Protocol

This trial protocol has been provided by the authors to give readers additional information about their work.

This supplement contains the following items:

1. Original protocol (pp. 2-12), summary of changes (p. 13), and the final protocol (pp. 14-24).

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PROTOCOL TITLE: Reducing Risky Drinking using Smartphone Paired Breathalyzer

INTRODUCTION AND PURPOSE:

The proposed project will test six commercial cellphone breathalyzers against a police grade breathalyzer device.The study will test the accuracy of these smartphone breathalyzers at assessing Breath Alcohol Content (BrAC) against a standard police grade breathalyzer. This study aims to fill the knowledge gap by determining the validity of smartphone paired breathalyzer devices to accurately assess BrAC. Data collection includes collection of BrAC measurements, as well as survey data.

OBJECTIVES:

Given the popularity of these devices and the ability to share these data in a secure and automated fashion, if reliable, these devices could be used for implementing strategies to reduce risky drinking on a much broader scale than previously possible. Contingency management is the systematic use of behavioral rewards or disincentives to reinforce desired behaviors, and shows promise as one of the most effective means of prevention of drug and alcohol abuse. By using automated remote monitoring, innovative contingency management strategies incorporating insights from behavioral economics could be more easily implemented by providing immediate rewards and feedback and by taking advantage of group-based incentives and norms. However the validity of smartphone-paired breathalyzer measurements has not been independently confirmed, impeding further research application and funding. Informal assessments by the national media suggest that commercial smartphone paired breathalyzers may vary in reliability. This study aims to fill the knowledge gap by determining the validity of smartphone paired breathalyzer devices to accurately assess BrAC when compared against a police grade breathalyzer. By testing these devices against a police grade breathalyzer, the reliability of breathalyzers that pair with smartphones will be better understood, and we can determine if there are measurable differences in the blow rates of the commercial grade breathalyzers that connect to smart phone apps compared with police grade breathalyzers. By understanding the reliability of these technologies in measuring breath alcohol content, their potential utility in behavioral intervention strategies can be better understood. Our long-term objective is to leverage smartphone-paired breathalyzers to implement cost-effective and scalable behavioral interventions to reduce risky drinking behaviors such as drinking and driving.

BACKGROUND:

Nearly 88,000 people die annually from alcohol-related causes, making it the third leading cause of preventable death in the US.(National Institute on Alcohol Abuse and Alcoholism, 2015) Excessive alcohol consumption is a major risk factor for injury, assault, and suicide.(Easton, C.J., Swan, S., & Sinha, 2000; McNeill, Sherwood, Starck, & Thompson, 1998; White & Hingson, 2014) In 2013, 10,076 people were killed in drinking and driving-related motor vehicle crashes, accounting for one-third of all driving-related deaths.(National Highway Traffic Safety Administration, 2015) Individuals who engage in drinking and driving, compared to those do not, have similar cognitive abilities, actually understand legal consequences *better*, but are *poorer* planners and *more present-biased*, heavily weighing immediate costs and benefits relative to future ones when making decisions.(Sloan, Eldred, & Xu, 2014) This suggests that strategies such as planning a designated driver and providing immediate reinforcement of the benefit of moderating alcohol consumption are particularly promising approaches to reduce drinking and driving and binge drinking. Nationally, 17% of individuals aged 18 and older report binge drinking in the past month.(Centers for Disease Control and Prevention, 2015; Substance Abuse and Mental Health Services Administration, 2015) Importantly, binge drinkers are 14 times more likely to report alcohol-impaired driving than non-binge drinkers.(Naimi et al., 2003)

Contingency management, the systematic use of behavioral rewards or disincentives to reinforce desired behaviors, is one of the most effective approaches to reduce drug use,(Alessi & Petry, 2013; Kosten & O'Connor, 2003; N. M. Petry, 2000; Prendergast, Podus, Finney, Greenwell, & Roll, 2006; Roll et al., 2006) likely because heavy substance abusers are consistently more present biased.(MacKillop et al., 2011) Our prior work demonstrates the effectiveness of contingency management among dependent drinkers using daily visits to a treatment center.(Nancy M Petry, Martin, Cooney, & Kranzler, 2000) The effectiveness of contingency management relies on readily being able to detect substance use. However, alcohol is metabolized more quickly than most drugs, making it difficult to monitor in the community. In the last two years, breathalyzers that pair with smartphones have come on the market,("Alcohoot Smartphone Breathalyzer," n.d., "BACtrack Mobile Pro," n.d.; Drivesafe Evoc, n.d. "Floome: Smartphone Breathalyzer," n.d; "DrinkMate," n.d; "BACtrack Ultra-Portable Personal Keychain Breathalyzer," n.d) allowing individuals to monitor and more easily track their own breath alcohol concentration (BrAC). Given the popularity of these devices,("A smartphone breathalyzer," 2015; Jolly, 2015) booming sales (an $816 million dollar market),(Wintergreen Research, 2016) and the ability to share the data they generate in a secure and automated fashion, the devices could be used to implement contingency management strategies to reduce risky drinking on a much broader scale. These could be combined with contingency management strategies that incorporate insights from

behavioral economics to provide immediate rewards and feedback and take advantage of group-based incentives and norms.(Loewenstein et al., 2007; MS et al., 2015)
In the last two years, three companies have begun to sell breathalyzers that pair with smartphones,11–13 allowing individuals to monitor and track their own Breath Alcohol Content (BrAC).14,15 Given the popularity of these devices and the ability to share these data in a secure and automated fashion, if reliable, these devices could be used for implementing contingency management strategies to reduce risky drinking on a much broader scale than previously possible. Furthermore, by using automated remote monitoring, innovative contingency management strategies incorporating insights from behavioral economics could be more easily implemented by providing immediate rewards and feedback and by taking advantage of group-based incentives and norms.16,17 However the validity of smartphone-paired breathalyzer measurements has not been independently confirmed in the peer-reviewed literature, impeding further research application and funding. Informal assessments by the national media suggest that commercial smartphone paired breathalyzers may vary in reliability.18,19,14 By testing these devices against a police grade breathalyzer, the reliability of breathalyzers that pair with smartphones will be better understood, and we can determine if there are measurable differences in the blow rates of the commercial grade breathalyzers that connect to smart phone apps compared with police grade breathalyzers. By understanding the reliability of these technologies in measuring breath alcohol content, their potential utility in behavioral intervention strategies can be better understood.

CHARACTERISTICS OF THE STUDY POPULATION:

1. Target Population and Accrual:

Approximately 20 men and women, ages 21-39, will be enrolled who self-report as moderate drinkers, who are not seeking treatment for alcohol abuse (i.e. no treatment in the past year and current verbal report of not wanting treatment) do not have alcohol use disorder, as defined by the DSM-V, and do not have any medical conditions that limit or prevent alcohol consumption. Because there are well known risks of alcohol to the unborn fetus, women will be screened with a urine pregnancy test and must confirm a negative result before alcohol is administered. Children will not be recruited for this protocol because alcohol will be administered and the legal drinking age is 21 years. Due to the risks involved with drinking and driving, participants will only be enrolled in the study if they are willing to take public transportation or an uber rideshare home from the study visit.

Subjects will be healthy volunteers, 21-39 years old. They will be non-treatment seeking community drinkers who have previously consumed 4 or more standard drinks of alcohol for women and 5 or more standard drinks of alcohol for men, without problems. Subjects will be included if they drink socially on a drinking level of 4 or more standard drinking days, but excluded if they consume on average 12 or more drinks per week. They will be excluded if they have met criteria for DSM-V (American Psychiatric Association 2013) alcohol or drug dependence (lifetime) or for alcohol or drug abuse currently or in the past 12-months or another major psychiatric disorder,) are using psychotropic medications or are pregnant or nursing. Subjects will undergo a brief medical screening, female subjects will confirm that they are not pregnant using a urine screening.

2. Key Inclusion Criteria:

Inclusion criteria will be: (a) age 21-39 old, (b) Less than 4 drinking days and less than12 drinks per week on average in the past 2 months, (c) have previously consumed four (women) or five (men) or more standard drinks without problems (d) a valid photo ID (e) willing to take public transportation home, via septa or an uber rideshare credit.

