Disclaimer: The following information is fictional and is only intended for the purpose of illustrating key concepts for results data entry in the Protocol Registration and Results System (PRS).

Micro-Randomized Study Design Example

Maryland Alcohol-Dependent Moms Abstinence (MAMA) Study

Methods

Study Design

The Maryland Alcohol-Dependent Moms Abstinence (MAMA) Study was a micro-randomized optimization trial (MRT) conducted to gather evidence to inform the development of a just-in-time adaptive intervention (JITAI) to reduce risky drinking among pregnant women (18 years or older) during the first trimester. The ultimate goal of the study was to create a full-scale JITAI with the most effective strategies for helping participants abstain from alcohol during their pregnancy in order to prevent fetal alcohol spectrum disorders (FASDs). The study duration was 1 year, from January 1, 2018, to December 31, 2018. Each woman remained in the study for 37 days from the date of her enrollment.

Study Participants

Participants were recruited from Federally Qualified Health Centers (FQHCs) in Maryland. All pregnant women in the first trimester of pregnancy were screened for risky drinking during the first appointment at which pregnancy was confirmed. The first screening step used the AUDIT 1-3 (US) tool, as recommended by the Centers for Disease Control and Prevention (CDC). This tool consists of the first three questions of the full AUDIT (US) screening tool. Each question has seven possible answers, scored from low risk (0) to high risk (6); scores are summed for a total ranging from 0 to 18. Women who scored ≥ 7, or "positive" for excessive drinking, on the AUDIT 1-3 (US) were then assessed using the full AUDIT (US). The AUDIT (US) is a 10-item instrument that asks questions about alcohol consumption during the past year, symptoms of alcohol dependence, and alcohol-related problems or harm. The full AUDIT (US) includes the AUDIT 1-3 (US) and an additional seven questions with answer options that vary by question but range from low risk (0) to high risk (4); the scores for all 10 questions are summed, for a total of 0 to 46. Scores of 8–15 suggest drinking in excess of screening guidelines, and scores of 16–19 might indicate additional alcohol-related harm. Women who scored from 8 to 19 on this measure were eligible for the study and were encouraged to enroll. According to CDC guidelines, risky drinking for women is defined as > 3 drinks on any single day or > 7 drinks per week. Consuming ≥ 4 drinks within 2 hours is defined as binge drinking. A drink consists of 0.6 ounces (14 grams) of alcohol, such as 12 ounces of most beers, 5 ounces of most table wines, or one shot (1.5 ounces) of 80-proof spirits. All enrolled participants exhibited the risky drinking behavior described by these guidelines.

Women were excluded from the study if they were in the second or third trimester of pregnancy, had very high-risk pregnancies that required bed rest, or were identified as using other teratogenic substances. In addition, women were excluded if they were unable to use a cell phone or did not have cellular service at home.

Participants who met the eligibility criteria, gave informed consent to participate, and were enrolled in the study received, as part of their regular prenatal visit, an intake counseling session that promoted abstaining from alcohol. Participants consented to wear a wristband

sensor, the SerenRUS from ZenLabs, to monitor their electrodermal activity (EDA), a physiological measure of skin conductance that is used to assess stress levels. Participants also consented to use a study-provided Android phone as their primary phone for the duration of the study.

The study protocol was reviewed and approved by Virginia University's School of Medicine Institutional Review Board. Because personal sensor data were collected by systems that run on Wi-Fi, we built additional safeguards into the software to reduce the possibility of hacking, which could compromise sensitive personal data. Each participant provided written informed consent to collect these data.

The MAMA Intervention

The MAMA intervention was delivered through the Addiction-Comprehensive Health Support System (A-CHESS) app, which was available to participants on the study-provided mobile phone throughout their time in the study (Gustafson, McTavish, Chih, Atwood, Johnson, et al., 2014). A-CHESS included two types of intervention components. "Pull" components were always available through the app. Most were active, requiring participants to decide to use them, except the count of days and times that the participant had refrained from drinking, which was considered passive. The "push" component, comprised of messages sent by the A-CHESS system, was randomly delivered (or not delivered) according to a decision rule. All messages were created according to evidence-based cognitive behavioral principles (Crane, et al., 2018) and the Treatment Improvement Protocol for Addressing Fetal Alcohol Spectrum Disorders (Substance Abuse and Mental Health Services Administration, 2014). The complete list of pull and push components is provided in Table 1.

