# Research Protocol

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**Study Title:** Remember to abstain: Assessment of working memory training on delay discounting in low-SES cigarette smokers

**NCT #**: NCT05210608

**Co- Investigator(s):** N/A

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## I. Purpose, Background and Rationale

### A. Aim and Hypotheses

1. Brief Introduction: Despite widespread awareness of significant negative health consequences, cigarette smoking remains the leading cause of preventable morbidity and mortality in the US (Creamer et al., 2019; Jamal, 2018). Moreover, the highest rate of smoking and heaviest burden of smoking-related illness occurs among low-socioeconomic status (SES) individuals relative to higher SES groups (Businelle et al., 2010; Clegg et al., 2009). Low SES individuals are also 40% less likely to succeed in quitting smoking when they attempt to do so (National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health, 2014). One potential explanation for the disparity in rate of smoking and successful quit attempts may be differences in individual rates of delay discounting (DD), i.e., the degree to which rewards loses their value as the delays to their receipt increase (Odum, 2011). A proposed way to reduce steep DD and, potentially, substance use has been computer training for working memory, which has shown favorable results in a sample of individuals with stimulant dependence (Bickel et al., 2011) and substance use broadly (Felton et al., 2019), with the latter even showing decreases in cigarette smoking in a subset of the sample.

2. Aims: The current study will assess delay discounting (DD), working memory (WM) training, and cigarette smoking cessation outcomes. The aims of the project are the following:

- Assess efficacy of WM training
    - Assess efficacy of WM training on cigarette smoking
    - Assess efficacy of WM training on DD

## B. Background and Significance

1. Study Significance: The development of effective, theoretically coherent interventions addressing cigarette smoking is imperative, particularly interventions that would be feasible, efficacious, and acceptable in low-SES individuals. The proposed research is an innovative approach that capitalizes on previous findings showing reductions in delay discounting and even cigarette smoking. If working memory training is found to improve smoking cessation outcomes as a function of reductions in delay discounting, the project results could be helpful in future development of low-cost interventions for cigarette smoking.

2. The highest rate of smoking and heaviest burden of smoking-related illness occurs among low-SES individuals (Businelle et al., 2010; Clegg et al., 2009). One explanation for this disparity may be differences in individual rates of DD, which have been showed to be reduced with working memory training. (Bickel et al., 2011; Felton et al., 2019). Given the low cost of administering working memory training, such an intervention may be favorable for low-SES populations to improve smoking cessation outcomes.

3. Literature Review: DD has significant associations with:

   - **Cigarette smoking** (smokers tend to have higher rates of DD compared to non-smokers; Bickel et al., 1999);
   - **Smoking treatment outcome** (individuals who remained smoke free after a smoking cessation intervention had lower DD compared to those who didn't; González-Roz et al., 2019; Krishnan-Sarin et al., 2007; MacKillop & Kahler, 2009; Yoon et al., 2007);
   - **SES** (individuals with lower education and income have higher DD rates compared to those who are more educated and affluent; de Wit et al., 2007; Reimers et al., 2009).

   An innovative way to reduce DD that has been proposed is via working memory (WM) training. WM refers to one's capacity to hold information while engaging in complex mental tasks, including reasoning, comprehension, and learning (Baddeley, 2010). Previous research has shown that DD and WM correlate negatively (Shamosh et al., 2008), that individuals with higher DD rates show neural deficits in WM (Herting et al., 2010), and that acute nicotine abstinence is associated with WM deficits (Mendrek et al., 2006; Patterson et al., 2010). Furthermore, previous studies targeting WM to reduce DD have shown favorable results in a sample of individuals with stimulant dependence (Bickel et al., 2011) and substance use broadly (Felton et al., 2019), with the latter even showing decreases in cigarette smoking in a subset of the sample.

## C. Rationale

1. Although previous research has shown WM training to reduce DD, and cigarette use in a small subsample, the hypotheses of this study are largely exploratory. However, given the theoretical connections between DD, SES, and WM, it is expected that the hypotheses of this project will be supported.