3. Key Exclusion Criteria:

Exclusion criteria will be (a) desire alcohol treatment now or received it in the past 6 months, (b) alcohol dependence with withdrawal per DSM-V criteria and (c) non-English-speaking (d) individuals who have a medical condition or who are taking medication which limits or prevents the consumption of alcohol. We are excluding non-english speaking individuals due to the fact that we do not have translated materials so they will be unable to consent to participate in the study activities. We are also excluding individuals who are under 21 years in age due to legal restrictions of consuming alcohol. We are excluding individuals who have psychological or medical conditions, or are taking medication, that limit or prevent the consumption of alcohol.

4. Subject Recruitment and Screening:

Subjects for this study will be recruited primarily from individuals who present themselves for evaluation for study inclusion by calling our research facility. It is expected that the majority of subjects will volunteer to participate after responding to IRB-approved advertisements on mass transit; and broadcast email messages at institutions (including the University of Pennsylvania Health System) that offer such a service; and by posting/distributing recruitment materials in community settings with public posting areas or other means of providing community access to materials (such as hospitals, town halls,

public libraries, YMCAs, health fairs/organizations). We will obtain permission before distributing or posting the approved recruitment materials.

5. Early Withdrawal of Subjects:

During the intake survey participants will be assessed for suicidal ideation and behavior using the Columbia-Suicide Severity Rating Scale. Participants who exhibit suicidal ideation or behavior will be withdrawn from the study and provided resources.

6. Vulnerable Populations:

This study will not include vulnerable populations.

7. Populations vulnerable to undue influence or coercion:

This study may enroll employees or students of Penn. These participants will not be recruited directly or incentivized differently than other subjects in the study. During informed consent study staff will review the voluntary nature of their participation and reminded that they are able to leave the study at any time during the study procedures.

STUDY DESIGN:

This study tests three commercial cellphone breathalyzers (Alcohoot, BacTrack, evoc) and a wearable device that measures blood alcohol content through the skin (BacTrack Skyn) against a police grade breathalyzer device (Intoxilyzer 240)(Test, n.d.). These devices were chosen as the only currently commercially available breathalyzers that pair with smartphones and the only device that moniters alcohol content through the skin. This study will test the accuracy of these smartphone breathalyzers at assessing BrAC against a standard police grade breathalyzer, which is widely used to test BrAC.

In a controlled setting, 20 participants, aged 21-39, will attend a session where they receive 3 doses of a standard amount of alcohol, based on weight and gender(Watson, Watson, & Batt, 1981), designed to raise Blood Alcohol Content to 1.02g/dL. Breath alcohol content (BrAC) will first be measured with each of the three commercial smartphone-paired breathalyzer (Drivesafe Evoc (Drivesafe Evoc, n.d.), Alcohoot(Alcohoot Smartphone Breathalyzer, n.d.), BacTrack Pro(BACtrack Mobile Pro, n.d.)) and Intoxilyzer 240. Some participants will be instructed to wear the Bactrack skyn at the beginning of the study). After which, the self-report survey will be administered. The order in which the Breathalyzers are administered will change for each use, per a pre-determined, randomized, order, which only the study staff will have access to. A second dose and third dose will be given and this process will be repeated at 40 minutes and 80 minutes after the first dose. Participants will be blinded to all breathalyzer measurements. A study smartphone will be used to collect smartphone-paired breathalyzer readings. We will also measure self-reported intoxication rating using measures subjective intoxication: Personal Drinking Habits Questionnaire (PDHQ)(Vogel-Sprott, 1992), Perceived Driver Fitness(Van Dyke & Fillmore, 2014)and Perceived intoxication and BAC estimation(Harrison & Fillmore, 2005; Harrison, Marczinski, & Fillmore, 2007) administered by the study staff.

All research activities will be conducted in the CTRC and alcohol will be provided from Investigational Drug Service. All research staff will be fully trained in the pilot protocol and their role in the study, will be supervised by the PI, Dr. Mucio (Kit) Delgado, MD (Assistant Professor of Emergency Medicine), and will be trained to refer patients to the appropriate provider (emergency department, outpatient doctor/clinic, social worker) as warranted. A nurse, trained in the protocol, will be onsite at all times and able to assist if any adverse effects occur.

METHODS:

There will be 4 phases of the study:

1. Recruitment: We will use broad-based and cost-effective recruitment strategies including: a) advertisements in UPHS and CHOP employee weekly emails; and b) posting of flyers.Individuals, who are interested in the study, will be contacted and screened over the telephone.
2. Phone Screening: General information will be provided to the prospective subject. Study screening form (attached) will be administered, eligibility confirmed, and research staff will go over informed consent with participant. There will be an optional pre-study in person visit if necessary. Inclusion criteria will be: (a) age 21-39 old, (b) Less than 4 drinking days and 12 drinks per week on average in the past 2 months, (c) have consumed either 4 (women)or 5 (men) or more standard drinks on a single occasion without problems (d) a valid photo ID (e) willing to take public transportation home, via septa or an uber rideshare credit. Exclusion criteria will be (a) desire alcohol treatment now or received it in the past 6 months, (b) alcohol dependence with withdrawal per DSM-V criteria (c) non-English-speaking, and (d) individuals who have a medical

condition or who are taking medication which limits or prevents the consumption of alcohol.Interested and eligible participants will schedule their study visit. .

3. Study Visit: On a predetermined study date, eligible subjects will come to the study site for a bar-lab session (timeline below), which will be conducted in the Clinical and Translational Research Center. Each study session will comprise of up to 4 participants, one per bed, and last about 5-6 hours. The space will be configured as a bar-like setting. Prior to the test sessions they will be instructed to east a small meal before fasting for 2 hours, abstain from caffeine for 8 hours and alcohol for 24 hours. Upon arrival, subjects will sign written informed consent. After which the subjects will undergo BrAC measurement, confirming a breath sample of 0 BrAC, using the Intoxilyzer 240.(Test, n.d.) and complete a screening and medical history. At the CTRC participants will undergo a brief medical screening which will include measuring their blood pressure, heart rate, a urine pregnancy test for female participants, and complete the columbia-suidcide severity rating scale. This screening will be performed by a CTRC nurse, who will be trained in the protocol.

4. Intake Survey: After which an intake survey will be administered by study staff, which Includes a) Driving History and Experience Questionnaire DHEQ(Harrison & Fillmore, 2005), b) Drinking and Driving Questionnaire(McCarthy, Niculete, Treloar, Morris, & Bartholow, 2012), c) , this survey measures participants drinking habits during a single week, frequency of drinking, typical duration of drinking events, and number of months an individual has been drinking on a regular basis. Participants will then complete the Decision Making Survey, which has questions related to their Delayed discounting and measures of impulsivity (Senecal, Wang, Thompson, & Kable, 2012).

4. Dose Administration: Before dose administration a portion of particpants will be instructed to wear the Bactrack skyn wearable device. All subjects will first be given a priming dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 0.03-0.04 g/dL based on weight and gender(Watson et al., 1981). Subjective ratings of alcohols effects and BrAC will be obtained after each dose. Each dose will be consumed within a standard 10-minute block to minimize inter-subject variability in the consumption rate. After each drink, participants will wait 20 minutes, and be instructed to rinse their mouth with a nonalcoholic mouthwash to ensure proper results. Breath alcohol content (BrAC) will first be measured with each of the three commercial smartphone-paired breathalyzer (Drivesafe Evoc (Drivesafe Evoc, n.d.), Alcohoot(Alcohoot Smartphone Breathalyzer, n.d.), BacTrack Pro(BACtrack Mobile Pro, n.d.)) and the Intoxilyzer 240, which will be tested in a randomized order and recorded. The order in which the devices are tested will change for each use, per a pre-determined, randomized, order; this order will be blinded to the participants. Participants will also be blinded to all breathalyzer measurements. A study smartphone will be used to collect smartphone-paired breathalyzer readings. This process will be repeated two times at minute 40 and minute 80. After each BrAC measurement has been obtained, we will also measure self-reported intoxication rating using: Self-Reported intoxication Survey: Includes a) Perceived DriverFitness(Van Dyke & Fillmore, 2014) and b) Perceived intoxication and BAC estimation.(Harrison & Fillmore, 2005; Harrison et al., 2007) (survey attached).
At 110 minutes, a nurse will perform a blood draw on the participants, which will be used to determine blood alcohol content. This will administered through a survey given by a study staff trained in the protocol. After 150 minutes if participants BrAC does not measure .02 or below, participants will be tested at intervals of 20 minutes until their blood alcohol content has reached a level of .02 or below at which time they will be provided with transportation home. Midway through the study participants will receive a small meal provided by the CTRC.