Table 1. Pull and push intervention components

Intervention Component	Description
Pull components	
Daily abstinence counter (passive)	The counter and graph of days abstinent appeared on the home page of the app to remind participants of their days of abstinence. Participants recorded their number of drinks per day by time of day in the A-CHESS app for the duration of the study.
Discussion groups (active)	Participants could chat online anonymously with others in the MAMA Study to receive instant support.
Personal stories (active)	Professionally produced text and videos of abstinence stories from other mothers, focusing on ways to manage addiction and cope with challenges
Instant library (active)	Summaries of articles, chapters, and other publications on addiction management for women
Frequently asked questions (active)	Brief and encouraging answers to questions about addiction, such as "How do I deal with cravings for alcohol?" The responses included links to information and services for more support.
Web links (active)	Links to evidence-based addiction-related websites and specific pages within those sites, including Alcoholics Anonymous resources
Easing distress (active)	A computerized cognitive-behavioral therapy program designed to help women cope with inaccurate thoughts that hinder their efforts to remain abstinent. The program helped assess logical errors, attributional mistakes, and the tendency to amplify distress, and it offered exercises to sharpen problem-solving skills.

Intervention Component	Description
Push component	
Stress-management prompts, randomized according to the decision rule	Messages prompted participants to manage their stress by using coping mechanisms or to maintain their current affect, depending on whether the wristband stress sensor detected a stress event in the 10 minutes prior to a decision point. If participants experienced a stress event during this period, they were encouraged to access coping strategies in the A-CHESS app and consider attending a support group meeting. If they did not experience a stress event during this period, they received a message of encouragement to remain stress-free.

Study Procedure and Randomization

Baseline Period

During the intake session, a study staff member explained the use of the wristband sensor and assessed the participant's baseline levels of electrodermal activity, a measure of skin conductance, to establish the amplitude above which stress peaks would be documented. Then, during the next 7 days, we collected baseline measures on each participant's stress events and alcohol consumption.

We asked participants to define a 13-hour period each day during which they would be awake and available for either monitoring (during the baseline period) or monitoring and receiving messages (during the intervention period) at decision points once every hour at the top of the hour, or at 13 points during each 24-hour period. During the baseline period, there were 91 (13 x 7) possible decision points per participant. Participants' wristband sensors detected EDA through continuous recording and were monitored by the central study servers.

The wrist sensors sampled EDA in the range 0.01–0.89 μS with ±0.01 μS resolution at 10 Hz. Participants whose EDA increased at a rate of ≥ 0.004 μS per second to an amplitude of 0.50 μS or more above their personal resting conductance were considered to be experiencing a single stress peak (Sano & Picard, 2013; Walker, Thomson, Pfingst, Viemincx, Aidman, et al., 2019). Throughout the study, we defined a "stress event" as ≥ 6 stress peaks during a 10-minute monitoring period (Figure 1). For each decision point for which a participant was available, the occurrence of a stress event in the subsequent hour was monitored to establish the proportion of

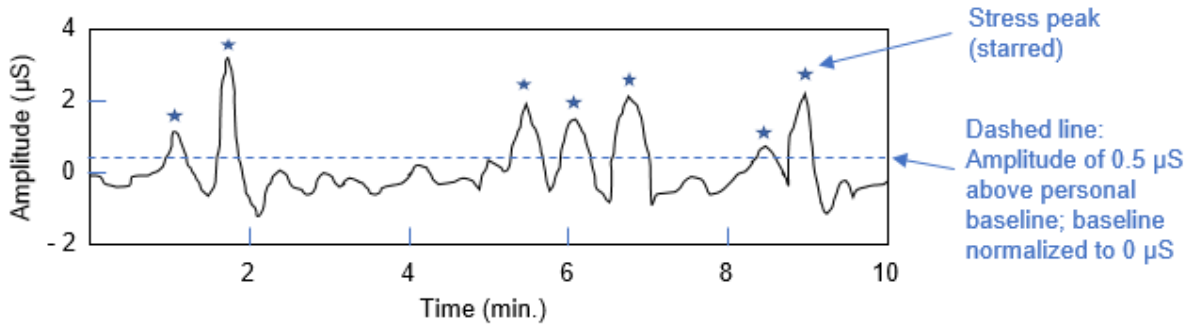

Figure 1. Illustration of a stress event (≥ 6 stress peaks within 10 minutes)

decision points followed by a stress event. A participant was not considered available at a decision point if her wristband sensor wasn't maintaining a constant reading of EDA (for example, if the sensor's battery had died, if the sensor wasn't worn, or if the sensor didn't make appropriate contact with the skin). Proportions were determined for each participant, then averaged across participants.

