REMOTE GUIDED CAFFEINE REDUCTION

Protocol

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JHM IRB - eForm A – Protocol

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1. Abstract

a. Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

There is emerging evidence that some individuals have difficulty cutting down or eliminating their caffeine consumption in spite of clinically significant problems exacerbated by caffeine use. Some of the most commonly reported caffeine-related problems are anxiety, insomnia, and gastrointestinal distress. However, prior in-person trials examining the benefits of a gradual, manualized caffeine reduction program did not specifically measure improvement in these symptoms before and after caffeine reduction. We recently led an in-person clinical trial examining the effects of a very brief intervention to provide instructions for a gradual, manualized caffeine reduction program in individuals with DSM-defined problematic caffeine use. We found that as a result of our brief intervention, participants were successful at reducing caffeine use. However, we did not measure symptoms improvement with respect to anxiety, insomnia, or gastrointestinal distress, in spite of the fact that these are common problems that can be exacerbated by caffeine. This time- and cost-effective, very brief intervention may be ideal to implement remotely (i.e., online), but the acceptability and feasibility of a remote intervention has not yet been assessed. In the proposed study, we will implement our brief, manualized caffeine reduction intervention entirely remotely (online), and determine to what extent: 1. participants will engage with a remote caffeine reduction intervention and find it acceptable, 2. participants are able to reduce their caffeine use, 3. participants report improvement in common caffeine-related problems (e.g., anxiety, insomnia, or gastrointestinal concerns), and 4. participants randomized to the immediate intervention group (at 7 weeks post enrollment and treatment) show greater caffeine reductions or greater improvements in caffeine-related problems relative to the delayed treatment group at 7 weeks post-enrollment (before treatment). Participants will complete four remote visits (Screening, Treatment, Week 7 Follow-up, Week 14 Follow-up) via HIPAA-compliant Zoom meetings created by study staff or through other approved Johns Hopkins Telemedicine Services (e.g., Polycom). Participants will complete surveys/intake assessments via shareable JHMI-credentialed Qualtrics links provided to them by the study staff during remote meetings and weekly via email/text during the gradual caffeine reduction period (Weeks 1-6). Participants will provide contact information for a community observer who will be sent email links to complete two surveys via shareable JHMI-

credentialed Qualtrics links provided to them by the study staff. Our study staff is experienced in implementing Qualtrics surveys remotely in prior studies and has extensive experience providing brief intervention for caffeine reduction using the manual-only approach. These data will support feasibility and initial efficacy of future randomized controlled trials in populations experiencing specific caffeine-related problems.

2. Objectives (include all primary and secondary objectives)

Primary objective. Determine to what extent participants will engage with a remote caffeine reduction intervention for caffeine-related problems and find it acceptable.

Secondary objective (a). Determine to what extent participants are successfully able to reduce their caffeine consumption following the remote intervention.

Secondary objective (b). Determine to what extent participants report improvement in common caffeine-related problems (e.g., insomnia, anxiety, gastrointestinal distress) following the remote intervention.

Secondary objective (c). Determine whether participants randomized to the immediate intervention group (at 7-weeks post enrollment and post-treatment) show greater caffeine reductions or greater improvements in caffeine-related problems relative to the delayed treatment group at 7-weeks post-enrollment (prior to delayed treatment). This randomization will allow us to compare the initial efficacy of our intervention with caffeine reductions that may occur spontaneously over the same duration.

3. Background (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

An estimated 89% of adults in the United States consume caffeine daily (Fulgoni et al., 2015). Although moderate caffeine consumption is not generally associated with negative health consequences (Nawrot et al., 2003; Wykoff et al., 2017), approximately 14% of adults consume more than the recommended limit of 400 mg of caffeine per day (Fulgoni et al., 2015; USDA, 2015). Caffeine may negatively affect conditions such as anxiety, insomnia, tachycardia, urinary incontinence, gastrointestinal upset, and is associated with complications during pregnancy (see Temple et al., 2017 or Sweeney et al., 2018 for review). It is common for physicians or other medical professionals to recommend reduction of caffeine use for individuals who have contraindicated psychological or medical conditions (Hughes et al. 1988; Griffiths and Reissig, 2008). Further, a large percentage of caffeine users in the general population report a desire or unsuccessful efforts to stop or reduce caffeine use (Hughes et al., 1998; Sweeney et al., 2020).