Timeline: Study activities at Site Visit

Time	**Procedures ***
00 - 10 minutes	• Participant is given a priming dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 0.03-0.04 g/dL based on calculations based on weight and gender
10-30 minutes	• Participant rinses with alcohol free mouthwash.
30-40 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Survey
40-50 minutes	• Second dose of alcohol designed to raise BrAC to 0.07-.08’
50-70 minutes	• Participant rinses with alcohol free mouthwash.
70-80 minutes	4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • 2. Self Report of Intoxication Survey

80-90 minutes	• Participant receives third dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 1.01-1.02 g/dL •
90-110 minutes	• Participant rinses with alcohol free mouthwash.
110-120 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Blood draw to determine Blood Alcohol Content • Self Report of Intoxication Survey
135 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
150 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
175 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
190 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
205 minutes until study completion	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey: • Breathalyzer measurements will be obtained until participant is at .02 or lower

* Please note the above table is for participants 1-10. For participants 11-20, the same format will be used but the breathalyzers will be swapped for the following: Backtrack Keychain, DrinkMate, and Floome.

1. Study Instruments:

1. Intake Survey

a) Driving History and Experience Questionnaire DHEQ (Harrison & Fillmore, 2005)This self-report questionnaire gathered information on driving history and behaviors. Included in the questionnaire are measures of driving experience such as length of time holding a driver's license and number of days and miles driven per week. The questionnaire also gathered information about participants driving behaviors, such as license revocations, presence and number of DUI citations and punishments, traffic accidents, traffic tickets, typical driving environment (rural, urban, and interstate), and the type of vehicle transmission (manual, automatic, or both).

b.) Drinking and driving questionnaire (McCarthy et al)This self-report questionnaire gathered information on individuals drinking and driving history. The questionnaire asked participants to respond to questions about drinking and driving history on 4 or 5 point Likert scales. The questionnaire included a measure of frequency of drinking and driving and typical quantity of alcohol consumed before driving. The items were obtained from a scale reported by McCarthy et al. (2012).

2. Decision making survey

a). the Delayed discounting questionnaire (Senecal et al 2012).

b). Barratt Impulsiveness Scale BIS-11 (Patton et al., 1995)This 30-item self- report questionnaire is designed to measure the personality dimension of impulsivity. Participants rated 30 different statements on a 4-point Likert-type scale ranging from Rarely/Never to Almost Always/Always. Higher total scores indicate higher levels of self-reported impulsiveness (score range 30120).

3. Self-Reported intoxication Survey (attached to the protocol): Includes visual analogue scales which measure self-reports of:

a) Perceived Driver Fitness (Van Dyke and Fillmore 2014)

b) Perceived intoxication and BAC estimation.(Harrison and Fillmore 2005; Harrison et al 2007)

4. Intoxilyzer 8000: The Intoxilyzer breathalyzer is a police grade breathalyzer that has been used in various studies in order to achieve an accurate estimate of BrAC (Fillmore 2001; Harrison and Fillmore 2005;)

5. Smartphone Breathalyzers (Alcohoot, BacTrack, DriveSafe Evoc, Floome, Drink Mate, Keychain Backtrack) These devices were chosen as the only currently commercially available breathalyzers that pair with smartphones, which have received growing attention in the national media. (A smartphone breathalyzer, 2015; Jolly, 2015)

6. Bactrack Skyn: Bactrack skyn is a wearable device that tracks breath alcohol content. A portion of participants will be selected to wear these devices in order to validate their ability to measure and estimate blood alcohol content. (https://www.bactrack.com/pages/bactrack-skyn-wearable-alcohol-monitor).

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Floome: https://floome.com/

Drink Mate: http://www.getdrinkmate.com/

BACtrack Keychain: https://www.bactrack.com/products/bactrack-keychain-breathalyzer?&mkwid=Ch2zPSsL&pcrid=102311672917&pkw=bactrack%20keychain&pmt=e&pdv=c&ring-central=google-ppc&gclid=CjwKEAiAs_PCBRD5nIun9cyu01kSJAA-WD-ruugi8IvC2_Z7nN_Mz40Fd2MYTiexYL2MMobRXXZfIRoCLLvw_wcB

2. Group Modifications:

Because there are no trial arms in this study, all participants will complete the same study activities, and there will be no group modifications necessary. Because of the limited availability of the Bactrack Skyn measurement tool, only a portion of our participants will receive this device depending on availability of the device.

3. Method for Assigning Subjects to Groups:

There will be no randomization for this study. All participants will receive the same study protocol. Except a selection of participants will be instructed to wear the Bactrack skin wristband for the duration of the study. This will not effect any other aspect of the study protocol.

4. Administration of Surveys and/or Process:

Interested participants will call the study hotline where an IRB-approved research assistant or project manager, will answer any questions, administer the study screening and go over the written informed consent. There will be an optional in person study visit for the participant to come in and review study procedures, and sign written informed consent, in person. At the study visit, which occurs at a predetermined time, the participant will first sign written informed consent to participate. They will then take an initial survey, with questions related to their past alcohol use and habits including Driving History and Experience Questionnaire DHEQ1, Drinking and Driving Questionnaire. Participants will also take the Decision making survey, which includes The Barratt Impulsiveness Scale, and the Delayed discounting questionnaire. Some participants will then be instructed to wear the BACtrack skyn wrist device. Participants will then receive three doses of vodka mixed with juice based on their gender and weight designed to reach a peak blood alcohol level of .08 g/dL. After each dose their Breath Alcohol Content (BrAC) will be measured using the three smartphone breathalyzers and the intoxilyzer, measured in a random order. After each breathalyzer measurement, participants will receive the Self-Report of Intoxication Survey, which will include Perceived Driver Fitness and Perceived intoxication and BAC estimation, which are measured using a visual analogue scale.

Besides a preliminary study visit for participants to consent to the study and complete the eligibility survey, all research activities will take place in one of the four CTRC study sites and will occur in a study session of approximately six hours in length with up to four participants at each session for a total of five study sessions. Participants will be separated by curtains and fill out individual paper surveys on paper sheets in order to maintain confidentiality.

Data collection will include contact information, medical history, and history of alcohol use, various measurements of Breath Alcohol Content (BrAC), as well as survey data from the self-reported intoxication survey. The informed consent process during study enrollment will describe all of these aspects of data collection.

5. Data Management:

Paper forms will be used to collect data and a research assistant will create and maintain the research database. All source documents will be identified by study identification (ID) number, and the key to that ID number will be kept in a locked file cabinet. All personally identifiable information also will be kept separately in a locked file cabinet. No results will be reported in a personally identifiable manner. All tracking system data and research database information will be password-protected with several levels of protection: first, a password will be required to access the computer of the user who has access to the

6. Statistical Analysis Plan:

Primary Outcome Measures

1. Blood Alcohol Content Variability

Mean paired-difference between the peak BrAC and phlebotomy drawn BAC among the police-grade and personal breath testing devices

Secondary Outcome Measures :

1. Differences in Breath Testing Device Readings

Mean difference in BrAC between the police-grade and personal breath testing devices

Other Outcome Measures:

1. Driving Limit Threshold Detection The sensitivity to detect driving-limit thresholds of > 0.05% and > 0.08% relative to the police-grade breath testing devices

To determine differences in 1) peak BrAC and phlebotomy drawn BAC among the police-grade and personal breath testing devices and 2) differences in BrAC between the police-grade and personal breath testing devices, we will use analysis of variance in repeated measures where the instrument was the repeated measure. To adjust for multiple comparisons we will use Tukey-Kramer tests. Results will be presented as mean paired differences with 95% confidence intervals. Additionally, we will assess the sensitivity to detect driving-limit thresholds of $\geq$ 0.05% and $\geq$ 0.08% relative to the police-grade breath testing devices and report 95% confidence limits.