To establish a baseline for alcohol consumption, we measured the number of drinks within the hour following each decision point for which a participant was available. We asked participants to document their alcohol use for each baseline day, including an approximation of the time of day they consumed each drink. (We acknowledge the limitations of this method and the potential for inaccuracy in self-reports, especially reports of behaviors affected by social desirability bias.) If participants had one or more drinks within the hour after a decision point, then those drinks were assigned to that decision point. The number of drinks per decision point was determined for each participant, then averaged across participants.

Intervention Study Period

The same 13-hour blocks of active monitoring time established in the baseline period for each participant were used for the intervention period. The A-CHESS system could deliver a single message at each decision point, and it randomized delivery as a message or no message. The messages had one of two purposes: (1) if a stress event occurred within the 10 minutes immediately before a decision point, the message encouraged the participant to access stress reduction resources or (2) if there was no stress event in the 10 minutes before the decision point, the message encouraged the participant to remain stress-free.

At each decision point, the randomization was independent of previous randomizations and of participants' responses to previous suggestions. During the 30-day intervention period, messages were randomized up to 390 (13 x 30) times for each participant. To keep participant burden low and also provide sufficient opportunities to assess the effectiveness of the intervention strategies, we used a probability of 0.2 for receiving a message and a probability of 0.8 for receiving no message at each decision point when participants were available for the intervention.

A-CHESS randomized delivery of a message or no message to participants only if they were considered available. A participant was not considered available if her wristband sensor wasn't maintaining a constant reading of EDA, if she was driving, or if her phone was offline. As in the baseline period, we asked participants to document their alcohol use for each day of the intervention.

Outcomes and Measures

The aim of this study was to identify which strategies were most effective in helping participants achieve full abstinence during pregnancy, so that we could compile a suite of intervention components to test with a larger group of women. The ultimate goal was for pregnant women to abstain from alcohol.

Proximal Outcome Measure

Failure to maintain abstinence often occurs after stressful situations which can lead to alcohol craving. Therefore, this study's primary proximal, or short-term, outcome was the effect of messaging on stress levels, determined by assessing the occurrence of a stress event in the hour after the decision point in the presence or absence of messaging. Proportions were determined for each participant (dichotomized according to randomized receipt of messages or no messages), then averaged across participants.

The study's secondary proximal outcome was short-term alcohol

consumption, defined as the number of drinks within the hour following a decision point. As in baseline, if participants had one or more drinks within the hour after a decision point, then those drinks were assigned to that decision point. We used two questions in the A-CHESS app to assess a participant's abstinence or level of alcohol consumption daily throughout the intervention: "How many drinks did you have today?" and "When did you have those drinks?" Participants recorded their answers directly in the app, where they were saved and displayed in a daily abstinence graph. The number of drinks per decision point was determined for each participant (dichotomized according to randomized receipt of messages or no messages), then averaged across participants.

Distal Outcome Measure

The distal, or long-term, exploratory outcome was the average number of drinks per woman throughout the 30-day intervention. The conceptual model underlying this MRT is that if the proposed intervention reduces stress, women will be less likely to drink. Given the exploratory nature of this objective, results are not presented for this outcome.

Statistical Analysis

We designed the study to have 80% power to detect a small effect size of relative risk (RR = 1.05) in the probability of experiencing stress in the hour after a decision point with 5% type I error control. In conducting a simulation-based sample size calculation, we assume that participants are available for 70% of the 390 (13 x 30) decision points. Our study sample of 50 participants exceeded the minimum sample size of 49. We continuously monitored each individual's stress level. For each decision point, we collected data on participants' stress levels in the previous 10 minutes and in the subsequent hour as measured by EDA; the day of the study; and the number of drinks consumed in the subsequent hour.

For prespecified analyses, we used the estimator for marginal excursion effect for binary/count outcomes to analyze the proximal effect of messages on (1) whether a stress event was experienced in the subsequent hour and (2) the near-term alcohol consumption at available decision points (Qian, Yoo, Klasnja, Almirall, & Murphy, 2019). We used generalized estimating equations to assess the association between the two proximal outcomes at available decision points. (See the appendix for additional details.) Analyses were conducted using SAS software, version 9.4 (SAS Institute).