In spite of the widespread use of caffeine, and growing recognition that some caffeine users experience caffeine-related problems, few studies have been conducted to develop and validate caffeine cessation treatments. Gradual reduction of caffeine over a period of several weeks has shown to be effective in prior controlled studies with heavy caffeine users and individuals with urinary incontinence (James et al., 1985, 1988; Foxx & Rubinoff, 1979; Bryant et al., 2002; Bernard et al., 1981). Further, two recent investigations from our laboratory treated participants and characterized their problematic caffeine use according to DSM criteria. Evatt, Juliano, and Griffiths (2016) evaluated a gradual caffeine cessation treatment among individuals seeking treatment for problematic caffeine use using a wait-list control design. Participants received a 1-hour in-person counseling session and received a manual incorporating cognitive-behavioral strategies to reduce caffeine consumption over a period of 5 weeks. On average, treatment resulted in significant reductions in self-reported caffeine use and salivary caffeine following the manualized intervention, with no significant increases in self-reported caffeine use observed for up to 1 year follow-up.

Because the requirement of a 1-hour individual counseling session as in Evatt et al. (2016) may still be considered burdensome for health care professionals with limited time and expertise dedicated to behavioral interventions, we recently completed a follow-up study examining examined the efficacy of simplified, manual-only treatment for caffeine reduction and cessation in individuals seeking treatment for their caffeine use (Sweeney et al., 2019). Individuals meeting at least two proposed DSM-5 diagnostic criteria for Caffeine Use Disorder were randomly assigned to receive either immediate treatment or treatment delayed by 7 weeks. The treatment consisted of an in-person meeting, at which study staff provided a manual containing information about caffeine and instructions for gradually reducing caffeine consumption over a period of 6 weeks. No counseling or additional support was provided. Caffeine consumption and caffeine-related distress was assessed before treatment and 7 weeks after receiving the treatment manual (End-of-Treatment) during in-person meetings, and 20 weeks post-treatment via phone. The treatment resulted in significant reductions in participants' caffeine consumption and caffeine-related distress at End-of-Treatment that were sustained at 20 weeks post-treatment. Comparisons between the immediate and delayed treatment groups suggest the treatment effects were attributable to the manualized treatment rather than spontaneous with the passage of time. Feedback from volunteer-nominated community observers in both groups provided further evidence for participant self-reported caffeine reduction.

This efficacious, very brief, manual-only intervention for caffeine reduction is time- and cost-effective, and may be an ideal candidate for use through remote (online) implementation. However, the feasibility, acceptability, and initial efficacy of a remote intervention remains to be determined. In the proposed study, we will extend this line of research to determine to what extent: 1. participants will engage with a remote caffeine reduction intervention and find it acceptable, 2. participants are successfully able to reduce their caffeine consumption, and 3. participants report improvement in common caffeine-related problems.

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

There will be no in-person visits for the proposed study. Study interactions will be conducted entirely remotely via JHMI-credentialed Qualtrics surveys, HIPAA-compliant Zoom meetings created by study staff (i.e., using the JHMI HIPAA-compliant instance), or through other approved Johns Hopkins Telemedicine Services (e.g., Polycom). The present study will consist of a *preliminary online screening* (via JHMI-credentialed Qualtrics survey), followed by a more detailed screening televisit for those individuals who meet preliminary screening criteria. Individuals determined to be eligible following the screening televisit will complete three additional televisits: *Treatment*, *Week 7 follow-up*, and *Week 14 follow-up*. Participants will provide contact information for a community observer who will complete two online surveys, one near the *Treatment* visit and one near the *Week 7 follow-up*. Between the treatment visit and the Week 7 follow-up, participants will complete online surveys once per week. In Table 1 below, we provide a summary of the assessments to be administered at each study time point. Detailed measures and descriptions are also appended to the current application in the "Measures" document.