2. The performance of this project may advance our knowledge of the relevant clinical targets for smoking cessation in low-SES individuals. In particular, this project is expected to shed light on DD as the putative mechanism in smoking for low-SES individuals and the durability of reductions in smoking as a result of reductions in DD through WM training.

3. Despite the evidence for some successful techniques for reducing DD, little of this work has been translated into intervention approaches to target clinical outcomes. This application seeks to capitalize on the emerging literatures indicating (1) WM training may be an effective and efficient way to reduce DD, and (2) DD is associated with SES, cigarette smoking, and treatment outcomes. Though WM training has been successfully implemented in laboratory-controlled experiments to reduce DD, we are not aware of any interventions for clinical disorders that specifically seek to do so and potentially enhance treatment outcomes.

## II. Research Plan and Design

**A. Study Objectives:** The main aims of this project are to examine the observed efficacy of WM training.

**B. Study Type and Design:** This study is an open-label trial longitudinal (participants will be assessed through their 1-month quit date) trial.

**C. Sample size, statistical methods, and power calculation**

1. Consistent with Stage 1a pilot trials, the current trial included a small sample size of completers ($N = 15$) to determine the initial outcomes of the WM intervention and its perceived feasibility/acceptability.
2. DD will be estimated by fitting the hyperbolic function specified in Eq. 1 to the indifference points computed during the task in order to estimate each individual's discount rate, where $v$ represents the discounted value of an outcome, $V$ is the undiscounted value, $D$ is the delay and $k$ is the discounting parameter, which specifies the degree to which the value of a given reward is discounted when it is delayed (with higher values representing greater discounting).

$$v = \frac{V}{1 + kD}$$

Eq. 1

While $k$ distributions tend to be skewed, post-hoc natural logarithmic transformations will be performed, which have been shown to approximate normal distributions. We will calculate $k$ values for each magnitude ($50, $200, $1000). Due to varying degrees of goodness-of-fit associated with nonlinear regression functions, we will also calculate area-under-the-curve (AUC) estimates (Borges et al., 2016). Hypotheses encompassed will be tested using Hierarchical Linear Modeling (HLM; Raudenbusch & Bryk, 2002), which allows the analysis of repeated measures and has been recommended because of its ability to: 1) accommodate missing data, 2) examine individual change over time in outcomes, and 3) include the average change and the individual variation around this average change which is especially important

in a small sample (Raudenbusch & Bryk, 2002; Singer. & Willett, 2003), even in smaller samples (Collado et al., 2019). Hypotheses encompassed within Aim 1 will be tested using Hierarchical Linear Modeling (HLM; Raudenbusch & Bryk, 2002), which allows the analysis of repeated measures and has been recommended because of its ability to: 1) accommodate missing data, 2) examine individual change over time in outcomes, and 3) include the average change and the individual variation around this average change which is especially important in a small sample (Raudenbusch & Bryk, 2002; Singer. & Willett, 2003), even in smaller samples (Collado et al., 2019).

3. Individuals who smoke cigarette and who are low in SES and receptive to a future quit attempt will be recruited for this study. Participants will be recruited from the greater Kansas City area.

**D. Subject Criteria (See Vulnerable Populations appendix, if applicable)**: The subject age range will be over 18 years old. Participants will be able to participate in the study regardless of gender and race. Special populations, such as minors and pregnant women, will not be targeted for inclusion.

1. **Inclusion criteria**: To be included in this study, a participant must be 18 years of age or older, who have smoked at least four cigarettes per day for at least 6 months, are interested in quitting cigarette smoking, are at or below the federal poverty line based on persons in family/household and annual household income:
    - 1 -- $12,880
    - 2 -- $17,420
    - 3 -- $21,960
    - 4 – $26,500
    - 5 -- $31,040
    - 6 -- $35,580
    - 7 -- $40,120
    - 8 -- $44,660
    - ≥ 9 – add $4,540 for each additional person,

    OR they or their child(ren) utilize a federal program for low-income individuals, and are willing to participate in a 5-week working memory training program as a pretreatment adjunct to behavioral group therapy.