Results

Study Participants

A total of 76 pregnant women at FQHCs in Maryland were assessed for eligibility for the study. Of those, 10 were found to be ineligible because they met exclusion criteria: 3 had high-risk pregnancies that required bed rest, 4 were diagnosed with alcohol use disorder and referred for inpatient treatment, and 3 did not have cellular service at home. The remaining 66 women were offered enrollment in the study; 3 refused, so 63 participants were enrolled. During the course of the study, 13 participants withdrew or were lost to follow-up, so 50 were included in the final analysis (Figure 2).

There were no systematic or significant differences between those enrolled and those analyzed. Demographic characteristics and baseline data for participants are shown in Table 2. Participants in the population analyzed for outcome measure assessments were available during 3,668 of a total of 4,550 possible decision points (50 participants x 91 decision points per participant) in the baseline period.

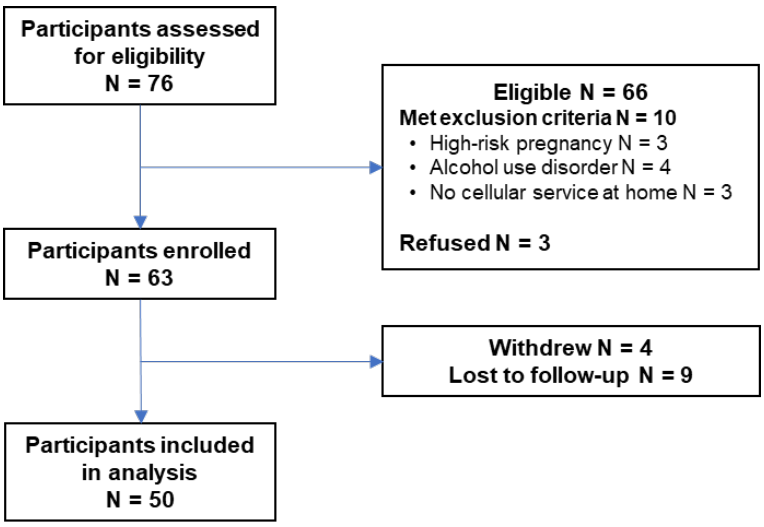

Figure 2. CONSORT flow diagram for participants

Table 2. Participant characteristics for the enrolled population (N = 63) and baseline data for the primary outcome measures for the analyzed population (50 participants, 3,668 baseline decision points)

Participant Characteristics for Enrolled Population	**Total** *(N = 63)*
Age *(mean, SD)*	23.7 (1.7)
Female *(number, percentage)*	63 (100%)
AUDIT (US) score *(mean, SD)*	15.4 (2.3)
Race *(number, percentage)*	
American Indian/Alaska Native	0 (0%)
Asian	5 (8%)
Black or African American	18 (29%)
Native Hawaiian or Other Pacific Islander	0 (0%)
White	40 (63%)
Ethnicity *(number, percentage)*	
Hispanic or Latino	9 (14%)
Not Hispanic or Latino	54 (86%)
Baseline Assessments for Analyzed Population	**Total** *(N = 50)*
Proportion of decision points followed by a stress event *(mean, SD)*	0.56 (0.08)
Number of drinks within the hour following a decision point	
Drinks per decision point *(mean, SD)*	0.24 (0.04)

Outcomes

Decision Points, Participant Availability, and Messages Delivered

For the 50 study participants, there were 390 possible decision points per person during the 30 days of the intervention period, for a total of 19,500 possible person-decision points among all participants. Participants were available for the intervention during 15,586 of the 19,500 decision points (80%), a percentage that remained relatively constant throughout the intervention period. Participants received an average of 2.0 messages daily (SD = 1.3), or 3,056 total stress-management messages delivered throughout the study. Of these, 69%, or 2,096 messages, were delivered at decision points where the participant had not experienced a stress event in the prior 10 minutes, while the remainder (960 messages) were delivered at decision points where the participant had experienced a stress event in the prior 10 minutes. Of the 12,530 decision points that were not randomized to receipt of a message, 4,975, or 40%, were associated with a stress event. In the following analysis, we use the term "prior-stressed" to refer to the status of having experienced a stress event in the 10 minutes prior to a decision point.