Preliminary Screening. We have created a preliminary screening survey assessing basic demographics and initial eligibility via JHMI-credentialed Qualtrics survey. Links to the survey will be provided via online or paper flyer advertisements (e.g., Psychiatry department website, Google/Facebook ads) or in response to email/telephone inquiry. Individuals who complete the preliminary screening and indicate interest in participation will provide their first name and telephone number as part of the survey. Individuals who meet initial eligibility criteria will be contacted via phone to determine a time for the screening televisit and to receive instructions.

Screening Televisit. Study staff will create a HIPAA-compliant Zoom meeting with the participant, or using other approved Johns Hopkins Telemedicine Services (e.g., Polycom) in the event of technical or other issues with Zoom. The visits will be password-protected and will require the participant to use video

during the call. Study staff will also use video whenever possible. The study staff will use the Zoom chat function or email to send the participant survey links and will verbally instruct them on how to complete the surveys, beginning with the consent survey. The oral consent form document will be embedded within the Qualtrics survey such that the participant can download the consent form document, or alternatively may be emailed to the participant. The study staff will ask the participant to read aloud the first part of the consent form in order to confirm that they were able to download the document and are able to read English fluently. Then the participant will be provided the opportunity to review the document and ask the study staff any questions they have about participation. This will be followed by a consent quiz administered via Qualtrics survey link. Participants will provide oral consent and answer all of the consent quiz questions correctly prior to proceeding with the remaining screening questionnaires. Following consent, participants will complete standardized medical/substance use history questionnaires as well as surveys to determine their caffeine/cigarette use, caffeine-related problems, and standardized assessments of anxiety, sleep, and gastrointestinal problems as outlined in Table 1. The participant will fill out the surveys via Qualtrics links, or the study staff will interview them and enter their responses on the study staff computers. Study staff will provide instructions to guide them through the assessment completions, review their responses on Qualtrics, and may ask follow-up questions if necessary, to supplement their survey responses. After determining eligibility, participants will be randomized to either the Immediate or Delayed treatment group using an urn randomization procedure accounting for caffeine consumption, age, and sex as was utilized in prior research in our laboratory (Evatt et al., 2016; Sweeney et al., 2019).

Community Observer. During the screening or treatment visit, participants will be asked to provide the name and contact information (phone number and email address; email will be the preferred method of contact) for a family member, friend, roommate, or significant other for the purposes of online surveys about their caffeine use. The participant will be asked to confirm with their observer that the study team has permission to contact them. The observer will be contacted twice to complete a brief online survey regarding the participants' caffeine use. The first contact will occur soon after the participant has the *Treatment* visit. The second contact will occur near the time of the participant's *Week 7 follow-up* visit.

Treatment Televisit. Participants determined to be eligible following the screening televisit will be scheduled to complete the treatment televisit shortly after screening. For the immediate treatment group, the treatment the *Treatment* visit will generally occur within one week of the screening televisit. The delayed treatment group will have their *Treatment* visit scheduled for a date approximately 7 weeks after screening. During the *Treatment* televisit, study staff will provide the participants with a digital copy of the caffeine reduction treatment manual used in prior studies (Evatt et al., 2016; Sweeney et al., 2019). As in prior research (Sweeney et al., 2019), study staff will give a brief (i.e., generally less than five minutes) description of the manual and instructions on how to gradually reduce their caffeine consumption over a period of six weeks. Participants will also complete assessments to determine their caffeine consumption and cigarette use over the past 7 days as outlined in Table 1. Participants will also be provided with information about their follow-up visits and how to complete weekly surveys.

Weekly Surveys. At seven days following the treatment televisit, participants will receive a request to complete a survey via Qualtrics link sent via email/text. The survey will consist of standard assessments of anxiety, depressed mood, sleep problems, gastrointestinal problems, past week caffeine/cigarette intake, and problems related to caffeine as outlined in Table 1. They will receive a request to complete the same survey once per week (weeks 1-6) until the Week 7 follow-up televisit.