RISK/BENEFIT ASSESSMENT:

1. Risks:

There is some risk that subjects will be identified as participants in the study and that the confidential information provided regarding psychiatric and substance use history will be inadvertently disclosed without the subjects' permission.
Urine pregnancy testing is performed for all women of reproductive potential, prior to alcohol administration, to avoid the potential for adverse fetal effects of alcohol. These procedures should add no additional risks beyond the minimal risks normally associated with them.Over a period of 120 minutes, participants will be given three doses of alcohol, which will result in a BrAC of 1.01-1.02g/dL. This amount of alcohol is equivalent to 4-5 standard drinks, an amount that these moderate-drinking subjects have ingested previously. Although the amount of alcohol available to them will produce only moderate blood alcohol levels, subjects could feel intoxicated or react negatively to the alcohol, such as nausea or dehydration. Engaging in any dangerous activities during this period would increase risk of self-harm. Precautions to minimize these risks are discussed below.

After consuming alcohol, participants may be unsafe to operate a vehicle. This risk will be mitigated by providing participants transportation home with either a septa token or rideshare credits for uber of up to $30, depending on their location.
Study activities will be performed in a special clinical research room located in a hospital setting in close proximity to an inpatient care. Nursing and medical personnel will be available to assist in the care of the subject if any adverse event occurs. Participants' breath alcohol concentration (BrAC) and their general condition will be monitored during all aspects of the procedure. The bar-lab will be located in a safe and secure area in in a hospital where medically trained staff will be onsite and there will be ready access to emergency care should it be necessary. All subjects will remain in the test area until their BrAC will be below 0.02 g/dL. All study activities will occur in the afternoon, no earlier than 11am, to minimize nausea and vomiting that could occur with morning alcohol consumption. A meal will be provided.

Rating Scales and Questionnaires. To avoid breach of confidentiality, subjects' names will appear only on a consent form, a telephone screening form and a "key" form kept in a locked cabinet. All forms that contain identifying information will be kept double locked (i.e., in a locked cabinet, in a locked room) to maintain their security. All study data forms will contain only the subject's unique study identification number, using a reference system maintained by the study staff. Completed study forms will be kept in a locked cabinet, the key to which will be available only to the PI and staff working on this study. Subject visits will be scheduled and no information about the subject will be provided to anyone (except in emergencies as defined above) in person or by telephone.

All paper research records will be stored in locked cabinets and only the investigators and only IRB approved study will have access to those records.

2. Benefits:

There are no direct benefits to participation. Participants are contributing to preparation of a larger study, which in turn may have benefits to society in general. Given that anecdotal research shows variation in Breathalyzer readings, understanding the validity of smartphone paired breathalyzers has potential to benefit society in general.

3. Subject Privacy:

Participants will be screened for eligibility over the telephone with a trained research team member in a private office. The participant will review the paper consent form in a private room on the day of the study visit. The participant will have a private room in the research lab during the study visit.

4. Subject Confidentiality:

Participants who have seen recruitment material will call a study line in order to sign up for the study. At this pre-screening phone call, the research project manager will briefly go over study procedures. If the participant is interested, they will be complete a brief (less than ten minute) screening over the phone to determine eligibility. Participants may be asked to meet with the study staff prior to scheduling their study visit to determine eligibility. At the study visit, eligible participants will sign written informed consent, and be administered the study protocol; all study documents will be de-identified after all contact has been made. Participant information will be stored in a locked filing cabinet only accessible by the research assistants, PI, and project manager. Personal information will not be stored with study data and will be destroyed after data collection.

How will confidentiality of data be maintained? Check all that apply.

☒ Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

☒ Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.

☒ Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

☒ Whenever feasible, identifiers will be removed from study-related information.

☐ A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

☒ A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

☐ Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

☐ Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

☐ Other (specify):

We will require a waiver of consent written consent in order to administer the screening survey over the phone because it is not feasible for each participant to be required to come in, in order to answer questions in the screening survey. Before the screening survey is administered, participants will be prompted to provide verbal consent (attached to this protocol) over the phone, using the verbal consent script that is attached to this protocol. Once a participant is screened, using the screener, and has set up a study session, participants will signed written informed consent at the beginning of their study visit prior to any other activities being completed.

5. Protected Health Information

- Name
- Street address, city, county, precinct, zip code, and equivalent geocodes
- All elements of dates (except year) for dates directly related to an individual and all ages over 89
- Telephone and fax number
- Electronic mail addresses

6. Compensation:

Each subject will receive a $100 cash card as an incentive for completing the 6 hour study session. This cashcard will work through the Greenphire clincard system (SOP attached to this submission). Information about the greenphire system will be provided in the consent document for the participant. Information, including social security number, will be collected from the participant at the intake phone call in order to set up an online account that the participant will be able to access. Participants will be reimbursed for travel and ensured a ride home by receiving either a septa token or up to $30 in rideshare credits from Uber.

7. Investigator's Risk/Benefit Assessment:

In general the benefits outweigh the risks in this study. Participants will receive information on alcohol consumption and health. Participants are also contributing to preparation of a larger study, which in turn may have benefits to society in general. Although there are some risks involved in participating in this study, as mentioned above, these can be minimized to ensure that the potential benefits exceed the potential risks, so that the risk/benefit ratio is favorable.

INFORMED CONSENT:

1. Consent Process:

Participants will respond to recruitment material by calling the study hotline. After calling the study hotline, participants will be screened for eligibility and will schedule a visit. At the study visit, participants will sign written informed consent. Consent will be obtained by explaining the study objectives, procedures, and potential risks to subjects verbally and in writing at a pre-screening and / or screening visit. Subjects will be given an opportunity to ask questions and will be provided with complete and accurate answers to any questions they may have. Written documentation of this process will be obtained using the IRB-approved consent form. Subjects are given a signed copy of the consent form for his or her reference.

2. Waiver of Informed Consent:

This research in general involves minimal risks to the participants because the benefits outweigh the risks in this study. Specifically the waiver of consent only applies to administration of the screening survey, and completing this survey involves minimal risk to participants, such as there is some risk that confidential information provided regarding psychiatric and substance use history will be inadvertently disclosed without the subjects' permission. Methods outlined elsewhere in this protocol will be in place to protect participant information to minimize this risk. Also the benefits for allowing participants to take screening over the phone and not having to come in for two study visits outweighs this risk.

It is not always feasible for participants to schedule a separate study visit to answer a brief screening survey. In order to accommodate participants who cannot schedule a separate study visit, we are requesting a waiver of written informed consent only to administer the screening survey over the phone. Allowing this step in the process to be completed over the phone will make the study more feasible to be completed by participants.

Once a participant is screened, using the screener, and has set up a study session, participants will sign written informed consent at the beginning of their study visit prior to any other activities being completed.

RESOURCES NECESSARY FOR HUMAN RESEARCH PROTECTION:

All research activities will be conducted in the CTRC and alcohol will be provided from Investigational Drug Service. The project manager will oversee all study operations and two research assistants will be trained in the protocol and present at the study sessions. All research staff will be fully trained in the pilot protocol and their role in the study, will be supervised by the PI, Dr. Mucio (Kit) Delgado, MD (Assistant Professor of Emergency Medicine), and will be trained to refer patients to the appropriate provider (emergency department, outpatient doctor/clinic, social worker) as warranted. A nurse, trained in the protocol, will be onsite at all times and able to assist if any adverse effects occur.

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Summary of changes to the research protocol.