Effect of Stress-Management Messages on Experience of a Stress Event in the Subsequent Hour after a Decision Point

Our primary analysis showed that among all the available decision points throughout the 30-day intervention period, the average proportion of decision points after which a stress event occurred in the subsequent hour for the 12,530 available decision points at which the participant did not receive a stress-management message was 0.58 (SD = 0.07); for the 3,056 available decision points at which the participant did receive a stress-management message, the average proportion of decision points after which a stress event occurred in the subsequent hour was 0.55 (SD = 0.09). Table A-1 (see the appendix) provides details for Model 1 and shows the coefficients from the estimator for marginal excursion effect for assessing the effect of stress-management messages on whether a stress event is experienced in the subsequent hour after a decision point, averaging over all the available decision points and all participants. Receiving a stress-management message, compared to no message, reduced the probability of experiencing a stress event in the subsequent hour by a factor of 4.9% ($100\% * [e^{-0.05} - 1]$) ($p = 0.017$).

We also assessed the extent to which stress-management messages were moderated by the day in the study and prior-stressed status in the estimator for marginal excursion effect. Time in the study since the intervention period started was coded by day as 0, 1, … , 29. Details of the model are included in Model 2 in the appendix. The fitted coefficients are presented in Table A-2 (see the appendix). The estimated effect of messages decreased by a factor of 0.3% ($100\% * [1 - e^{0.003}]$) for each additional day in the study since the intervention period started ($p = 0.155$), and this effect increased by a factor of 6.1% ($100\% * [e^{-(-0.059)} - 1]$) if the participant was prior-stressed ($p = 0.054$).

Effects of Stress-Management Messages on Near-Term Alcohol Consumption

Our secondary analysis showed that among all the available decision points throughout the 30-day intervention period, the average number of drinks consumed per decision point was 0.22 (SD = 0.02) for the 12,530 decision points at which participants did not receive a stress-management message; for the 3,096 decision points at which participants did receive a stress-management message, the average number of drinks consumed per decision point was 0.21 (SD = 0.04). Table A-3 (see the appendix) shows the coefficients from the estimator for marginal excursion effect for assessing the effect of stress-management messages on the number of

drinks following the decision point, averaging over all the available decision points and over all participants. Details of the model are included in Model 3 in the appendix. Receiving a stress-management message, compared to no message, reduced the number of drinks consumed following the decision point by 6.0% (100% * [$e^{-0.062}$ – 1]) (p = 0.004).

We also assessed the extent to which stress-management messages were moderated by day in the study and prior-stressed status in the estimator for marginal excursion effect. Details of the model are included in Model 4 in the appendix. The fitted coefficients are presented in Table A-4 (see the appendix). This estimated effect decreased by a factor of 0.2% (100% * [1 – $e^{0.002}$]) for each additional day in the study since the intervention period started (p = 0.447), and this effect increased by a factor of 8.2% (100% * [$e^{-(-0.079)}$ – 1]) if the participant was prior-stressed (p = 0.091).

Association between Experience of a Stress Event in the Subsequent Hour after a Decision Point and Near-Term Alcohol Consumption

As an exploratory analysis, we assessed the association between the two proximal outcomes, experiencing stress in the subsequent hour after a decision point and near-term alcohol consumption, by generalized estimating equations for all available decision points. Details of the model are included in Model 5 in the appendix. The fitted coefficients are presented in Table A-5 (see the appendix). After accounting for day in the study, prior-stressed status, and whether a stress-management message was delivered or not, the number of drinks following a decision point increased by a factor of 2.0% (100% * [$e^{0.020}$ – 1]) if the participant experienced stress in the subsequent hour (p = 0.242), compared to the number of drinks if the participant did not experience stress in the subsequent hour. Under strong causal assumptions, including no unmeasured confounders that influenced both proximal outcomes and that a stress event in the subsequent hour always occurred before any alcohol was consumed, this association may be interpreted as the causal effect of stress management on near-term alcohol consumption. However, it is possible that a participant would self-medicate during a stress event by drinking, which would make it invalid to interpret the association result as causal.

Adverse Events

We collected information on adverse events that might have been related to the MAMA Study using patient records from the time of enrollment in the study through 2 days after participation in the intervention ended. Four nonserious and five serious events were reported (Table 3).

Table 3. Adverse events for the enrolled population, N = 63. Each event was experienced by a different participant (i.e., no participant experienced more than one event).