Week 7 Follow-up Televisit. At approximately 7 weeks after the treatment televisit, participants will complete a follow-up televisit at which they will complete the same measures as previously administered to assess anxiety, depressed mood, sleep problems, gastrointestinal problems, past week caffeine/cigarette use, and caffeine-related problems as outlined in Table 1. Participants will also complete a treatment acceptability survey.

Week 14 Follow-up Televisit. Finally, participants will complete a follow-up visit approximately 14 weeks after the treatment televisit. They will complete all the same assessments as the Week 7 televisit, except they will not repeat the treatment acceptability survey.

Table 1. *Study measures according to visit*

	Preliminary Online Screening	Screening Televisit	Treatment Televisit	Weekly Surveys (Weeks 1-6)	Week 7 Televisit	Week 14 Televisit
Basic screening questions/demographics[1]	X					
Typical Week Caffeine Survey	X					
AUDIT-C[2]	X					
DAST-10[3]	X					
PROMIS-Anxiety-8a[4]	X			X	X	X
PROMIS-SleepDisturbance-8a[4]	X			X	X	X
PROMIS-GIDiarrhea-6a[4]	X			X	X	X
PROMIS-GIReflux-13a1.0[4]	X			X	X	X
PROMIS-Depression-8a[4]	X			X	X	X
Consent Quiz[1]		X				
Medical History Survey[1]		X				
Drug Use History Matrix[1]		X				
Caffeine Timeline Follow-back[1]		X	X		X	X
Past 7 Days Caffeine Survey[1]		X	X	X	X	X
Past 7 Days Cigarette Survey (smokers only)[1]		X	X	X	X	X
Caffeine Problems Survey[1]		X				
Caffeine Use Disorder Questionnaire[1]		X		X	X	X
Caffeine Use Disorder Interview[1]		X				
GAD-7[5]		X			X	X
PSQ-I[6]		X			X	X
Insomnia Severity Index[7]		X			X	X
GSRS[8]		X			X	X
Treatment Acceptability Survey/Interview[1]					X	
Observer Rating Survey (Completed by Community Observer)[1]			X		X	

Note. Detailed descriptions of all measures are appended to the present IRB application in the "Measures" document. [1]Study team-generated measure/survey based on prior research (e.g., Sweeney et al. 2019, 2020). [2]Alcohol Use Disorders Identification Test-C, Bush et al., 1998. [3]Drug Abuse Screening Test, Skinner 1982. [4]Patient-Reported Outcomes Measurement Information System, Cella et al., 2010, Rothrock et al., 2010. [5]Generalized Anxiety Disorder-7, Spitzer et al., 2006. [6]Pittsburgh Sleep Quality Index, Buysse et al., 1989. [7]Bastien et al., 2001. [8]Gastrointestinal Symptom Rating Scale, Svedlund et al., 1988.

b. If your study involves data/biospecimens from participants enrolled under other research studies with a written consent or under a waiver of consent, please list the IRB application numbers for those studies. Please note: Certificate of Confidentiality (CoC) protections applied to the data in source studies funded by NIH or CDC will extend to this new study if the funding was active in 2016. If this situation applies, Section 36, question 4 in the application will need to be answered "Yes" and "Hopkins Faculty" should be selected in question 7. No other documents are required.

This study does not involve data or biospecimens from participants enrolled in other research studies.

c. Study duration and number of study visits required of research participants.

Participants will be asked to complete online preliminary screening via Qualtrics survey, four televisits (screening, treatment, 7 week follow-up, 14 week follow-up), and complete six surveys over six weeks

(weeks 1-6 following treatment televisit), as described in detail above in study procedures and in Table 1. The screening televisit is anticipated to take less than 1.5 hours. All other televisits are expected to take less than 30 minutes. The six weekly surveys (weeks 1-6 following treatment televisit) are anticipated to take approximately 5-10 minutes once per week. The anticipated study duration is approximately 15 weeks from the time of the screening televisit to the final televisit at 14-weeks for those in the immediate intervention group. For those in the delayed intervention group, the anticipated study duration is approximately 21 weeks due to the programmed delay between the screening televisit and the treatment televisit. The duration of participation will be in part dependent on participant and study staff scheduling and availability. There is no evidence to suggest that the difference in timing of visits and measures will adversely affect the participants or the validity of the study. On those occasions on which the timing of meetings, sessions or measures deviate substantially from the time frames in the protocol, we will report these as deviations in the Continuing Review.

d. Blinding, including justification for blinding or not blinding the trial, if applicable.

