# Estimating the effects of early adulthood alcohol use on late life cognition using a synthetic lifecourse cohort

Scott C Zimmerman✵, Peter T Buto✵, Katrina Kezios✦, Jillian Hebert✵, Anusha Vable✵, Adina Zeki Al Hazzouri✦, M Maria Glymour✧

✵University of California San Francisco, ✦Columbia University, ✧Boston University

**Introduction**:

Adolescent and early adulthood alcohol use may influence cognitive aging, but few data sets measure alcohol use across the life course and late life cognition.

We generated a synthetic cohort fusing the National Longitudinal Study of Youth 1979 (NLSY79) and the Health and Retirement Study (HRS).

We used the synthetic cohort to evaluate the effect of early life alcohol use on later life memory and memory decline.

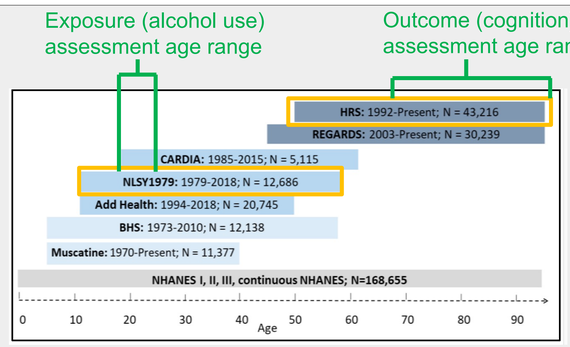


**Figure 1:** Data from available cohorts cover different parts of the life course. In this analysis we use NLSY79 as an early life cohort and HRS as a later life cohort.

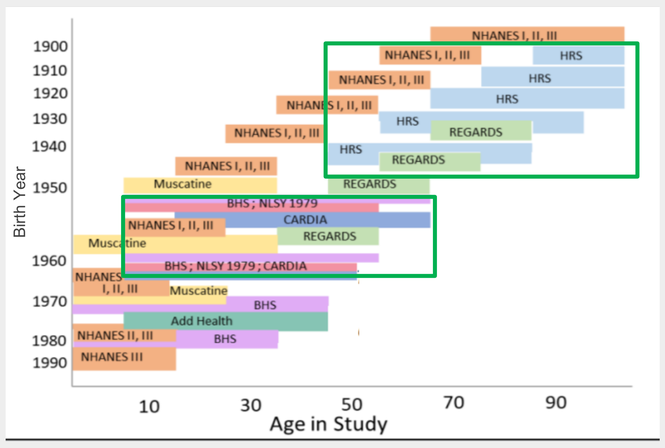


**Figure 2:** Data from available cohorts were collected at different times. These cohorts overlap in the age range 42-64 years (born 1957-1964 in NLSY79 and 1932-1978 in HRS).

**Methods**:

- **Samples**: NLSY79 (measured 1979-2020, born 1957-1964) and HRS (measured 1995-2020, born 1932-1978).
- **Exposure**: alcohol use reported in 1983 in NLSY79 as drinks/week (none; light-to-moderate: <=7 drinks/week for women, 14 for men; or heavy drinking) and any binge drinking in the last 30 days.
- **Outcome**: Longitudinal memory assessment in HRS (sum of 10-item immediate and delayed word list recall scores).

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**Github.com/ScottZimmerman/SER_2023a**