2. **Exclusion criteria:** Participants must not indicate a severe substance use disorder according to the DSM-V with any substance other than tobacco or have any significant medical or psychiatric condition. Such conditions could include traumatic brain injury, dementia, significant learning disability, or psychotic symptoms. Participants must be at least at a 5$^{th}$-grade reading level. In case that participants are excluded, they will be provided with

resources in the community and provided with contact information for the Kansas Tobacco Quitline.

3. **Withdrawal/Termination criteria:** Participants may withdraw from the study at any time without penalty. The researcher reserves the right to discontinue individuals who evidence inability to comply to study conditions. The researcher will also exclude participants if they seem at risk for COVID-19 infection.

4. Participants can partake in other studies while participating in this research study if it does not interfere with their method of smoking cigarettes.

**E. Specific methods and techniques used throughout the study:**

1. **Laboratory tests:** Participants will provide breath and saliva samples to confirm smoking abstinence. Breath samples will be collected using the coVita Micro+ basic Smokerlyzer and saliva samples will be collected using the NicConfirm mouth swab tests. Timing of the samples are described in the Study Procedures section. Amount cannot be readily estimated for either test. Saliva samples will only be labeled using participant ID #'s, and breath samples will be stored on the Smokerlyzer. Saliva samples will be photographed for study records and then discarded.

## Study Procedures

**COVID-19 safety procedures**: These procedures will be followed for each in-person study session, and study staff will be trained prior to any data collection. Prior to departing, the project coordinator (PC) and/or research assistant (RA) will be screened for COVID-19 risk and will make sure all items and equipment (e.g., pens, laptop computers) are sanitized. The PC/RA will also wash and sanitize their hands as well as wear a surgical mask. The PC/RA will bring surgical masks and sanitizing wipes to the study location as well. The PC/RA will screen participants 24 hours before a session and at the study location prior to entering the building.

High-touch surfaces and chairs would have been sanitized before any individuals enter the space. Participants and will have been screened according to aCOVID screening form. Social distancing (6 feet or more) will be enforced at all parts of the study session unless close contact is absolutely necessary. All individuals will wear a face mask unless participants need to provide breath/saliva samples.

**Note**: If at any point a participant displays behavior inconsistent with COVID-19 safety procedures (e.g., not wearing their mask properly for extended periods of time, not social distancing), they will be reminded of the procedures. If the person refuses to engage in COVID-19 safety procedures, their participation will be terminated for the day. Individuals whose participation is terminated for the day will be asked if they are willing to follow COVID-19 safety procedures for future appointments. If participants deny their intention to meet the safety procedures, their participation in the study will be terminated. These participants will be provided with resources in the community as well as with contact information for the Kansas/Missouri Quitline. In the event that a participant reports any COVID-like symptoms, participants will be asked to leave the study location and reach out to Swope Health Services for further guidance.

Upon session conclusion, the RA will collect the laptop computer from the participant and disinfect. All high-touch surfaces and chairs will also be sanitized.

After participants complete 5 or more of the working memory trainings, they can begin attending a weekly 60-minute group based on an evidence-based behavioral treatment manual (MacPherson et al., 2016, 2017). Group topics include identifying values and goals within a variety of life areas (including achieving a non-smoking lifestyle), structuring and scheduling activities according to these personal values, identifying high-risk situations and developing appropriate coping strategies, enlisting social support assertively, discussing the benefits of a non-smoking lifestyle, receiving social support from the group, and managing lapses in smoking. Participants can attend as many sessions as they would like and join groups on a rolling basis.