There is no blinding component to the proposed research.

e. Justification of why participants will not receive routine care or will have current therapy stopped.

There will be no anticipated disruption to any ongoing treatment or routine care.

f. Justification for inclusion of a placebo or non-treatment group.

There will be no anticipated placebo or non-treatment group. These are pilot or preliminary data that may support a future randomized trial which would have a separate IRB approval.

g. Definition of treatment failure or participant removal criteria.

Participants who are not eligible or who are noncompliant with study tasks will be removed from the study early. There are no other early stopping rules in the study.

h. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

The intervention consists solely of the treatment manual and brief instructions provided at the treatment televisit, and is not accompanied by any ongoing therapy (Sweeney et al., 2019). All participants who complete the treatment televisit will be able to keep their copy of the treatment manual.

5. Inclusion/Exclusion Criteria

Inclusion Criteria

1. Between 18-75 years old
2. Reside in the United States
3. Read, write, and speak English fluently
4. Able to access a video camera on a smartphone, tablet, or other computer
5. Able to receive text messages or emails (or both)
6. Consume greater than or equal to 200 mg caffeine per day in a typical week
7. Indicate a problem that is caused or worsened by caffeine from among the following options: sleep problems, anxiety or nervousness, frequent urination, heartburn or other digestive issues, feel dependent on or addicted to caffeine

8. Interested in getting help to gradually reduce or eliminate caffeine consumption as part of a research study

Exclusion Criteria

1. Evidence of significant depressive symptoms assessed via PROMIS-Depression-8a and medical history
2. Evidence of problematic alcohol use assessed via the AUDIT-C and medical/substance use history
3. Evidence of problematic substance use other than alcohol, nicotine, or caffeine assessed via the DAST-10 and medical/substance use history
4. Evidence of a significant psychiatric disorder, presentation of acute psychiatric symptoms, or any other mental illness that, in the opinion of the investigators, may complicate participation in the study. [Anxiety and sleep disorders are not anticipated to interfere with study participation and will not generally be exclusionary]
5. Any medical condition that, in the opinion of the investigators, may interfere with or preclude completion of the study

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.

There are no proposed drugs or devices in the proposed research study.

b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.

N/A

c. Justification and safety information if non-FDA approved drugs without an IND will be administered.

N/A

7. Study Statistics

a. Primary outcome variable.

To determine to what extent participants will engage with a remote caffeine reduction intervention for caffeine-related problems and find it acceptable (*Primary objective*), we will calculate the percentage of completed assessments for each televisit (Treatment, 7 Week Follow-Up, 14 Week Follow-Up) among eligible participants, as well as self-reported agreement with the items on the treatment acceptability survey completed at the 7 Week Follow-Up televisit (e.g., “I read all or most of the Guide to Caffeine Reduction and Cessation,” “Overall, the guide was helpful during my attempt to reduce or quit caffeine.”)

b. Secondary outcome variables.

To determine to what extent participants are successfully able to reduce their caffeine consumption following the remote intervention (*Secondary objective (a)*), we will assess caffeine consumption as determined by the caffeine surveys at 7-and 14-week post-treatment follow-ups and compare this with consumption at the screening and treatment televisits.

To determine to what extent participants report improvement in common caffeine-related problems (e.g., insomnia, anxiety, gastrointestinal distress) following the remote intervention (*Secondary objective (b)*),we will assess caffeine related problems, anxiety, sleep problems, and gastrointestinal distress via standardized measures (see Table 1) at 7 and 14 weeks post treatment follow-ups and compare this with scores on these assessments at the screening and treatment televisits.

