037e-01	2.771e-01	-1.268	0.2047
## as.factor(RACE)3	-3.810e-02	9.626e-01	5.899e-01	-0.065	0.9485
## GRADES	3.648e-02	1.037e+00	2.195e-02	1.662	0.0965 .
## as.factor(MARRY)3	1.812e-01	1.199e+00	1.624e-01	1.116	0.2643
## as.factor(MARRY)4	2.890e-01	1.335e+00	2.519e-01	1.148	0.2511
## as.factor(MARRY)5	1.023e-01	1.108e+00	5.251e-01	0.195	0.8455
## as.factor(MARRY)6	-5.407e-01	5.824e-01	3.937e-01	-1.373	0.1697
## as.factor(MARRY)8	7.725e-02	1.080e+00	1.010e+00	0.077	0.9390
## as.factor(SIZE)2	5.776e-02	1.059e+00	2.565e-01	0.225	0.8218
## as.factor(SIZE)3	1.403e-01	1.151e+00	2.664e-01	0.527	0.5985
## as.factor(SIZE)4	-1.325e-02	9.868e-01	2.982e-01	-0.044	0.9646
## as.factor(SIZE)5	-3.917e-01	6.759e-01	5.549e-01	-0.706	0.4803
## as.factor(SIZE)6	5.865e-01	1.798e+00	4.052e-01	1.448	0.1477
## as.factor(SIZE)7	-1.499e-01	8.608e-01	3.995e-01	-0.375	0.7076
## as.factor(SIZE)8	-1.109e+01	1.534e+05	1.125e+03	-0.010	0.9921
## AVGSMK	2.910e-02	1.030e+00	4.956e-03	5.871	4.33e-09 ***
## as.factor(SMSA)2	-2.106e-01	8.101e-01	2.085e-01	-1.010	0.3125
## as.factor(SMSA)4	-4.605e-01	6.309e-01	3.278e-01	-1.405	0.1600
## URBAN	1.143e+01	9.180e+04	1.125e+03	0.010	0.9919
## HTN_REP	1.046e-01	1.110e+00	1.407e-01	0.744	0.4572
## RBC	1.351e-01	1.145e+00	7.611e-02	1.776	0.0758 .
## DRMI	-3.575e-01	6.994e-01	3.875e-01	-0.922	0.3563
## DIAB	-2.536e-01	7.760e-01	3.007e-01	-0.843	0.3990

```
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
```

	exp(coef)	exp(-coef)	lower .95	upper .95
## BOOZE	1.014e+00	9.859e-01	0.9734	1.057
## AGEYRS	1.063e+00	9.407e-01	1.0479	1.078
## as.factor(RACE)2	7.037e-01	1.421e+00	0.4088	1.211
## as.factor(RACE)3	9.626e-01	1.039e+00	0.3029	3.059
## GRADES	1.037e+00	9.642e-01	0.9935	1.083
## as.factor(MARRY)3	1.199e+00	8.342e-01	0.8720	1.648
## as.factor(MARRY)4	1.335e+00	7.490e-01	0.8150	2.187
## as.factor(MARRY)5	1.108e+00	9.027e-01	0.3958	3.100

```
## as.factor(MARRY)6 5.824e-01 1.717e+00 0.2692 1.260
## as.factor(MARRY)8 1.080e+00 9.257e-01 0.1493 7.819
## as.factor(SIZE)2 1.059e+00 9.439e-01 0.6409 1.751
## as.factor(SIZE)3 1.151e+00 8.691e-01 0.6826 1.939
## as.factor(SIZE)4 9.868e-01 1.013e+00 0.5501 1.770
## as.factor(SIZE)5 6.759e-01 1.480e+00 0.2278 2.006
## as.factor(SIZE)6 1.798e+00 5.563e-01 0.8125 3.977
## as.factor(SIZE)7 8.608e-01 1.162e+00 0.3934 1.884
## as.factor(SIZE)8 1.534e-05 6.520e+04 0.0000 Inf
## AVGSMK 1.030e+00 9.713e-01 1.0196 1.040
## as.factor(SMSA)2 8.101e-01 1.234e+00 0.5384 1.219
## as.factor(SMSA)4 6.309e-01 1.585e+00 0.3319 1.199
## URBAN 9.180e+04 1.089e-05 0.0000 Inf
## HTN_REP 1.110e+00 9.006e-01 0.8426 1.463
## RBC 1.145e+00 8.736e-01 0.9861 1.329
## DRMI 6.994e-01 1.430e+00 0.3272 1.495
## DIAB 7.760e-01 1.289e+00 0.4304 1.399
##
## Concordance= 0.716 (se = 0.016 )
## Likelihood ratio test= 138.9 on 25 df, p=<2e-16
## Wald test = 123.3 on 25 df, p=6e-15
## Score (logrank) test = 131.1 on 25 df, p=2e-16

z <- (coef(fit6_cont_f)[1] - coef(fit6_cont_m)[1])/sqrt(vcov(fit6_cont_f)[1,1] + vcov(fit6_cont_m)[1,1])
1 - pnorm(z)

## BOOZE
## 0.7171777
```

