

Procedure:

Individual characteristics will be assessed in the initial laboratory session and include a combination of questionnaire and task measures. Daily information, including details on each drinking episode, will be compiled from a combination of EMA morning reports and geospatial data. Finally, within-event variables will be collected from a combination of EMA report and TAC. A key aspect of the project is that the four core AID risk factors from the original project will be assessed under multiple conditions: 1) while participants are sober, 2) during intoxication under controlled laboratory conditions, and 3) while participants are drinking in the natural environment. The method of measurement across different modalities will be as consistent as possible, with appropriate formatting changes when necessary.

Below we describe the assessment of each of these constructs across modalities (see Appendix). AID attitudes (perceived danger of AID). At baseline, participants will indicate how dangerous it is to drive after

consuming 1, 3, and 5 drinks in 2 hours, using a 4-point Likert scale. As in Amlung et al., 2015 & Morris et al., 2014, questions will be linked to estimated BrAC for each participant based on weight and sex.

During the alcohol laboratory session, participants will be asked an in-the-moment version of these questions ("How dangerous it is for you to drive right now?") at multiple points of the BrAC curve.

During the AA portion of the project, participants in the Full AA conditions will be asked to rate the perceived danger of driving "right now" at each of the evening reports after a drink has been reported.

They will also be asked

to provide a retrospective rating of the danger of driving the previous evening during morning reports following a drinking session. Impulsivity. At baseline, participants will complete measures of trait impulsivity (UPPS-P (Cyders et al., 2007), delay discounting (Monetary-Choice Questionnaire; Kirby et

al., 1999) and inhibitory control (cued Go/NoGo; Fillmore et al., 2008). During the laboratory session, they will complete measures of state impulsivity (Momentary Impulsivity Scale (MIS; Tomko et al., 2014)) and delay discounting (5-Trial Adjusting Delay Discounting Task (Koffarnus & Bickel, 2014)) at multiple points on the BrAC curve. They will also complete a measure of inhibitory control (cued Go/NoGo) at matched BrAC's on the ascending and descending limbs. During the AA arm of the project, all participants will complete measures of state impulsivity (MIS) and delay discounting (5-Trial Adjusting Delay Discounting Task) at each evening report. Research Strategy Page 66 Contact PD/PI: MCCARTHY,

DENIS M Alcohol demand. Behavioral economic demand for alcohol will be assessed at baseline using the

Alcohol Purchase Task (APT; Murphy & MacKillop, 2006). During the laboratory session, demand will be assessed at multiple points of the BrAC curve using three items corresponding to the APT indices (intensity, breakpoint, Omax) developed in Amlung et al., 2015. All participants will also complete these indices in evening AA reports. Subjective intoxication. Participants will rate their level of subjective intoxication, from 1 ("Not intoxicated at all") to 10 ("More intoxicated than I've ever been") (Morris et al.,

2014). During the laboratory session, they will provide this rating at multiple points along the ascending and descending limb of the BrAC curve. During the AA arm of the project, participants will respond at each evening report where drinking is reported and will answer a retrospective version of this question about their previous day's peak intoxication in morning reports. Laboratory Session The laboratory session is estimated to take approximately five hours. Prior to beverage administration, participants will complete a battery of questionnaire measures and computer tasks for baseline assessment. The battery will include a range of measures, including demographics, typical/recent alcohol and substance use and related behaviors, and typical/recent driving behavior. In addition to the measure of the four core constructs (described

above), we will also collect a baseline assessment of Working memory capacity (OSPA; Unsworth et al.,