To determine whether participants randomized to the immediate intervention group show greater caffeine reductions or greater improvements in caffeine-related problems (*Secondary objective (c)*) at the *7-week follow-up* relative to the delayed treatment group over the same time-period, we will compare all of the secondary outcome variables described above between the two treatment groups to compare our intervention relative to spontaneous reduction that may occur with the passage of time.

c. Statistical plan including sample size justification and interim data analysis.

Because the primary purpose of this study is to collect pilot and feasibility data rather than determine efficacy via randomized controlled trial, the statistical analysis will be primarily descriptive. Primary outcomes will be reported as the proportion of completed televisits among eligible participants as well as the mean and standard deviation agreement (visual analog scale) with items on the treatment acceptability survey. With respect to secondary outcomes, means and standard deviations for the standardized assessments in Table 1 will be calculated for screening, treatment, 7 Week Follow-Up and 14-Week Follow-Up visits, and we will also visually inspect individual subject data. With respect to comparisons between the immediate and delayed intervention group, we will use a mixed effects regression model with between-subjects factors of group, a within subjects factor of time, and a group x time interaction term. A power analysis indicates that with two groups, four measurements, an alpha of .05, a desired power of .95, correlation among repeated measures of .5, and conservatively estimating a small effect (e.g., partial eta squared = .02), a sample size of 100 will be sufficient to detect a treatment effect. Further, we will calculate Cohen's *d* and partial eta squared effect sizes using means and standard deviations for pre-and post-treatment for all secondary outcomes. These effect size calculations will be used to determine the necessary sample size for any future large-scale randomized controlled trials to assess clinical effects in different treatment populations. The desired sample size of 100 is also based on our laboratory's proven participant capacity for prior randomized clinical trials and long-term human laboratory studies (e.g., Evatt et al., 2016; Sweeney et al., 2017, Sweeney et al., 2019).

d. Early stopping rules.

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Risks of the study procedures: The procedures employed in this study are benign. There are also no specific risks related to the questionnaire assessments. It is possible that interview questions pertaining to psychological health or other medical history could cause participants to feel uncomfortable. Participants may feel tired, bored or annoyed when responding to surveys. Heavier caffeine users may experience unpleasant withdrawal symptoms when reducing caffeine consumption, though the gradual reduction over a period of weeks was specifically designed to reduce the frequency and severity of withdrawal. Common withdrawal symptoms include headache, tiredness/fatigue, decreased energy/activeness, decreased alertness/attentiveness, drowsiness/sleepiness, decreased contentedness/well-being, depressed mood, difficulty concentrating, irritability, muzzy/foggy/not clearheaded, muscle pain/stiffness, flu-like symptoms, or nausea and/or vomiting (Juliano & Griffiths, 2004). Caffeine withdrawal is a transient phenomenon with little medical risk. There is no evidence to suggest caffeine reduction is contraindicated to pregnancy (and in fact caffeine reduction may be beneficial for pregnant women; Chen et al., 2016).

Thus, pregnant women, breastfeeding women, or women who are not using an effective means of birth control may be included in the study sample.

Risks of a breach in confidentiality: Although we make every attempt to keep participant information and data private and stored in a secure place, there is always a risk that sensitive participant information might be accidentally disclosed to someone outside of the research project.

b. Steps taken to minimize the risks.

Protection against risks of the study procedures: All participants in this study will be thoroughly informed of the potential risks, including of caffeine withdrawal, during the oral informed consent process. Because participation is voluntary, participants can withdraw at any time if they find the behavioral procedures or caffeine withdrawal effects undesirable. The gradual reduction over a period of weeks was specifically designed to reduce the frequency and severity of caffeine withdrawal. The study team carefully reviews medical and social history information from Screening to determine eligibility, and a member of the Behavioral Pharmacology Research Unit (BPRU) medical staff will be consulted if there are medical concerns judged to potentially impact participation.