**Screener call:** Interested individuals will take part in a phone call (~10 minutes) with the proje

coordinator to determine their eligibility. The project coordinator will ensure that participants do not meet exclusion criteria, which include: not being a smoker who has smoked 4 cigarettes/day for at least 6 months, not being interested in quitting smoking, not qualifying as low-income, having significant medical or psychiatric conditions, having severe substance use disorder for any substance other than tobacco, or being below a 5$^{th}$ grade reading level (asked via a self-report of educational attainment). Participants would qualify as low-income if they are at or below the federal poverty line for their respective household size OR if they or their child utilize a federal program for low-income individuals (e.g., Supplemental Security Income, Supplemental Nutrition Assistance Program, Children's Health Insurance Program, etc.; https://aspe.hhs.gov/topics/poverty-economic-mobility/poverty-guidelines/frequently-asked-questions-related-poverty-guidelines-poverty). Participants will be screened on any alcohol and drug use within the past 12 months and DSM-5 SUD symptoms will be assessed for any frequent substance use (2-4 times a week or more for any non-prescribed drug, 3-5 times a week or more for alcohol) other than tobacco. Participants who do not meet eligibility requirements will be informed that they will not be able to continue with the study, but the reason for this will not be disclosed. This is to ensure that participants do not attempt to alter their responses on disqualifying criteria in order to continue with the study. Contact information, in whatever medium the participant chooses (e.g., email, phone call, SMS text), and contacting preferences (e.g., medium, time of day) will also be collected for future session scheduling purposes. All individuals will be provided with a referral document which lists medical, substance use, and case management services in the Kansas City area. Individuals will be asked if they would like to receive the document over email, sent through mail, texted via SMS, or have it read out loud to them over a phone call.

**Baseline session**: This session will take approximately 1 to 1.5 hour to complete and will include informed consent and initial assessments. Participants will complete an informed consent process, which will include time and space to read the informed consent form (ICF), followed by thorough discussion with a study staff member about the nature of the study, potential risks and benefits, and participant rights. If the individual wishes to continue following this discussion, they will digitally sign the ICF via Qualtrics. At the point at which the ICF is signed by the individual, s/he will be considered an enrolled participant. Participants will also report demographic information (age, sex, race/ethnicity, current income, employment, and education level) and report on their cigarette smoking behavior. If at any point during the study a participant reports elevated suicidality, they will be thoroughly assessed for suicidality risk by the PI, who was extensive clinical experience, and participants will be referred to immediate care (e.g., Emergency department, Kansas City crisis response) depending on level of risk. All individuals will be provided with a referral document which lists medical, substance use, and case management services in the Kansas City area. Participants will also complete a reading test (Wide Range Achievement Test-4; WRAT-4) to confirm reading level from self-reported educational attainment.

Participants will also complete baseline assessments of DD, WM, and health-relevant behaviors and outcomes (*Measures* described in detail below). DD will be assessed using computerized binary choice tasks that asks participants to choose between smaller, immediate (either money or cigarettes) and larger, delayed (money) amounts after a specified delay and which adjusts the amount of the smaller, immediate amount based on participant choices. Point prevalence of tobacco smoking in the prior 7 days will be assessed using the semi-structured Timeline Followback (TLFB). WM will be assessed using the Tower of Hanoi task (TOH; asks participants to sequentially move a series of disks of varying sizes across 3 pegs), Hopkins Verbal Learning Test-Revised (HVLT-R; asks participants to recall and recognize a series of words), and Letter Number Sequencing task (LNS; asks participants to recall a set of numbers and letters). Participants will also be asked to provide an expired breath carbon monoxide (CO) sample using a coVita Micro+basic Smokerlyzer to biochemically verify smoking status/abstinence.

**Training sessions:** Participants will then be scheduled for the first of 10 training sessions. For each of the 10 training sessions, participants will complete four EF training programs. These programs have been used successfully to decrease DD (Bickel et al., 2011). These programs are: Sequenced Recall of Digits – Auditory, Sequenced Reverse Recall of Digits – Auditory, Sequenced Recall of Words – Visual, Verbal Memory – Visual. Each session will take 30 minutes to complete. For the control training program, the tasks will be matched on all essential features (e.g., stimulus, response, feedback) with four exceptions: (1) correct answers are provided or indicated to participants within each trial as part of the program interface, and (2) instruction indicates how to identify and respond to the stimulus that indicates the correct response. This will ensure that the sensory/motor experience of participants in the active training vs control training conditions are as similar as possible, with the exception of the memory requirement. Participants will also be given a set of noise-cancelling headphones during the training sessions to help offset any ambient noise in the environment.

Training sessions will take approximately 30 minutes to complete, will occur 2–3 times per week, and completed in 3-5 weeks in most instances. Each participant will be assigned a unique computer login for the self-guided training sessions, and progress (attendance, performance) will be monitored.