2005) and AID Perceptions (positive AID expectancies (PEDD-Y; McCarthy et al., 2006), perceived personal limit (Amlung et al., 2016) perceived negative consequences (Grube & Voas, 1996), and normative beliefs about AID (Treloar et al., 2012)). After completing the baseline battery, participants will receive an alcoholic beverage. To minimize participant risk, and consistent with ongoing work in the PI's

lab, we will follow procedures outlined in the NIAAA Recommended Council Guidelines on Ethyl Alcohol Administration in Human Experimentation (NIAAA, 2005). The dose of alcohol will be calculated to produce a peak BrAC of 0.10g% (Curtin & Fairchild, 2003), the equivalent of

approximately 0.85g/kg alcohol for males, 0.73g/kg alcohol for females. This target BrAC was selected to ensure that the majority of participants reach the legal limit of .08g%, given individual variability in metabolism. Further, this dose

level results in an ascending limb period of approximately 60 minutes, which allows sufficient time for the assessment of primary study variables at matched BrAC on the ascending and descending limb (for assessment of acute tolerance) and at peak BrAC. In addition to the four core constructs, during the alcohol session we will also assess BrAC (Alco-sensor FST, Intoximeters, Inc.) at 10 minute intervals on the ascending limb and every 20 minutes on the descending limb to match assessment BrAC for study tasks;

Subjective Response to Alcohol (Subjective Effects of Alcohol Scale; Morean et al., 2013) and AID Intentions (willingness to drive) at multiple points on the BrAC curve. In addition, as part of K25

AA024182 (PI Davis-Stober), ongoing work in the PI's lab is focused on developing multiple novel decision making tasks relevant to AID. The laboratory component of the project will include tasks from this line of research that are both associated with AID and sensitive to acute alcohol effects. Ambulatory Assessment The ambulatory assessment arm of the project will involve 6 weeks of data collection for all study participants. During this period, data will be collected via self-report (EMA), the BActrack Skyn (TAC), and location and movement data passively collected from the GPS and accelerometer of the smartphone. Participants will be randomly assigned to two Full AA groups and the MA control group. EMA. During their AA participation, participants will provide self-report data using a study-provided smartphone. Following previous research (Trull et al., 2008a), participants will attend initial orientation sessions to be trained in completing assessments. Participants will return to the lab every 7 days for a brief session to review compliance and receive interim payment, which has proven to increase compliance (Trull et al., 2008b). Participants will complete 5 reports per day – a morning report and 4 “evening” reports. The “evening” reports will be scheduled for 6pm, 8pm, 10pm, and midnight.

However, participants will be able to reschedule or self-initiate the reports if they are consuming alcohol (or using other substances) at other times. The morning report will be scheduled on an individual basis, 30 minutes after participant's self- reported standard waking time. If participants go to bed prior to the midnight assessment, they will

complete a final assessment and put the smartphone to “sleep”, which will terminate follow-up prompts. To

facilitate compliance, assessments are designed to be short, with each assessment requiring less than 3 minutes to complete. For the Full AA conditions, the morning report will include a retrospective report on drinking and transportation the previous day, including drinking location(s), transportation used and options available; social context of drinking episodes (Thrul & Kuntsche, 2015); and intentions/plans for drinking and transportation the Research Strategy Page 67 Contact PD/PI: MCCARTHY, DENIS M upcoming evening. For the evening reports, participants will report on their mood, craving, core study variables, current drinking behavior (if any) and AID intentions. When participants do not report drinking, additional “filler” questions on current mood will be assessed to equalize time to complete the report. For

the MA control condition, participants will complete abbreviated versions of each report, with no questions

specific to AID. The morning report will ask about drinking location, transportation, and social context the previous day, with no questions on plans/intentions. The evening reports will assess mood, craving, core study variables (except for AID attitudes), and current drinking behavior. In addition to the four core constructs, the EMA Evening Assessments will also include: Mood. Questions from the Positive and Negative Affect Schedule (PANAS-X; Watson & Clark, 1999); Alcohol craving. Using a single 100-point visual analog scale, asking “How much do you want a drink right now?”; Social Context. Participants will be provided a list of who they are currently with and asked to check all that apply, including 1) romantic partner, friend, coworker, child(ren), parent, other family, someone else. This measure is used in EMA studies of drinking behavior by Co-investigator Trull (Lane et al., 2015); AID Intentions. Will be assessed at each evening assessment for those in the Full AA conditions.