Protocol Version	**Amendment or Clarification**	**Dates**
Version 2	Changes made to the protocol: --- Study completion changed from a BrAC reading of 0.02 to 0.03. Reason: As participants agree not to operate a vehicle after leaving the laboratory and there is not a significant difference in impairment or loss of coordination between a BAC of 0.02 and 0.03 (Bailey, 1993; Compton et al., 2002, National Institute on Alcohol Abuse and Alcoholism, 1994), we are making this adjustment to reduce undue burden on the participant, particularly because it has often taken participants more than 6 hours to reach a BAC reading of 0.02. -- Included a second phase of enrollment as we had not met our enrollment goals with phase 1. Enrollment increased from 20 to 30 participants.	3/21/17 IRB Approval
Version 1.0 Initial IRB approval	The approved IRB protocol was considered Version 1.0 of the protocol. Approval was granted 11-18-2014.	12/8/2016 IRB Approval, Full Protocol

Version Date: 11.28.2016

PRINCIPAL INVESTIGATOR: M. Kit Delgado, MD, MS, FACEP

PROTOCOL TITLE: Reducing Risky Drinking using Smartphone Paired Breathalyzer

INTRODUCTION AND PURPOSE:

The proposed project will test six commercial cellphone breathalyzers against a police grade breathalyzer device.The study will test the accuracy of these smartphone breathalyzers at assessing Breath Alcohol Content (BrAC) against a standard police grade breathalyzer. This study aims to fill the knowledge gap by determining the validity of smartphone paired breathalyzer devices to accurately assess BrAC. Data collection includes collection of BrAC measurements, as well as survey data.

OBJECTIVES:

Given the popularity of these devices and the ability to share these data in a secure and automated fashion, if reliable, these devices could be used for implementing strategies to reduce risky drinking on a much broader scale than previously possible. Contingency management is the systematic use of behavioral rewards or disincentives to reinforce desired behaviors, and shows promise as one of the most effective means of prevention of drug and alcohol abuse. By using automated remote monitoring, innovative contingency management strategies incorporating insights from behavioral economics could be more easily implemented by providing immediate rewards and feedback and by taking advantage of group-based incentives and norms. However the validity of smartphone-paired breathalyzer measurements has not been independently confirmed, impeding further research application and funding. Informal assessments by the national media suggest that commercial smartphone paired breathalyzers may vary in reliability. This study aims to fill the knowledge gap by determining the validity of smartphone paired breathalyzer devices to accurately assess BrAC when compared against a police grade breathalyzer. By testing these devices against a police grade breathalyzer, the reliability of breathalyzers that pair with smartphones will be better understood, and we can determine if there are measurable differences in the blow rates of the commercial grade breathalyzers that connect to smart phone apps compared with police grade breathalyzers. By understanding the reliability of these technologies in measuring breath alcohol content, their potential utility in behavioral intervention strategies can be better understood. Our long-term objective is to leverage smartphone-paired breathalyzers to implement cost-effective and scalable behavioral interventions to reduce risky drinking behaviors such as drinking and driving.

BACKGROUND:

Nearly 88,000 people die annually from alcohol-related causes, making it the third leading cause of preventable death in the US.(National Institute on Alcohol Abuse and Alcoholism, 2015) Excessive alcohol consumption is a major risk factor for injury, assault, and suicide.(Easton, C.J., Swan, S., & Sinha, 2000; McNeill, Sherwood, Starck, & Thompson, 1998; White & Hingson, 2014) In 2013, 10,076 people were killed in drinking and driving-related motor vehicle crashes, accounting for one-third of all driving-related deaths.(National Highway Traffic Safety Administration, 2015) Individuals who engage in drinking and driving, compared to those do not, have similar cognitive abilities, actually understand legal consequences *better*, but are *poorer* planners and *more present-biased*, heavily weighing immediate costs and benefits relative to future ones when making decisions.(Sloan, Eldred, & Xu, 2014) This suggests that strategies such as planning a designated driver and providing immediate reinforcement of the benefit of moderating alcohol consumption are particularly promising approaches to reduce drinking and driving and binge drinking. Nationally, 17% of individuals aged 18 and older report binge drinking in the

past month.(Centers for Disease Control and Prevention, 2015; Substance Abuse and Mental Health Services Administration, 2015) Importantly, binge drinkers are 14 times more likely to report alcohol-impaired driving than non-binge drinkers.(Naimi et al., 2003)

Contingency management, the systematic use of behavioral rewards or disincentives to reinforce desired behaviors, is one of the most effective approaches to reduce drug use,(Alessi & Petry, 2013; Kosten & O'Connor, 2003; N. M. Petry, 2000; Prendergast, Podus, Finney, Greenwell, & Roll, 2006; Roll et al., 2006) likely because heavy substance abusers are consistently more present biased.(MacKillop et al., 2011) Our prior work demonstrates the effectiveness of contingency management among dependent drinkers using daily visits to a treatment center.(Nancy M Petry, Martin, Cooney, & Kranzler, 2000) The effectiveness of contingency management relies on readily being able to detect substance use. However, alcohol is metabolized more quickly than most drugs, making it difficult to monitor in the community. In the last two years, breathalyzers that pair with smartphones have come on the market,("Alcohoot Smartphone Breathalyzer," n.d., "BACtrack Mobile Pro," n.d.; Drivesafe Evoc, n.d. "Floome: Smartphone Breathalyzer," n.d; "DrinkMate," n.d; "BACtrack Ultra-Portable Personal Keychain Breathalyzer," n.d) allowing individuals to monitor and more easily track their own breath alcohol concentration (BrAC). Given the popularity of these devices,("A smartphone breathalyzer," 2015; Jolly, 2015) booming sales (an $816 million dollar market),(Wintergreen Research, 2016) and the ability to share the data they generate in a secure and automated fashion, the devices could be used to implement contingency management strategies to reduce risky drinking on a much broader scale. These could be combined with contingency management strategies that incorporate insights from *behavioral economics* to provide immediate rewards and feedback and take advantage of group-based incentives and norms.(Loewenstein et al., 2007; MS et al., 2015)

In the last two years, three companies have begun to sell breathalyzers that pair with smartphones,11–13 allowing individuals to monitor and track their own Breath Alcohol Content (BrAC).14,15 Given the popularity of these devices and the ability to share these data in a secure and automated fashion, if reliable, these devices could be used for implementing contingency management strategies to reduce risky drinking on a much broader scale than previously possible. Furthermore, by using automated remote monitoring, innovative contingency management strategies incorporating insights from behavioral economics could be more easily implemented by providing immediate rewards and feedback and by taking advantage of group-based incentives and norms.16,17 However the validity of smartphone-paired breathalyzer measurements has not been independently confirmed in the peer-reviewed literature, impeding further research application and funding. Informal assessments by the national media suggest that commercial smartphone paired breathalyzers may vary in reliability.18,19,14 By testing these devices against a police grade breathalyzer, the reliability of breathalyzers that pair with smartphones will be better understood, and we can determine if there are measurable differences in the blow rates of the commercial grade breathalyzers that connect to smart phone apps compared with police grade breathalyzers. By understanding the reliability of these technologies in measuring breath alcohol content, their potential utility in behavioral intervention strategies can be better understood.

CHARACTERISTICS OF THE STUDY POPULATION:

1. Target Population and Accrual:

Approximately 20 men and women, ages 21-39, will be enrolled who self-report as moderate drinkers, who are not seeking treatment for alcohol abuse (i.e. no treatment in the past year and current verbal report of not wanting treatment) do not have alcohol use disorder, as defined by the DSM-V, and do not have any medical conditions that limit or prevent alcohol consumption. Because there are well known risks of alcohol to the unborn fetus, women will be screened with a urine pregnancy test and must confirm a negative result before alcohol is administered. Children will not be recruited for this protocol because alcohol will be administered and the legal drinking age is 21 years. Due to the risks involved with drinking and driving, participants will only be enrolled in the study if they are willing to take public transportation or an uber rideshare home from the study visit.

Subjects will be healthy volunteers, 21-39 years old. They will be non-treatment seeking community drinkers who have previously consumed 4 or more standard drinks of alcohol for women and 5 or more standard drinks of alcohol for men, without problems. Subjects will be included if they drink socially on a drinking level of 4 or more standard drinking days, but excluded if they consume on average 12 or more drinks per week. They will be excluded if they have met criteria for DSM-V (American Psychiatric Association 2013) alcohol or drug dependence (lifetime) or for alcohol or drug abuse currently or in the past 12-months or another major psychiatric disorder,) are using psychotropic medications or are pregnant or nursing. Subjects will undergo a brief medical screening, female subjects will confirm that they are not pregnant using a urine screening.