**BA groups**: Once participants complete 50% or more of their training sessions, the project coordinator will work with participants to find a time to begin the behavioral group sessions with the PI (i.e., Clinician), who will administer the intervention, over Zoom.

1. Session 1: Clinician will let everyone introduce themselves, go over group guidelines (including confidentiality), explain program rationale (engaging in pleasurable, smoke-free activities improves chances of quitting smoking), make note of barriers and benefits to quitting smoking, provide a copy of the National Cancer Institute *Clearing the Air* pamphlet, discuss previous quit attempts with the group participants as well as the upcoming quit attempt as part of the program, and introduce the Daily Activity, Mood, and Smoking Log, which asks participants to list hour-by-hour what they did during each day, the enjoyment of activity/event, the importance of it, the number of cigarettes smoked during each activity/event, and the overall mood of the day.
2. Session 2: Clinician will go over participants' use of the Daily Activity, Mood, and Smoking log, explain Life Areas, Values, and Activities (LAVA; major life areas, such as social relationships, and activities to strengthen those areas, such as spending more time with family on weekends), and ask participants to choose 15 activities related to their life areas and rank them by difficulty to accomplish.

3. Session 3 (1 week pre-quit date): Clinician will go over participants' use of the Daily Activity, Mood, and Smoking log, review participants' LAVA inventory, explain how to plan activities and integrate them with their daily log, discuss high-risk situations for relapse and how to identify them, and scheduling the quit date (and what to do in case of a "slip," i.e., smoking after quit date).
4. Session 4 (quit week): Clinician will go over participants' use of the Daily Activity, Mood, and Smoking log, discuss quit dates and quitting experience (e.g., withdrawal and immediate plans) for each participant, discuss success in accomplishing LAVA activities, identify obstacles to abstinence, offer support, talk about maintaining a healthy lifestyle (i.e., proper diet and exercise), and highlight social support, particularly by encouraging participants to form a "Contract" with a supportive person in their life (i.e., ask someone to take part in an activity with them to help them remain abstinent, such as riding bicycles together).
5. Session 5: Clinician will go over participants' use of the Daily Activity, Mood, and Smoking log, participants' contracts, quitting experience (e.g., withdrawal symptoms), strategies to avoid smoking, perceived benefits and disadvantages to quitting smoking, and identifying high-risk situations.
6. Session 6: Clinician will go over participants' use of the Daily Activity, Mood, and Smoking log, quitting experience (e.g., withdrawal symptoms), strategies to avoid smoking, perceived benefits and disadvantages to quitting smoking, discuss time management as a tool for abstinence, help identify high-risk situations, and offer support.
7. Session 7: This session will mirror Session 6.
8. Session 8: This session will mirror Sessions 6 & 7, and will include a discussion on developing a post-program plan to maintain abstinence by engaging and monitoring activities after the BA group and dealing with negative feelings, triggers, and immediate cravings. The clinician will also review the overall program progress and remind participants about the upcoming follow-up sessions.

**Post-training session**: This session is expected to take 1 to 1.5 hours to complete. 2-3 days following their last training session, participants will complete the DD task, TLFB, TOH, HVLT-R, LNS, and provide a CO breath sample. Participants will be asked to set a quit date for their cigarette smoking at this session and will be encouraged to connect to the tobacco quitline (1-800-QUIT-NOW).

**1-week post quit date session**: This session is expected to take about 30 minutes to complete. Around 7 days after their quit date, participants will complete the DD task, TLFB, and provide a CO breath sample. Participants will also provide a saliva sample to test for salivary cotinine, a metabolite of nicotine to biochemically verify smoking status/abstinence.

**1-month post quit date session**: This session is expected to take about 45 minutes to complete. Around 30 days after their quit date, participants will complete the DD task, TLFB, TOH, HVLT-R, LNS, provide a CO breath sample, and provide a saliva sample.

***Measures***

*SCID DSM-5*. If a participant reports frequent drug or alcohol use, they will fill out questionnaires on their DSM-5 symptoms for the respective substance (other than tobacco). Data will be recorded on Qualtrics, only identified by participant ID.

