- 1. Submit a written report that includes:
  - a. Objective (1 sentence)
  - Methods text. Describe your methods with the same level of detail as you would in a scientific manuscript. Justify your approach (DAG, choice of covariates, modeling decisions, etc.)
  - c. Results text and tables/figures (manuscript-level detail)
  - d. A brief summary of your conclusions (1-3 sentences)
  - e. Provide any necessary supplementary materials
  - f. Provide a clean/labeled dataset with all variables required for analysis, data dictionary, and codebook.
  - g. Provide a link to your code on GitHub

## a. Objective

The objective of this analysis is to describe the association of mid-life alcohol use on mortality over a 20-year follow-up period from baseline.

## b. Methods

## Sample

Participants aged 18-64 years old were sampled from a population sample of adults in a northern German region using registry data. Of the 5,829 eligible individuals at baseline, 4,093 individuals completed interviews between July 1996 to March 1997. Baseline data was analyzed among 4075 individuals, and vital status at follow-up was obtained from April 2017 to April 2018 among a final analytic sample of 4028 individuals.

#### Measurement

## Baseline measures

Alcohol abstinence and consumption 12 months prior to baseline was assessed using items from the Alcohol Use Disorder Identification Test-Consumption (AUDIT-C) questionnaire. This tool was selected due to ease of administration, common use, and standardization. A score was calculated to summarize frequency and quantity of alcohol consumption by the following categories: abstinence (0), low to moderate (1 to 3), moderate to high (4), high (5), very high (6 to 7), and extremely high alcohol consumption (8 to 12).

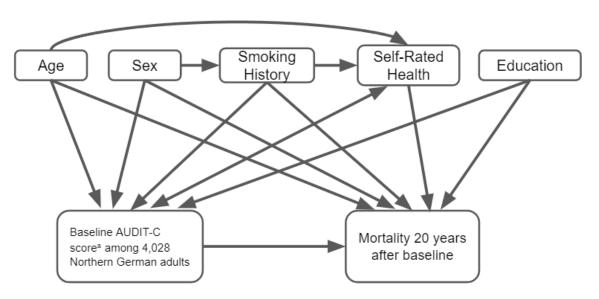
## Outcome measures

Mortality assessment was conducted from April 2017 to April 2018. Total mortality was determined by death certificate information obtained from local health authorities where participants resided at baseline.

## Covariates

Smoking status at baseline was collected as a 5-level categorical variable, including never smokers, former limited smokers, former daily smokers, current lighter (less than 20 cigarettes per day) smokers and current heavy (20 or more cigarettes per day) smokers. Smoking is a clear confounder between alcohol use and mortality. Educational status was assessed as 12 or more, 10 to 11, or 9 or less years. Educational status has been demonstrated to confound many exposures and mortality, as it acts as a proxy for early life conditions and opportunity. Age and sex at baseline was also assessed and included as covariates. Self-rated health was collected as a 5-level categorical scale variable from excellent to poor, and re-coded as a 3category variable by John et al. Self-rated health at baseline might have two different roles in the causal path between alcohol consumption and mortality. At baseline, self-rated health might act as a proxy confounder in the relationship between alcohol consumption and mortality, as those with medical conditions that limit alcohol consumption might also rate their health as 'poor'. Alternatively, self-rated health might mediate the relationship between alcohol consumption and mortality, as alcohol consumption over the previous 12-month period might directly impact the subject's perception of health at the time of interview, especially among heavy drinkers.

Figure 1. DAG demonstrating proposed association between AUDIT-C and mortality



a AUDIT-C score (Alcohol Use Disorders Identification Test score) is used to measure alcohol consumption and abstinence at baseline

# **Data analysis**

Descriptive summary statistics (frequencies, means) were performed to describe the study sample and follow-up time by study sample characteristics. Simple and multivariate Cox proportional hazards models were used to describe the associations of baseline AUDIT-C scores with mortality over the follow-up period. Model 1 adjusted for sex, age, education, and smoking history, but did not adjust for self-rated health at baseline under the assumption that it might be an intermediary between alcohol consumption and mortality during follow-up. Model 2 included self-rated health at baseline under the assumption that adjustment for self-rated health at baseline might de-confound the relationship between alcohol consumption and mortality during follow-up.

## c. Results

We found that among 4028 study participants, 447 individuals (11%) were alcohol abstainers at baseline and slightly over half (54%) of individuals were low to moderate alcohol consumers (Table 1). The mean age was 41.7 years (SD  $\pm$  12.9), and roughly half of individuals were female (49.8%) and attained 9 years of education or less (47.8%). Self-rated health status was reported as very good to excellent among 35% of participants. Respective average and maximum follow-up time was 20.7 and 22.0 years.

Table 1. Demographic and baseline characteristics of population-based cohort of 4,028 northern German adults, 1996-1997.