2. Key Inclusion Criteria:

Inclusion criteria will be: (a) age 21-39 old, (b) Less than 4 drinking days and less than12 drinks per week on average in the past 2 months, (c) have previously consumed four (women) or five (men) or more standard drinks without problems (d) a valid photo ID (e) willing to take public transportation home, via septa or an uber rideshare credit.

3. Key Exclusion Criteria:

Exclusion criteria will be (a) desire alcohol treatment now or received it in the past 6 months, (b) alcohol dependence with withdrawal per DSM-V criteria and (c) non-English-speaking (d) individuals who have a medical condition or who are taking medication which limits or prevents the consumption of alcohol. We are excluding non-english speaking individuals due to the fact that we do not have translated materials so they will be unable to consent to participate in the study activities. We are also excluding individuals who are under 21 years in age due to legal restrictions of consuming alcohol. We are excluding individuals who have psychological or medical conditions, or are taking medication, that limit or prevent the consumption of alcohol.

4. Subject Recruitment and Screening:

Subjects for this study will be recruited primarily from individuals who present themselves for evaluation for study inclusion by calling our research facility. It is expected that the majority of subjects will volunteer to participate after responding to IRB-approved advertisements on mass transit; and broadcast email messages at institutions (including the University of Pennsylvania Health System) that offer such a service; and by posting/distributing recruitment materials in community settings with public posting areas or other means of providing community access to materials (such as hospitals, town halls, public libraries, YMCAs, health fairs/organizations). We will obtain permission before distributing or posting the approved recruitment materials.

5. Early Withdrawal of Subjects:

During the intake survey participants will be assessed for suicidal ideation and behavior using the Columbia-Suicide Severity Rating Scale. Participants who exhibit suicidal ideation or behavior will be withdrawn from the study and provided resources.

6. Vulnerable Populations:

This study will not include vulnerable populations.

7. Populations vulnerable to undue influence or coercion:

This study may enroll employees or students of Penn. These participants will not be recruited directly or incentivized differently than other subjects in the study. During informed consent study staff will review the voluntary nature of their participation and reminded that they are able to leave the study at any time during the study procedures.

STUDY DESIGN:

This study tests three commercial cellphone breathalyzers (Alcohoot, BacTrack, evoc) and a wearable device that measures blood alcohol content through the skin (BacTrack Skyn) against a police grade breathalyzer device (Intoxilyzer 240)(Test, n.d.). These devices were chosen as the only currently commercially available breathalyzers that pair with smartphones and the only device that moniters alcohol content through the skin. This study will test the accuracy of these smartphone breathalyzers at assessing BrAC against a standard police grade breathalyzer, which is widely used to test BrAC.

In a controlled setting, 30 participants, aged 21-39, will attend a session where they receive 3 doses of a standard amount of alcohol, based on weight and gender(Watson, Watson, & Batt, 1981), designed to raise Blood Alcohol Content to 1.02g/dL. Breath alcohol content (BrAC) will first be measured with each of the three commercial smartphone-paired breathalyzer (Drivesafe Evoc (Drivesafe Evoc, n.d.), Alcohoot(Alcohoot Smartphone Breathalyzer, n.d.), BacTrack Pro(BACtrack Mobile Pro, n.d.)) and Intoxilyzer 240. Some participants will be instructed to wear the Bactrack skyn at the beginning of the study). After which, the self-report survey will be administered. The order in which the Breathalyzers are administered will change for each use, per a pre-determined, randomized, order, which only the study staff will have access to. A second dose and third dose will be given and this process will be repeated at 40 minutes and 80 minutes after the first dose. Participants will be blinded to all breathalyzer measurements. A study smartphone will be used to collect smartphone-paired breathalyzer readings. We will also measure self-reported intoxication rating using measures subjective intoxication: Personal Drinking Habits Questionnaire (PDHQ)(Vogel-Sprott, 1992), Perceived Driver Fitness(Van Dyke & Fillmore, 2014)and Perceived intoxication and BAC estimation(Harrison & Fillmore, 2005; Harrison, Marczinski, & Fillmore, 2007) administered by the study staff.

All research activities will be conducted in the CTRC and alcohol will be provided from Investigational Drug Service. All research staff will be fully trained in the pilot protocol and their role in the study, will be supervised by the PI, Dr. Mucio (Kit) Delgado, MD (Assistant Professor of Emergency Medicine), and will be trained to refer patients to the appropriate provider (emergency department, outpatient doctor/clinic, social worker) as warranted. A nurse, trained in the protocol, will be onsite at all times and able to assist if any adverse effects occur.

METHODS:

There will be 4 phases of the study:

1. Recruitment: We will use broad-based and cost-effective recruitment strategies including: a) advertisements in UPHS and CHOP employee weekly emails; and b) posting of flyers.Individuals, who are interested in the study, will be contacted and screened over the telephone.

2. Phone Screening: General information will be provided to the prospective subject. Study screening form (attached) will be administered, eligibility confirmed, and research staff will go over informed consent with participant. There will be an optional pre-study in person visit if necessary. Inclusion criteria will be: (a) age 21-39 old, (b) Less than 4 drinking days and 12 drinks per week on average in the past 2 months, (c) have consumed either 4 (women)or 5 (men) or more standard drinks on a single occasion without problems (d) a valid photo ID (e) willing to take public transportation home, via septa or an uber rideshare credit. Exclusion criteria will be (a) desire alcohol treatment now or received it in the past 6 months, (b) alcohol dependence with withdrawal per DSM-V criteria (c) non-English-speaking, and (d) individuals who have a medical condition or who are taking medication which limits or prevents the consumption of alcohol.Interested and eligible participants will schedule their study visit. .

3. Study Visit: On a predetermined study date, eligible subjects will come to the study site for a bar-lab session (timeline below), which will be conducted in the Clinical and Translational Research Center. Each study session will comprise of up to 4 participants, one per bed, and last about 5-6 hours. The space will be configured as a bar-like setting. Prior to the test sessions they will be instructed to east a small meal before fasting for 2 hours, abstain from caffeine for 8 hours and alcohol for 24 hours. Upon arrival, subjects will sign written informed consent. After which the subjects will undergo BrAC measurement, confirming a breath sample of 0 BrAC, using the Intoxilyzer 240.(Test, n.d.) and complete a screening and medical history. At the CTRC participants will undergo a brief medical screening which will include measuring their blood pressure, heart rate, a urine pregnancy test for female participants, and complete the columbia-suidcide severity rating scale. This screening will be performed by a CTRC nurse, who will be trained in the protocol.

4. Intake Survey: After which an intake survey will be administered by study staff, which Includes a) Driving History and Experience Questionnaire DHEQ(Harrison & Fillmore, 2005), b) Drinking and Driving Questionnaire(McCarthy, Niculete, Treloar, Morris, & Bartholow, 2012), c) , this survey measures participants drinking habits during a single week, frequency of drinking, typical duration of drinking events, and number of months an individual has been drinking on a regular basis. Participants will then complete the Decision Making Survey, which has questions related to their Delayed discounting and measures of impulsivity (Senecal, Wang, Thompson, & Kable, 2012).