## Checking PH-assumption

```
# categorical version
fit3_q <- coxph(Surv(fu_time, cancer_death) ~ BOOZE_q + AGEYRS +
                SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) + AVGSMK + as
                HTN_REP + RBC + DRMI + DIAB, data = dta)
cox.zph(fit3_q)

##          chisq df      p
## BOOZE_q    2.92259  3 0.404
## AGEYRS      0.99688  1 0.318
## SEX         3.50873  1 0.061
## as.factor(RACE) 0.06268  2 0.969
## GRADES      2.06122  1 0.151
## as.factor(SIZE) 3.88985  7 0.792
## as.factor(MARRY) 5.51469  5 0.356
## AVGSMK      0.00156  1 0.968
## as.factor(SMSA) 0.40469  2 0.817
## URBAN       0.27417  1 0.601
## HTN_REP     0.25422  1 0.614
## RBC         0.40691  1 0.524
## DRMI        0.00317  1 0.955
## DIAB        3.01364  1 0.083
## GLOBAL     24.54144 28 0.653
```

```
# continuous version
fit3_con <- coxph(Surv(fu_time, cancer_death) ~ BOOZE + AGEYRS +
                  SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) + AVGSMK + as
                  HTN_REP + RBC + DRMI + DIAB, data = dta)
cox.zph(fit3_con)

##               chisq df      p
## BOOZE          5.34e-01  1 0.465
## AGEYRS          1.01e+00  1 0.315
## SEX             3.41e+00  1 0.065
## as.factor(RACE)  5.92e-02  2 0.971
## GRADES           2.05e+00  1 0.152
## as.factor(SIZE)  3.85e+00  7 0.797
## as.factor(MARRY) 5.46e+00  5 0.362
## AVGSMK           2.26e-05  1 0.996
## as.factor(SMSA)  4.17e-01  2 0.812
## URBAN            2.58e-01  1 0.611
## HTN_REP          2.58e-01  1 0.612
## RBC              3.77e-01  1 0.539
## DRMI             2.93e-03  1 0.957
## DIAB             3.05e+00  1 0.081
## GLOBAL           2.23e+01 26 0.672
```

## Exploring Non-linearity

```
library(splines)
fit_nl <- coxph(Surv(fu_time, cancer_death) ~ ns(BOOZE, knots = 3) + AGEYRS +
                SEX + as.factor(RACE) + GRADES + as.factor(SIZE) + as.factor(MARRY) + AVGSMK + as
                HTN_REP + RBC + DRMI + DIAB, data = dta)
x <- seq(0,21, 0.5)
loghr <- ns(x, knots = 3) %*% coef(fit_nl)[c(1,2)]
vcov <- vcov(fit_nl)[c(1,2), c(1,2)]
var <- diag(ns(x, knots = 3) %*% vcov(fit_nl)[c(1,2), c(1,2)] %*% t(ns(x, knots = 3)))
se <- sqrt(var)
df <- tibble(x = x,
             y = loghr,
             ymin = loghr - 1.96*se,
             ymax = loghr + 1.96*se)
ggplot(df) +
  geom_line(aes(x = x, y = y), color = "red", linetype = "dashed")+
  geom_ribbon(aes(x = x, y = y, ymin = ymin, ymax = ymax),
            alpha = 0.5, fill = "#DB7093") +
  theme_bw() +
  labs(x = "Alcohol consumption (drinks/week)",
       y = "log(HR)")
```