*Wide Range Achievement Test 4 (WRAT 4).* A reading survey to measure participant's grade-level equivalent reading ability. This will be administered at the baseline session. Data will be recorded on paper, only identified by participant ID.

*Single Commodity Delay Discounting (DD).* A binary choice procedure will be conducted on a personal computer to assess DD. On each DD trial, two hypothetical money rewards will be presented on the screen. One outcome will be an amount of money available immediately; the other outcome will be a larger amount of money ($50, $1,000) available after some specified delay (1 week, 1 month, 6 months, 1 year, 5 years). Participants will indicate the preferred alternative with a mouse-click, and the computerized algorithm (Holt et al., 2003) will adjust the immediate reward over 6 trials to determine an indifference point for each amount/delay pairing, resulting in 7 indifference points (corresponding to the 7 delays) for each of 2 amounts ($50$1,000). Indifference points will be used to calculate delay discounting rates. Participants will be told to indicate preference on the task as if the outcomes were for real money; previous research has established the validity and reliability of DD tasks for hypothetical rewards (Matusiewicz et al., 2013). The results of this assessment will be recorded on a laptop computer, only identified by participant ID.

*Timeline Follow-Back* (TLFB; Sobell & Sobell, 1992). A 7-day TLFB methodology will be employed to assess point prevalence of tobacco use. Participants will be asked to report number of cigarettes smoked for each day. Participants will also be asked to report nicotine vape and marijuana use. Data will be recorded on Qualtrics, only identified by participant ID.

*Tower of Hanoi* (ToH). This assessment consists of a board with 3 pegs and 4 disks of differing sizes. Participants must move the stack of disks from one peg to another while following specific rules (i.e., all pegs must end up on the farthest peg and at no point can a larger disk be placed on top of a smaller disk). Task will be completed with a research assistant and data will be recorded on Qualtrics, only identified by participant ID.

*Hopkins Verbal Learning Test – Revised* (HVLT-R; Brandt & Beneditc, 2001). This standardized assessment of verbal learning and memory requires participants to memorize a list of words presented auditorily. Participants are then asked to recall or recognize as many words as possible, either immediately or following a delay. Task will be completed with a research assistant and data will be recorded on Qualtrics, only identified by participant ID.

*Letter Number Sequencing* (LNS). This measure of working memory is in the Adult Intelligence Scales–III (Wechsler, 1997). The participant is given a mixed string of letters and numbers that they must then put into a sequential order of numbers followed by a sequential order of letters. The string presentation increases in difficulty until the participant is no longer able to correctly sequence three strings of equivalent difficulty. Task will be completed with a research assistant and data will be recorded on Qualtrics, only identified by participant ID.

*Fagerstrom Test for Nicotine Dependence* (FTND; Heatherton et al., 1991). Nicotine dependence will be measured using the 6-item FTND, a standard instrument for assessing intensity of physical addiction to nicotine as it relates to smoking. Data will be recorded on Qualtrics, only identified by participant ID.

*Expired Breath Carbon Monoxide* (CO). Smoking status will be measured with an expired carbon monoxide (CO) level using a coVita Micro+basic Smokerlyzer monitor (https://www.covita.net/product/microbasic-smokerlyzer/). A CO level below 9 parts per million will indicate smoking abstinence for 12 hours or less. Trained research staff will administer this measure. Disposable mouthpieces will be used for each individual, and the results will be shared with the participants immediately following completion if they are interested. Data will be recorded on the CO monitor and on Qualtrics, only identified by participant ID.

*Salivary Cotinine*. Smoking status will also be measured with a salivary cotinine measure (saliva sample) using NicConfirm mouth swab cotinine tests (https://www.confirmbiosciences.com/products/retail-brands/nicconfirm-swab-cotinine-test/). A cotinine level below 30 ng/ml will indicate smoking abstinence for 1 week or less. The results will be shared with the participants immediately following completion if they

are interested. Data will be recorded on Qualtrics, and a picture will be taken of the salivary cotinine test for record-keeping, only identified by participant ID.