4. Dose Administration: Before dose administration a portion of particpants will be instructed to wear the Bactrack skyn wearable device. All subjects will first be given a priming dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 0.03-0.04 g/dL based on weight and gender(Watson et al., 1981). Subjective ratings of alcohols effects and BrAC will be obtained after each dose. Each dose will be consumed within a standard 10-minute block to minimize inter-subject variability in the consumption rate. After each drink, participants will wait 20 minutes, and be instructed to rinse their mouth with a nonalcoholic mouthwash to ensure proper results. Breath alcohol content (BrAC) will first be measured with each of the three commercial smartphone-paired breathalyzer (Drivesafe Evoc (Drivesafe Evoc, n.d.), Alcohoot(Alcohoot Smartphone Breathalyzer, n.d.), BacTrack Pro(BACtrack Mobile Pro, n.d.)) and the Intoxilyzer 240, which will be tested in a randomized order and recorded. The order in which the devices are tested will change for each use, per a pre-determined, randomized, order; this order will be blinded to the participants. Participants will also be blinded to all breathalyzer measurements. A study smartphone will be used to collect smartphone-paired breathalyzer readings. This process will be repeated two times at minute 40 and minute 80. After each BrAC measurement has been obtained, we will also measure self-reported intoxication rating using: Self-Reported intoxication Survey: Includes a) Perceived DriverFitness(Van Dyke & Fillmore, 2014) and b) Perceived intoxication and BAC estimation.(Harrison & Fillmore, 2005; Harrison et al., 2007) (survey attached).
At 110 minutes, a nurse will perform a blood draw on the participants, which will be used to determine blood alcohol content. This will administered through a survey given by a study staff trained in the protocol. After 150 minutes if participants BrAC does not measure .03 or below, participants will be tested at intervals of 20 minutes until their blood alcohol content has reached a level of .03 or below at which time they will be provided with transportation home. Midway through the study participants will receive a small meal provided by the CTRC.

Timeline: Study activities at Site Visit

Time	Procedures *
00 - 10 minutes	• Participant is given a priming dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 0.03-0.04 g/dL based on calculations based on weight and gender

10-30 minutes	• Participant rinses with alcohol free mouthwash.
30-40 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Survey
40-50 minutes	• Second dose of alcohol designed to raise BrAC to 0.07-.08'
50-70 minutes	• Participant rinses with alcohol free mouthwash.
70-80 minutes	4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • 2. Self Report of Intoxication Survey
80-90 minutes	• Participant receives third dose of alcohol containing vodka in fruit juice designed to raise the BrAC to 1.01-1.02 g/dL •
90-110 minutes	• Participant rinses with alcohol free mouthwash.
110-120 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Blood draw to determine Blood Alcohol Content • Self Report of Intoxication Survey
135 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
150 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
175 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
190 minutes	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey:
205 minutes until study completion	• 4 measurements of BrAC (Intoxilyzer, Alcohoot, Drivesafe Evoc, Bactrack) • Self Report of Intoxication Rating Survey: • Breathalyzer measurements will be obtained until participant is at .03 or lower

* Please note the above table is for participants 1-10. For participants 11-20, the same format will be used but the breathalyzers will be swapped for the following: Backtrack Keychain, DrinkMate, and Floome.

1. Study Instruments:

1. Intake Survey

a) Driving History and Experience Questionnaire DHEQ (Harrison & Fillmore, 2005)This self-report questionnaire gathered information on driving history and behaviors. Included in the questionnaire are measures of driving experience such as length of time holding a driver's license and number of days and miles driven per week. The questionnaire also gathered information about participants driving behaviors, such as license revocations, presence and number of DUI citations and punishments, traffic accidents, traffic tickets, typical driving environment (rural, urban, and interstate), and the type of vehicle transmission (manual, automatic, or both).

b.) Drinking and driving questionnaire (McCarthy et al)This self-report questionnaire gathered information on individuals drinking and driving history. The questionnaire asked participants to respond to questions about drinking and driving history on 4 or 5 point Likert scales. The questionnaire included a measure of frequency of drinking and

driving and typical quantity of alcohol consumed before driving. The items were obtained from a scale reported by McCarthy et al. (2012).

2. Decision making survey

a). the Delayed discounting questionnaire (Senecal et al 2012).

b). Barratt Impulsiveness Scale BIS-11 (Patton et al., 1995)This 30-item self- report questionnaire is designed to measure the personality dimension of impulsivity. Participants rated 30 different statements on a 4-point Likert-type scale ranging from Rarely/Never to Almost Always/Always. Higher total scores indicate higher levels of self-reported impulsiveness (score range 30120).

3. Self-Reported intoxication Survey (attached to the protocol): Includes visual analogue scales which measure self-reports of:

a) Perceived Driver Fitness (Van Dyke and Fillmore 2014)

b) Perceived intoxication and BAC estimation.(Harrison and Fillmore 2005; Harrison et al 2007)

4. Intoxilyzer 8000: The Intoxilyzer breathalyzer is a police grade breathalyzer that has been used in various studies in order to achieve an accurate estimate of BrAC (Fillmore 2001; Harrison and Fillmore 2005;)

5. Smartphone Breathalyzers (Alcohoot, BacTrack, DriveSafe Evoc, Floome, Drink Mate, Keychain Backtrack) These devices were chosen as the only currently commercially available breathalyzers that pair with smartphones, which have received growing attention in the national media. (A smartphone breathalyzer, 2015; Jolly, 2015)

6. Bactrack Skyn: Bactrack skyn is a wearable device that tracks breath alcohol content. A portion of participants will be selected to wear these devices in order to validate their ability to measure and estimate blood alcohol content. (https://www.bactrack.com/pages/bactrack-skyn-wearable-alcohol-monitor).

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Floome: https://floome.com/

Drink Mate: http://www.getdrinkmate.com/

BACtrack Keychain: https://www.bactrack.com/products/bactrack-keychain-breathalyzer?&mkwid=Ch2zPSsL&pcrid=102311672917&pkw=bactrack%20keychain&pmt=e&pdv=c&ring-central=google-ppc&gclid=CjwKEAiAs_PCBRD5nIun9cyu01kSJAA-WD-ruugi8IvC2_Z7nN_Mz40Fd2MYTiexYL2MMobRXXZfIRoCLLvw_wcB

2. Group Modifications:

Because there are no trial arms in this study, all participants will complete the same study activities, and there will be no group modifications necessary. Because of the limited availability of the Bactrack Skyn measurement tool, only a portion of our participants will receive this device depending on availability of the device.

3. Method for Assigning Subjects to Groups:

There will be no randomization for this study. All participants will receive the same study protocol. Except a selection of participants will be instructed to wear the Bactrack skin wristband for the duration of the study. This will not effect any other aspect of the study protocol.

4. Administration of Surveys and/or Process:

Interested participants will call the study hotline where an IRB-approved research assistant or project manager, will answer any questions, administer the study screening and go over the written informed consent. There will be an optional in person study visit for the participant to come in and review study procedures, and sign written informed consent, in person. At the study visit, which occurs at a predetermined time, the participant will first sign written informed consent to participate. They will then take an initial survey, with questions related to their past alcohol use and habits including Driving History and Experience Questionnaire DHEQ1, Drinking and Driving Questionnaire. Participants will also take the Decision making survey, which includes The Barratt Impulsiveness Scale, and the Delayed discounting questionnaire. Some participants will then be instructed to wear the BACtrack skyn wrist device. Participants will then receive three doses of vodka mixed with juice based on their gender and weight designed to reach a peak blood alcohol level of .08 g/dL. After each dose their Breath Alcohol Content (BrAC) will be measured using the three smartphone breathalyzers and the intoxilyzer, measured in a random order. After each breathalyzer measurement, participants will receive the Self-Report of Intoxication Survey, which will include Perceived Driver Fitness and Perceived intoxication and BAC estimation, which are measured using a visual analogue scale.

Besides a preliminary study visit for participants to consent to the study and complete the eligibility survey, all research activities will take place in one of the four CTRC study sites and will occur in a study session of approximately six hours in length with up to four participants at each session for a total of five study sessions. Participants will be separated by curtains and fill out individual paper surveys on paper sheets in order to maintain confidentiality.

Data collection will include contact information, medical history, and history of alcohol use, various measurements of Breath Alcohol Content (BrAC), as well as survey data from the self-reported intoxication survey. The informed consent process during study enrollment will describe all of these aspects of data collection.

5. Data Management:

Paper forms will be used to collect data and a research assistant will create and maintain the research database. All source documents will be identified by study identification (ID) number, and the key to that ID number will be kept in a locked file cabinet. All personally identifiable information also will be kept separately in a locked file cabinet. No results will be reported in a personally identifiable manner. All tracking system data and research database information will be password-protected with several levels of protection: first, a password will be required to access the computer of the user who has access to the

6. Statistical Analysis Plan:

Primary outcome: Interclass correlation coefficient between smartphone breathalyzer and wearable device readings and the police breathalyzer readings. (See: https://en.wikipedia.org/wiki/Intraclass_correlation).