Transdermal Alcohol Concentration (TAC). TAC measurement will be taken continuously by the Skyn. All participants will be asked to wear

their Skyn throughout the AA assessment period, but particularly during drinking episodes. A change in the revised application is that participants will not be able to see their current TAC at any time. However, for participants in the Full AA conditions, once the Skyn registers that they have reached .05 g/dl TAC, the app will prompt them to consider alternative transportation. Clickable links for local taxi/ride services will also be presented. Participants will be told that this prompt is based on their current TAC, and that it indicates it is not safe for them to drive, but will not be told the TAC trigger for this prompt. As noted, participants will wear the Skyn during their laboratory alcohol session. This will allow us to collect data on the accuracy of the Skyn's TAC estimates and, if necessary, develop individualized algorithms for estimating BrAC from TAC. Geospatial data. Throughout the AA assessment, participant location and movement data will be passively recorded on the study-provided smartphone. At the end of the AA period, this data will be combined with EMA data. When a participant reports drinking (or records a positive TAC), information about their drinking location, distance from home, travel using a motor vehicle, and what time they

returned home will be recorded. The most recent evidence for the accuracy of cellphone GPS systems indicate sufficient precision for our proposed use (Zandbergen & Barbeau, 2011). Using a much earlier generation of smartphones, they concluded that position estimation errors were uncommon, for example finding that horizontal location errors ranged from 5-21 meters in the least ideal conditions (static indoor testing). Data were more precise when moving outdoors, due to the clearer access to satellite data. Based on

this, we will use this geospatial information to provide a validity check on participant self-report. Discrepancies between participant selfreported location, use of motor vehicle, etc., will be probed during their next TLFB interview. As noted, Dr. Ken Sher will provide the project with a database of GPS locations for all nearby licensed drinking establishments

Statistical Analyses and Power:

Aim 1. Integrating laboratory and event-level predictors of AID. For Aim 1, we will employ a two-part (hurdle) model to test laboratory and AA predictors of AID. Part one of the model examines predictors of engagement in AID (or driving after any drinking). For this part of the model, we will employ a mixed logistic model examining factors that are predictive of a dichotomous variable indicative of whether, for a given drinking event, a participant drives after drinking alcohol. The second part of the model will employ a Gaussian linear mixed model, and examines predictors of a participant's TAC/BrAC level at the time of driving for drinking events where driving is reported. This analytic approach provides us with both increased flexibility and precision in our analyses. For example, we will be able to identify predictors of driving after any drinking as well as predictors that may be specific to driving at higher TAC. We believe that this flexibility is an important improvement to our approach in the revised application. For example, Hypothesis 1.3 will examine whether contextual factors increase the influence of AID risk factors on the likelihood of AID. Hypothesized contextual factors are based on studies demonstrating that drinking location (fewer miles to home; Kelley-Baker et al., 2013) and venue (drinking in restaurants; Gruenwald et al., 2002) are associated with increased AID risk. Our two-part model will allow us to test whether, for example, drinking venue increases the effect of AID risk factors for driving after any drinking, while drinking location increases the effect of AID risk factors when predicting driving at higher TAC/BrAC. In addition to examining TAC/BrAC at time of drinking as a continuous attribute, our approach will allow us to examine rational cutpoints for TAC – specifically, we will test models for cutpoints of TAC/BrAC of the current U.S. legal limit (.08) and NHTSA's proposed limit (.05). Research Strategy Page 68 Contact PD/PI: MCCARTHY, DENIS M Both models will have two levels, comprised of drinking events within participants. We will estimate models via both Maximum Likelihood methods and Generalized Estimating Equations; the former method can result in more accurate parameter estimates in certain situations (Stroup, 2013), whereas the latter method can be more flexibly extended to assumption violations (e.g., variance heterogeneity). Modeling will proceed by first fitting baseline GLMMs that establish associations between lower-level measures and the DV. The lower-level measures will be at the event level (including such variables as drinking venue), so they will directly address Hypothesis 1.2. Once these lower-level associations are established, we will then incorporate laboratory measures to address Hypothesis 1.1, followed by interactions to address Hypothesis 1.3. For example, consider studying the relationship between event-level impulsivity and AID. We will first person-center the impulsivity variable, so that the associated regression weight provides information about the effect of impulsivity as a participant departs from his/her mean level of impulsivity. We will then establish an association between impulsivity and AID using a two-level logistic model, where multiple eventlevel variables are included as IVs. The models will account for individual differences in associations between the event-level variables and AID, and they will be further extended (using level-2 IVs and cross-level interactions) to study the laboratory-based effects and moderation effects from Hypotheses 1.1 and 1.3. We will fit multiple versions of the models using different subsets of IVs, in order to establish that effects are robust to choice of predictors. This is important because unmodeled heterogeneity (resulting from omitted predictor variables) can adversely impact model estimates (Mood, 2009). To estimate power associated with these models, we adopted a simulation-based approach (Gelman & Hill, 2007). This involved generating artificial data from an assumed true model, fitting the proposed GLMM to each artificial dataset, and computing power based on the results. To estimate our power to detect an association between event-level impulsivity and AID, we specified parameter values for the true model based on previous studies. First, based on pilot data, we assumed that participants report driving following 15% of drinking events. We also assumed that each 5- point increase in impulsivity (as measured by delay discounting) was associated with (i) a 10% increase in the odds of driving after drinking (the low end of observed effect sizes for core study constructs) and (ii) a BrAC increase of .01, with random participant effects included in “maximal” models (Barr et al., 2013). In using these parameter values along with the anticipated sample sizes, our estimated power to detect these