Characteristic	Total n (column %)	Person-years of follow-up Mean (SD) 20.66 (4.0)		
Total	4028 (100)			
Demographic variables				
Age, mean (SD)	41.72 (12.9)			
Female	2006 (49.8)	21.0 (3.4)		
School education, n(%)				
9 or less years	1927 (47.8)	20.1 (4.7)		
10-11 years	1471 (36.5)	5) 21.2 (3.0)		
12 or more years	630 (15.6)	21.2 (3.2)		
Smoking status, n(%)				
Never smoker	676 (16.8)	20.9 (3.6)		
Ever less than daily	920 (22.8)	21.3 (2.9)		
Former daily	839 (20.8)	20.5 (4.3)		
Current daily <20 cpd	485 (12.0)	20.8 (3.6)		
Current daily >= 20 cpd	1108 (27.5)	20.0 (4.7)		
Self-rated health, n(%)				
Very good to excellent health	1427 (35.4)	21.2 (3.2)		
Good health	1926 (47.8)	20.7 (3.9)		
Poor to fair health	675 (16.8)	19.3 (5.3)		
AUDIT-C sum score, n(%)				
Abstinent (AUDIT-C=0)	447 (11.1)	19.3 (5.4)		

Low to Moderate (AUDIT-C=1-3)	2203 (54.7)	21.0 (3.5)	
Moderate to High (AUDIT-C =4)	674 (16.7)	20.9 (3.5)	
High (AUDIT-C=5)	383 (9.5)	20.7 (3.9)	
Very High (AUDIT-C=6-7)	228 (5.7)	20.3 (4.6)	
Extremely High (AUDIT-C =8-12)	93 (2.3)	18.9 (5.9)	

Abbreviations: AUDIT-C, Alcohol Use Disorders Identification Test-Consumption

Compared to baseline alcohol abstainers, baseline alcohol consumers at all levels except for extremely high alcohol consumption had reduced risk of mortality over the follow-up time in crude models and both adjusted models (Table 2). Adjusting for sex, age, smoking status, and years of education (Model 1) and self-reported health (Model 2) did reduce the strength of the association but did not eliminate it to null.

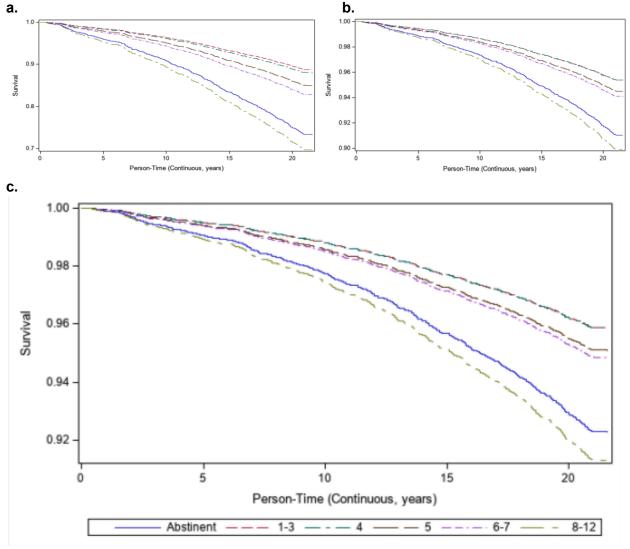
Table 2. Hazard of death 20 years after baseline by baseline alcohol consumption.

Alcohol Use At Baseline	N	Decease d n(%)	Unadjusted HR (95% CI)	Model 1ª HR (95% CI)	Model 2 <sup>b</sup> HR (95% CI)
Abstinent (AUDIT-C=0)	447	119 (26.6)	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]
Low to Moderate (AUDIT-C=1-3)	2203	248 (11.3)		0.502 (0.403-0.627)	0.523 (0.419-0.653)
Moderate to High (AUDIT-C =4)	674	181 <i>(</i> 12 N)			0.525 (0.392-0.701)
High (AUDIT-C=5)	383	158 (15 1)		0.602 (0.434-0.833)	0.626 (0.452-0.867)
Very High (AUDIT-C=6-7)	228	139 <i>(</i> 17 1)		0.649 (0.446-0.943)	0.657 (0.452-0.955)
Extremely High (AUDIT-C =8-12)	93	128 (30 1)		1.132 (0.741-1.729)	1.134 (0.734-1.734)

<sup>&</sup>lt;sup>a</sup> Model adjusted for sex, age, smoking status, and years of education at baseline

b Model adjusted for sex, age, smoking status, years of education, and self-reported health at baseline

Figure 2. Survival over 20 years of follow-up after baseline by baseline alcohol consumption.



a. Unadjusted survival curves of study participants by baseline alcohol consumption over 20 years follow-up.
b. Survival curves of study participants by baseline alcohol consumption, adjusted for age, sex, education, and smoking history. Cox Proportional Hazards model.
c. Survival curves of study participants by baseline alcohol consumption, adjusted for age, sex, education, smoking history, and self-rated health at baseline. Cox Proportional Hazards model.

#### d. Conclusion

Based on these study findings alone, it appears that low to high alcohol consumption over the prior 12 months, appears to reduce the risk of mortality over 20 years of follow up. These study findings are consistent with prior studies that have observed reduced risk of mortality among alcohol consumers over alcohol abstainers. However, this study, as others, suffers from lack of measurement on potential confounding factors, including factors determining mid-life abstinence from alcohol such as former heavy drinking or alcohol use disorders. Assessment of mid-life abstinence from alcohol alone does not sufficiently characterize prior alcohol-related exposures.

e. Supplementary materials

Code, raw data and analytic dataset are available in the Github repository, linked below.

f. Dataset, data dictionary and codebook

All project materials are available in the Github repository, linked below.

g. Provide a link to github repository

https://github.com/rfisher2022/Epidem207 JohnB