Secondary outcomes: mean relative differences in breathalyzer and wearable device readings relative to the police breathalyzer with standard deviations. These will be calculated for all measurements and by specific timepoints.

Other secondary analyses: We will conduct descriptive analyses of the association between self-reported measures of intoxication, predicted blood alcohol content, driving fitness, and willingness to drive with measured breath alcohol content by device. We will also explore the effect modification of these by self-reported measures of impulsivity and delay discounting.

RISK/BENEFIT ASSESSMENT:

1. Risks:

There is some risk that subjects will be identified as participants in the study and that the confidential information provided regarding psychiatric and substance use history will be inadvertently disclosed without the subjects' permission.
Urine pregnancy testing is performed for all women of reproductive potential, prior to alcohol administration, to avoid the potential for adverse fetal effects of alcohol. These procedures should add no additional risks beyond the minimal risks normally associated with them.Over a period of 120 minutes, participants will be given three doses of alcohol, which will result in a BrAC of 1.01-1.02g/dL. This amount of alcohol is equivalent to 4-5 standard drinks, an amount that these moderate-drinking subjects have ingested previously. Although the amount of alcohol available to them will produce only moderate blood alcohol levels, subjects could feel intoxicated or react negatively to the alcohol, such as nausea or dehydration. Engaging in any dangerous activities during this period would increase risk of self-harm. Precautions to minimize these risks are discussed below.

After consuming alcohol, participants may be unsafe to operate a vehicle. This risk will be mitigated by providing participants transportation home with either a septa token or rideshare credits for uber of up to $30, depending on their location.
Study activities will be performed in a special clinical research room located in a hospital setting in close proximity to an inpatient care. Nursing and medical personnel will be available to assist in the care of the subject if any adverse event occurs. Participants' breath alcohol concentration (BrAC) and their general condition will be monitored during all aspects of the procedure. The bar-lab will be located in a safe and secure area in in a hospital where medically trained staff will be onsite and there will be ready access to emergency care should it be necessary. All subjects will remain in the test area until their BrAC will be below 0.03 g/dL. All study activities will occur in the afternoon, no earlier than 11am, to minimize nausea and vomiting that could occur with morning alcohol consumption. A meal will be provided.

Rating Scales and Questionnaires. To avoid breach of confidentiality, subjects' names will appear only on a consent form, a telephone screening form and a "key" form kept in a locked cabinet. All forms that contain identifying information will be kept double locked (i.e., in a locked cabinet, in a locked room) to maintain their security. All study data forms will contain only the subject's unique study identification number, using a reference system maintained by the study staff. Completed study forms will be kept in a locked cabinet, the key to which will be available only to the PI and staff working on this study. Subject visits will be scheduled and no information about the subject will be provided to anyone (except in emergencies as defined above) in person or by telephone.

All paper research records will be stored in locked cabinets and only the investigators and only IRB approved study will have access to those records.

2. Benefits:
There are no direct benefits to participation. Participants are contributing to preparation of a larger study, which in turn may have benefits to society in general. Given that anecdotal research shows variation in Breathalyzer readings, understanding the validity of smartphone paired breathalyzers has potential to benefit society in general.

3. Subject Privacy:

Participants will be screened for eligibility over the telephone with a trained research team member in a private office. The participant will review the paper consent form in a private room on the day of the study visit. The participant will have a private room in the research lab during the study visit.

4. Subject Confidentiality:

Participants who have seen recruitment material will call a study line in order to sign up for the study. At this pre-screening phone call, the research project manager will briefly go over study procedures. If the participant is interested, they will be complete a brief (less than ten minute) screening over the phone to determine eligibility. Participants may be asked to meet with the study staff prior to scheduling their study visit to determine eligibility. At the study visit, eligible participants will sign written informed consent, and be administered the study protocol; all study documents will be de-identified after all contact has been made. Participant information will be stored in a locked filing cabinet only accessible by the research assistants, PI, and project manager. Personal information will not be stored with study data and will be destroyed after data collection.

How will confidentiality of data be maintained? Check all that apply.

☒ Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.

☒ Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.

☒ Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.

☒ Whenever feasible, identifiers will be removed from study-related information.

☐ A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

☒ A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

☐ Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

☐ Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

☐ Other (specify):

We will require a waiver of consent written consent in order to administer the screening survey over the phone because it is not feasible for each participant to be required to come in, in order to answer questions in the screening survey. Before the screening survey is administered, participants will be prompted to provide verbal consent (attached to this protocol) over the phone, using the verbal consent script that is attached to this protocol. Once a participant is screened, using the screener, and has set up a study session, participants will signed written informed consent at the beginning of their study visit prior to any other activities being completed.

5. Protected Health Information

- Name
- Street address, city, county, precinct, zip code, and equivalent geocodes
- All elements of dates (except year) for dates directly related to an individual and all ages over 89
- Telephone and fax number
- Electronic mail addresses

6. Compensation:

Each subject will receive a $100 cash card as an incentive for completing the 6 hour study session. This cashcard will work through the Greenphire clincard system (SOP attached to this submission). Information about the greenphire system will be provided in the consent document for the participant. Information, including social security number, will be collected from the participant at the intake phone call in order to set up an online account that the participant will be able to access. Participants will be reimbursed for travel and ensured a ride home by receiving either a septa token or up to $30 in rideshare credits from Uber.

7. Investigator's Risk/Benefit Assessment:

In general the benefits outweigh the risks in this study. Participants will receive information on alcohol consumption and health. Participants are also contributing to preparation of a larger study, which in turn may have benefits to society in general. Although there are some risks involved in participating in this study, as mentioned above, these can be minimized to ensure that the potential benefits exceed the potential risks, so that the risk/benefit ratio is favorable.

INFORMED CONSENT:

1. Consent Process:

Participants will respond to recruitment material by calling the study hotline. After calling the study hotline, participants will be screened for eligibility and will schedule a visit. At the study visit, participants will sign written informed consent. Consent will be obtained by explaining the study objectives, procedures, and potential risks to subjects verbally and in writing at a pre-screening and / or screening visit. Subjects will be given an opportunity to ask questions and will be provided with complete and accurate answers to any questions they may have. Written documentation of this process will be obtained using the IRB-approved consent form. Subjects are given a signed copy of the consent form for his or her reference.

2. Waiver of Informed Consent:

This research in general involves minimal risks to the participants because the benefits outweigh the risks in this study. Specifically the waiver of consent only applies to administration of the screening survey, and completing this survey involves minimal risk to participants, such as there is some risk that confidential information provided regarding psychiatric and substance use history will be inadvertently disclosed without the subjects' permission. Methods outlined elsewhere in this

protocol will be in place to protect participant information to minimize this risk. Also the benefits for allowing participants to take screening over the phone and not having to come in for two study visits outweighs this risk.

It is not always feasible for participants to schedule a separate study visit to answer a brief screening survey. In order to accommodate participants who cannot schedule a separate study visit, we are requesting a waiver of written informed consent only to administer the screening survey over the phone. Allowing this step in the process to be completed over the phone will make the study more feasible to be completed by participants.

Once a participant is screened, using the screener, and has set up a study session, participants will sign written informed consent at the beginning of their study visit prior to any other activities being completed.

RESOURCES NECESSARY FOR HUMAN RESEARCH PROTECTION:

All research activities will be conducted in the CTRC and alcohol will be provided from Investigational Drug Service. The project manager will oversee all study operations and two research assistants will be trained in the protocol and present at the study sessions. All research staff will be fully trained in the pilot protocol and their role in the study, will be supervised by the PI, Dr. Mucio (Kit) Delgado, MD (Assistant Professor of Emergency Medicine), and will be trained to refer patients to the appropriate provider (emergency department, outpatient doctor/clinic, social worker) as warranted. A nurse, trained in the protocol, will be onsite at all times and able to assist if any adverse effects occur.

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