Protection against risk of a breach in confidentiality: Research staff are highly trained to maintain participant confidentiality. Records and data are maintained on encrypted staff computers and HIPAA-compliant JHMI-credentialed Qualtrics surveys and will only be released outside of the study team with written authorization. Study IDs are used on data collection instruments and in electronic data storage wherever possible in place of any personally identifying information. The identity of subjects is not revealed in written records and documents with subjects' names are shredded before disposal. Televisits will only be arranged via password-protected Zoom meetings with study staff created in the JHMI HIPAA-compliant instance, or through other approved Johns Hopkins Telemedicine Services (e.g., Polycom) in the event of technical or other issues with Zoom. No recordings will be made of participant interactions. Regarding the observer ratings, participants are informed when they identify a community observer of the questions the observer will answer, and that none of the participant's other study information will be shared with the observer and that the observer ratings will not be shared with the participant. Staff have clear instructions to limit the information shared between participant and observer to only that described in the consent form and specified study measures.

c. Plan for reporting unanticipated problems or study deviations.

All unanticipated problems and adverse events will be reported to the IRB and other relevant agencies as required and described in the Data and Safety Monitoring Plan.

d. Legal risks such as the risks that would be associated with breach of confidentiality.

There is a theoretical risk that a breach in confidentiality will occur. In order to protect against this risk, research staff are trained in procedures for protecting participant privacy and personal health information. Data are managed to maximally protect participant confidentiality (e.g., in locked rooms, on encrypted computers, using participant ID codes rather than personal information). Records and data are maintained on encrypted computers and will only be released outside of the study team with written authorization from the participant. The identity of subjects is not revealed in written records and documents with subjects' names are shredded before disposal.

e. Financial risks to the participants.

There are no financial risks to the participants in this study.

9. Benefits

a. Description of the probable benefits for the participant and for society.

Participants in the proposed study may gain insights into their personal use of caffeine and how caffeine affects them. They may also gain insight into whether caffeine may cause or exacerbate any problems for them such as anxiety, insomnia, or gastrointestinal distress. The participants may find the facts and information about caffeine contained in the treatment manual interesting. If the intervention effects from our prior studies generalize to remote intervention, participants who have difficulty cutting down their caffeine consumption on their own may be able to cut down more effectively with the treatment manual.

The knowledge to be gained from the proposed study is important because it will demonstrate whether our previously time- and cost-effective brief intervention for caffeine reduction is feasible and acceptable to implement remotely. If this remote intervention is acceptable and feasible, it could be widely disseminable and its efficacy can be tested in larger trials. Although only a secondary outcome, the proposed pilot data may also demonstrate whether the intervention leads to successful caffeine reduction and successful reduction in caffeine-related problems in some individuals. The manual-only treatment is designed to be very brief such that health care providers with little experience related to caffeine dependence or behavioral interventions could implement the gradual reduction program, and such a widely disseminable treatment could have major impact.

10. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

Participants will not be paid for completing the preliminary screening. Participants will be paid $20 for the screening televisit, regardless of whether they qualify for subsequent visits. Qualified participants will be paid $20 for the treatment televisit, $20 for the Week 7 Follow-Up visit, $20 for the Week 14 Follow-Up visit, and will be paid $5 once per week for completing six surveys over six weeks. Participants who complete all of their study televisits will receive a $50 completion bonus, thus total compensation is anticipated to be $160 for completed participants. If additional televisits or surveys are necessary, such as in the event of survey or computer error, participants would be paid at the same per-session rate (i.e., $20 per televisit and $5 per survey). Compensation will be provided to participants via gift cards (deliverable via postal mail or email), or through creation of the participant as a vendor in the JHU system, where the participant can request a paper check or direct deposit. The payment strategy will depend on the most feasible option available to the study team and/or participant preference. If a participant discontinues caffeine reduction, such as due to adverse effects of caffeine withdrawal, they can still complete study assessments and receive payment and completion bonuses. If participants are withdrawn due to non-compliance or are lost to follow-up they will not receive the completion bonus. Similar to our past research, community observers will not be paid.

11. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

There are no costs to participants, although internet/email/video access is an eligibility requirement for participation in the study and the study team will not provide access to the internet or videocamera. The use of zoom or other telemedicine options will be free to participants. All other study costs will be paid for by the research project, which is funded by NIH grant R01DA003890.

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