Complete Title: Alcohol Labeling Study

Protocol Date: April 16, 2025
NCT #: NCT06835920

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Protocol Synopsis

Study title	Alcohol Labeling Study
Funder	National Institute on Alcohol Abuse and Alcoholism
Study rationale	• Policymakers and public health organizations are increasingly interested in communicating alcohol's harms to the public, including through mandated warning labels. • Communicating alcohol's harms through front-of-package alcohol health warnings could reduce alcohol consumption and alcohol-related health harms. • Few studies have experimentally evaluated whether front-of-package alcohol warnings change drinking behavior.
Study objectives	Primary • Evaluate whether front-of-package alcohol health warnings reduce the number of alcoholic drinks consumed per day. Secondary • Evaluate whether front-of-package alcohol health warnings affect other alcohol-related behaviors and inform consumers.
Study design	Randomized clinical trial
Number of participants	~720 participants.
Study duration	Each participant is in the trial for ~3 weeks. The trial enrollment period is expected to last ~24 months.
Study phases	The trial will have two phases: (1) Screening: screening for eligibility and obtaining consent and (2) Intervention: intervention/experimental treatment

Study protocol

Participants will be invited to attend 3 in-person visits, spaced ~1 week apart. Participants will be instructed to bring 8 days' worth of unopened alcohol containers to each trial visit. Study staff will randomize participants to 1 of 2 trial arms (front-of-package health warnings or control labels) at the first visit. At each visit, staff will apply labels per participants' assigned arm to the front of all alcohol containers. Participants will take a computer survey at each visit. Participants will take a final survey remotely approximately 1 week after the final in-person visit. Participants will answer two questions by text message each day they are in the study.

Statistical analysis plan

General principles

Analyses will be intent-to-treat, including all participants randomized at Visit 1, except when noted. We will use a critical alpha of 0.05 or 95% confidence intervals, and two-tailed tests to conduct all statistical tests.

Predictions

We predict that front-of-package alcohol health warnings will lead to fewer drinks consumed per day (primary outcome), compared to the control. In terms of secondary outcomes, we predict that compared to the control, front-of-package alcohol health warnings will lead to

greater intentions to limit drinking, forgoing a drink, perceived control over drinking, learning something new, knowledge of harms from alcohol in warnings, reminding of harms of alcohol, and perceived likelihood of harms from alcohol. We predict that, compared to the control, front-of-package alcohol health warnings will lead to lower maximum number of drinks consumed in a day, proportion of days drinking during the study, and perceived healthfulness of alcohol.

Statistical methods

We will descriptively present demographic characteristics separately for each trial arm but will not test for balance, following CONSORT guidelines. Assuming sufficient internal consistency (Cronbach's alpha>=0.70), we will average responses to all measures with 3 or more items.

All analyses will be intent-to-treat, except where noted. To examine the impact of trial arm on the primary outcome, we will run a mixed effects linear regression model to account for repeated measures across participants. This model will regress number of drinks consumed per day on indicators for trial day when drinking was reported (within subjects, level 1 variable, fixed effect), whether the trial day when drinking was reported was a weekend versus weekday (within subjects, level 1 variable, fixed effect), and trial arm (between subjects, level 2 variable, fixed effect). Analysis will treat the intercept as random. In “per protocol” sensitivity analyses, we will re-run the primary outcome model among those with high adherence to the labeling protocol.

We will explore whether the impact of trial arm on the primary outcome differs by the following participant characteristics: baseline alcohol use, baseline intentions to limit drinking, gender, age, and education. Using the same modeling approach as for the primary outcome and separate models for each moderator, we will regress number of drinks consumed per day on trial arm, the moderator, and interactions between trial arm and the moderator. We will report the statistical significance of the interaction terms. We will estimate the impact of trial arm on the outcome at each level of the moderator, adjusting for these post-hoc tests using a Bonferroni-Holm correction.

Next, we will examine the impact of trial arm on secondary outcomes. We will use mixed effects linear and logistic models for outcomes with repeated measures. The predictor will be trial arm (between subjects, level 2 variable, fixed effect); analyses will treat the intercept as random. We will use standard logistic and linear models for outcomes measured only once, with trial arm as the only predictor.

Sample size needs

To estimate sample size needs, we assumed 21 repeated daily diary measures, 2 trial arms of equal size, an intraclass correlation of .60, and 15% missingness for any given daily diary measure. Power analyses used mixed effects linear regression, with 1,000 simulations. A sample size of 720 people would provide >85% power to detect effect sizes of d=.18 or larger and >80% power to detect effect sizes of d=.17 or larger. These effect sizes are conservative estimates as prior studies of non-alcoholic beverages indicate effect sizes of sugary drink health warnings on behavior of d=.25[1] and d=.41.[2]

References

1. Grummon AH, Taillie LS, Golden SD, Hall MG, Ranney LM, Brewer NT. Sugar-sweetened beverage health warnings and purchases: A randomized controlled trial. *Am J Prev Med.* 2019;57(5):601-610.
2. Hall MG, Grummon AH, Higgins ICA, et al. The impact of pictorial health warnings on purchases of sugary drinks for children: A randomized controlled trial. *PLoS Med.* 2022.