associations is .91 in the logistic model and .99 in the linear mixed model. If Aim 2 is realized, then we can only use half of the Full AA group (the half that does not receive AA for the first six weeks), along with the

MA control group, to assess raw associations between lower-level variables and AID. In this case, we estimate power of .85 and of .99 to detect the associations (using the same values as above with a reduced sample size). We computed additional power estimates for moderation Hypotheses 1.3, using both the logistic model (where AID is a binary DV) and the Gaussian model (where TAC/BrAC is the DV). We assumed that Aim 2 was not realized, reducing the overall number of participants that we could enter into the analysis. For the logistic model, we assumed (as above, based on pilot data) that each 5-point increase in impulsivity was associated with a 10% increase in the odds of driving after drinking. We further assumed that this relationship was moderated by drinking venue, such that the relationship was diminished when participants were drinking at a restaurant. Under this scenario, power was .77 for the moderation

effect. For the Gaussian model, we assumed (as we did above) that each 5-point increase in impulsivity was associated with a mean BrAC increase of .01. We further assumed that this relationship was moderated by drinking location, such that the relationship was absent if a person was drinking 10 or more miles from home. Under this scenario, power was .96 for the moderation effect. Aim 2. Test potential effects of AA on AID behavior and intentions. For Aim 2, the study design affords us multiple manners in which we can examine the potential of mobile technology as an intervention for AID. We can estimate the effect of AA prospectively, examining whether or not AID changes from before a participant receives AA to after. We can also estimate the effect across experimental groups, examining whether or not AID differs between the groups with Full AA and the MA control group. To address this question, we will again employ the two DVs of driving after drinking and TAC in separate GLMMs (where drinking events are nested within participants). The IVs in each model will be dummy variables that are related to each participant's condition and to the time within the study. Specifically, the dummy variables will reflect whether or not the

individual is currently receiving AA, as well as whether or not the individual ever previously received AA. This will allow us to disentangle the effect of currently receiving AA from effects that may last after the individual has received AA. In computing power, we assumed 100 participants receiving AA at differing times (as described in Overview of Proposed Work) coupled with 100 participants in the control group. We further assumed that (i) active reception of AA reduces driving after Research Strategy Page 69 Contact PD/PI: MCCARTHY, DENIS M drinking from an average of twice per month to an average of 1.5 times per month (with individual differences in this effect), and (ii) active reception of AA reduces TAC of driving events by an average of .01. In employing assumption (i) in a logistic mixed model, we obtained a simulation-based power estimate of .79 to detect an intervention effect of active AA. In employing assumption (ii) in a Gaussian linear mixed model, we obtained a simulation-based power estimate of .97 to detect the intervention effect.