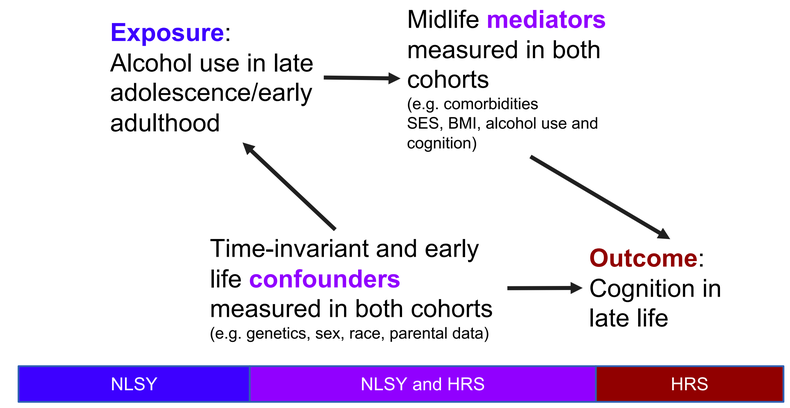


**Figure 3:** Conceptual directed acyclic graph (DAG) of pathways linking adolescent/early adulthood alcohol use and late life cognition, and the data sets in which variables are measured. Valid estimates of the association of the exposure and outcome require blocking all paths using variables measured in both cohorts.

- **Covariates**: Observations from HRS were matched to 10 NLSY79 participants based on variables measured in both data sets expected to confound or mediate the effects of adolescent/young adult alcohol use: sociodemographics, physical activity, general health, height, weight, depression, midlife alcohol use, midlife cognition, military status, current religion, comorbidities (heart problems, diabetes, hypertension, cancer).
- **Matching**: Exact and distance matching based on shared mediators and confounders measured in both HRS and NLSY79 (see matching process box).
- **Analysis**: HRS participants' exposures were imputed based on those of their NLSY matches. The outcome model then used linear mixed models adjusted for demographics, follow-up time, and a practice effect to estimate the association of imputed adolescent/young adult alcohol use with memory at age 50 and rate of change in memory in each data set and pooled the estimates and their variances using Rubin's rules.

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## Matching process

a) Calculate associations of each mediator and confounder with the exposure ($R^2$) and with the outcome (marginal $R^2$ linear mixed-effects models, accounting for practice effects).
b) **Exact time-invariant matching step:** For each HRS participant, find the exact matches from the pool NLSY79 participant based on time-invariant categorical covariates.
c) **Exact time-varying matching step:** Using the reference wave for the older cohort (i.e. the first wave with sufficiently complete data), determine at which waves the potential matches in the previous step would be eligible to match the older participant, based on the time-varying categorical covariates.
d) **Distance matching:** Again using the reference wave for the older, determine matching distance scores, based on the continuous covariates, weighted by the sum of the associations with the exposure and outcome from step a.
e) Determine match quality by comparing covariates for each matched pair, and drop matches of poor quality according to pre-specified thresholds.

**Results**:

- From 12,535 NLSY79 participants, we identified quality matches for 10,123 HRS enrollees.
- Compared to light-to-moderate drinkers who did not report binge drinking:
  - Other alcohol use categories were associated with lower memory scores at age 50 (imprecise estimates).
  - Adolescent/young adult binge drinking associated with faster memory decline, except among those reporting binge drinking in the past month but no drinking in the last week.
  - No reported drinking in the last week and heavy drinking without binging associated with slower memory decline.

| Variable | | Estimated effect on cognitive level, coef, (95%CI) | Estimated effect on cognitive change per decade of age, centered at 50 years (coef, 95%CI) |
|---|---|---|---|
| Age main term | | | -0.182 (-0.554,0.19) |
| **Past week drinking** | **Past 30-day binge drinking** | | |
| No alcohol | No | -0.175 (-0.635,0.285) | 0.015 (-0.453,0.483) |
| No alcohol | Yes | -0.063 (-0.722,0.596) | 0.044 (-0.416,0.504) |
| Light | No | Ref. | Ref. |
| Light | Yes | -0.021 (-0.532,0.49) | -0.033 (-0.505,0.439) |
| Heavy | No | -0.231 (-1.963,1.501) | 0.139 (-1.36,1.638) |
| Heavy | Yes | -0.065 (-0.553,0.423) | -0.069 (-0.637,0.499) |

**Table 1: Regression coefficients** from linear mixed effects models in HRS using the early life alcohol use from HRS participants' matched NLSY79 counterparts.

**Conclusions**

- In this synthetic cohort, we observed complex associations between early life alcohol use and late life cognition that were plausibly attributable to chance.
- Valid causal interpretation of early life exposures on late life outcomes in synthetic cohorts created with data fusion requires the assumption that all mediating and confounding pathways are accounted for.