Adverse Event	Number of Participants Affected
Total serious adverse events	**5**
Major depressive disorder diagnosis	2
Substance use disorder diagnosis	2
Hospitalization for substance use disorder	1
Total nonserious adverse events	**4**
Hypertension	2
Leg edema	2

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Appendix

Details for the Analysis of Effect of Stress-Management Messages on Experience of a Stress Event in the Subsequent Hour after a Decision Point

We use the following notations, where *t* indexes the decision point and each variable is indexed over all participants:

- Z_{t+1} = whether a stress event is experienced in the subsequent hour
- Z_0 = proportion of decision points where a stress event is experienced in the subsequent hour, averaged over all available decision points during the baseline period
- W_t = whether the participant experienced a stress event in the prior 10 minutes, i.e., is prior-stressed
- A_t = whether a stress-management message was delivered at decision point *t*
- D_t = day in the study (since the start of the intervention period) for decision point *t*, coded as 0, 1, … , 29

Model 1: Effect Averaged over Time

In the estimator for marginal excursion effect, in order to assess the average effect over time on the log relative risk scale, we specify the following components:

- Proximal outcome: Z_{t+1}
- Effect modifiers: Empty set
- Control variables: D_t, Z_0, W_t
- Centered treatment indicator: A_t - 0.5
- Weight: The availability indicator for the t^{th} decision point

Model 2: Effect Moderation by Day in the Study and Prior-Stressed Status

In the estimator for marginal excursion effect, in order to assess the average effect over time on the log relative risk scale, we specify the following components:

- Proximal outcome: Z_{t+1}
- Effect modifiers: D_t, W_t
- Control variables: D_t, Z_0, W_t
- Centered treatment indicator: A_t - 0.5
- Weight: The availability indicator for the t^{th} decision point

Table A-1. Fitted coefficients for the estimated effect, averaged over time in study and availability, of delivering a stress-management message vs. no message, on the probability of experiencing a stress event in the subsequent hour (Estimates reported are on the log relative risk scale.)

	Fitted Coefficient	95% LCL	95% UCL	SE	T-value	P-value
Intercept	-1.09	-1.22	-0.96	0.07	-16.62	< 0.001
Proportion of decision points followed by a stress event during the baseline period	1.03	0.79	1.27	0.12	8.37	< 0.001
Day in the study	-0.004	-0.005	-0.002	0.001	-4.29	< 0.001
Prior-stressed	0.028	-0.002	0.057	0.015	1.85	0.064
Delivering messaging vs. no messaging	-0.05	-0.09	-0.01	0.02	2.39	0.017

Table A-2. Fitted coefficients for the estimated effect moderation by day in the study since the intervention period started of delivering a stress-management message vs. no message on the probability of experiencing a stress event in the subsequent hour (Estimates reported are on the log relative risk scale.)

	Fitted Coefficient	95% LCL	95% UCL	SE	T-value	P-value
Intercept	-1.09	-1.22	-0.96	0.07	-16.41	< 0.001
Proportion of decision points followed by a stress event during the baseline period	1.02	0.78	1.13	0.12	8.25	< 0.001
Day in the study	-0.004	-0.005	-0.002	0.001	-4.34	< 0.001
Prior-stressed	0.027	-0.001	0.056	0.015	1.84	0.065
Delivering messaging	-0.074	-0.155	0.006	0.041	-1.79	0.073
Delivering messaging x day in the study	0.003	-0.001	0.008	0.002	1.42	0.155
Delivering messaging x prior-stressed	-0.059	-0.139	0.001	0.036	-1.93	0.054

Details for the Analysis of Effects of Stress-Management Intervention Messages on Alcohol Consumption

We use the following notations, where *t* indexes the decision point and each variable is indexed over all participants:

- Y_{t+1} = number of drinks consumed after the t^{th} decision point
- Y_0 = number of drinks consumed following a decision point, averaged over all available decision points during the baseline period
- W_t = whether the participant experienced a stress event in the prior 10 minutes, i.e., prior-stressed
- A_t = whether a stress-management message was delivered at decision point *t*
- D_t = day in the study (since the start of the intervention period) for decision point *t*, coded as 0, 1, … , 29

Model 3: Effect Averaged over Time

In the estimator for marginal excursion effect, in order to assess the average effect over time on the incidence rate ratio scale, we specify the following components:

- Proximal outcome: Y_{t+1}
- Effect modifiers: Empty set
- Control variables: D_t, Y_0, W_t
- Centered treatment indicator: A_t - 0.5
- Weight: The availability indicator multiplied by the indicator of the participant experiencing a stress event at the t^{th} decision point

Model 4: Effect Moderation by Day in the Study and Prior-Stressed Status

In the estimator for marginal excursion effect, in order to assess the average effect over time on the incidence rate ratio scale, we specify the following components:

- Proximal outcome: Y_{t+1}
- Effect modifiers: D_t, W_t

- Control variables: D_t, Y_0, W_t
- Centered treatment indicator: A_t - 0.5
- Weight: The availability indicator multiplied by the indicator of the participant experiencing a stress event at the t^{th} decision point

Table A-3. Fitted coefficients for the estimated effect, averaged over time in study and availability, of delivering a stress-management message vs. no message, on number of drinks following the decision point (Estimates reported are on the log incidence rate ratio scale.)

	Fitted Coefficient	95% LCL	95% UCL	SE	T-value	P-value
Intercept	-0.53	-0.70	-0.35	0.09	-5.97	< 0.001
Average number of drinks following a decision point during the baseline period	0.33	0.17	0.50	0.08	4.09	< 0.001
Day in the study	0.006	0.003	0.008	0.001	4.95	< 0.001
Prior-stressed	-0.015	-0.047	0.018	0.016	-0.89	0.372
Delivering messaging vs. no messaging	-0.062	-0.105	-0.019	0.022	-2.85	0.004

Table A-4. Fitted coefficients for the estimated effect moderation by day in the study since the intervention period started of delivering a stress-management message vs. no message on number of drinks following the decision point (Estimates reported are on the log incidence rate ratio scale.)

	Fitted Coefficient	95% LCL	95% UCL	SE	T-value	P-value
Intercept	-0.53	-0.70	-0.35	0.09	-5.98	< 0.001
Average number of drinks following a decision point during the baseline period	0.34	0.18	0.50	0.08	4.10	< 0.001
Day in the study	0.006	0.003	0.008	0.001	4.96	< 0.001
Prior-stressed	-0.015	-0.047	0.017	0.016	-0.91	0.364
Delivering messaging	-0.066	-0.159	0.028	0.048	-1.37	0.169
Delivering messaging x day in the study	0.002	-0.003	0.007	0.002	0.76	0.447
Delivering messaging x prior-stressed	-0.079	-0.171	0.013	0.047	-1.69	0.091

Details for the Analysis of Association between Experience of a Stress Event in the Subsequent Hour after a Decision Point and Near-Term Alcohol Consumption

Model 5: Generalized Estimating Equations

We use generalized estimating equations (GEE) with independence correlation structure and empirical/robust standard error. In the GEE model, where *t* indexes the decision point and each variable is indexed over all participants, we include as outcome the number of drinks consumed following the decision point, Y_{t+1}; we include as predictor whether a stress event is experienced in the subsequent hour, Z_{t+1}, whether a stress-management message is delivered, A_t, day in the study, D_t, average number of drinks following a stress event during the baseline period, Y_0, and prior-stressed, W_t; and we only use data from available decision points. Because the outcome of interest, number of drinks consumed following the stress event, is a count variable, we use log link in GEE; hence, the coefficients are interpreted on the log incidence ratio scale.

Table A-5. Fitted coefficients for the generalized estimating equation on the association between experience of a stress event in the subsequent hour after a decision point and near-term alcohol consumption, where near-term alcohol consumption is the outcome and experience of a stress event in the subsequent hour after a decision point is the predictor (Other control variables include day in the study, the indicator of delivering a stress-management message, and prior-stressed status. Estimates reported are on the log incidence rate ratio scale.)

	Fitted Coefficient	95% LCL	95% UCL	SE	T-value	P-value
Intercept	-0.53	-0.74	-0.33	0.11	25.56	< 0.001
Average number of drinks following a decision point during the baseline period	0.33	0.17	0.50	0.08	15.83	< 0.001
Proportion of decision points followed by a stress event during the baseline period	0.018	-0.273	0.309	0.148	0.02	0.901
Day in the study	0.006	0.004	0.008	0.002	1.37	< 0.001
Delivering messaging	-0.062	-0.105	-0.019	0.022	7.98	0.005
Stress in the subsequent hour	0.020	-0.014	0.054	0.017	1.37	0.242
Prior-stressed	-0.014	-0.047	0.018	0.017	0.74	0.391