**Timeline**

| *Measure* | Screener Call | Baseline | Computer Training (CT) [~3-5 weeks] | Post-CT | 1-week Post-Quit Date | 1-Month Post-Quit Date |
|---|---|---|---|---|---|---|
| Screener | X | | | | | |
| Demographics | | X | | | | |
| DD Tasks | | X | | X | X | X |
| Saliva Sample | | | | X | X | X |
| Breath Sample | | X | | X | X | X |
| Timeline Followback | | X | | X | X | X |
| WM Measures | | X | | X | | X |

Behavioral Activation Groups

**F. Risk/benefit assessment:** The risks associated with participation are minor, but there may be some risks possible: 1) Loss of confidentiality. This risk will be minimized by removing any link between personal information and data collection. 2) Embarrassment or negative feelings regarding their health behaviors or concerns. Participants can choose not to answer any questions. Information collected will be used for research purposes only. Participants will also be reminded that participation is completely voluntary and that they may withdraw at any time without penalty or losing any benefits to which they would otherwise qualify. 3) Minor physical discomfort from when giving saliva sample and carbon monoxide breath sample. We will do our best to minimize discomfort.

1. Physical risk: N/A
2. Psychological risk: N/A
3. Social risk: N/A
4. Economic risk: N/A

5. Potential benefit(s) of participating in the study:

    i. Participants are not guaranteed any benefits but may benefit from WM training and/or behavioral therapy centered on smoking cessation.
    ii. N/A.
    iii. This study may provide scientific and societal benefits by supporting this novel approach to improving health behaviors and outcomes via working memory training training.

**G. Location where study will be performed:** Research activities will take place at the Mazuma building in Kansas City (4001 Blue Parkway, Kansas City, MO 64130) in office space currently rented out by KUMC staff (including Tricia Snow). The behavioral activation groups will occur remotely on Zoom.

**H. Collaboration (with another institution, if applicable):** N/A.

**I. Single IRB Review for a Multi-site study (if applicable):** N/A.

**J. Community-Based Participatory Research (if applicable):** N/A.

**K. Personnel who will conduct the study, including:**

1. Indicate, by title, who will be present during study procedure(s): Dr. Anahi Collado, Ph.D., or the project coordinator, Sergej Grunevski, will facilitate the behavioral activation groups, the project coordinator and research assistant will be present as well. Project coordinator, Sergej Grunevski, will be present during consent and eligibility determination, the initial data collection, and the follow-up data collection. Research assistant, Archana Sundar, will be maintaining participant research records, managing study databases, and will be trained on conducting tests and procedures.

2. Primary responsibility for the following activities, for example:
    a. Determining eligibility: Sergej Grunevski and Archana Sundar
    b. Obtaining informed consent: Sergej Grunevski and Archana Sundar
    c. Providing on-going information to the study sponsor and the IRB: Dr. Anahi Collado and Sergej Grunevski
    d. Maintaining participant's research records: Sergej Grunevski and Archana Sundar
    e. Completing physical examination: N/A
    f. Taking vital signs, height, weight: N/A
    g. Drawing / collecting laboratory specimens: Sergej Grunevski and Archana Sundar

h. Performing / conducting tests, procedures, interventions, questionnaires: Dr. Anahi Collado, Sergej Grunevski, and Archana Sundar
i. Completing study data forms: Sergej Grunevski and Archana Sundar
j. Managing study database: Sergej Grunevski and Archana Sundar

**L. Assessment of Subject Safety and Development of a Data and Safety Monitoring Plan**

1. Details of the plan include:
    a. Persons/groups who will review the data (study team; independent safety monitor, data monitoring committee or formal DSMB). Dr. Anahi Collado, Sergej Grunevski, and Archana Sundar.
    b. Data/events that will be reviewed. Dates and events will be reviewed by the PI's and the research coordinator.
    c. Frequency of review will occur biweekly.
    d. Safety-related triggers that would cause the PI to stop or alter the study include COVID-19 infection or increased risk and cases in the greater Kansas City area.

2. Events will be determined as serious if they adversely impact the mental or physical health of the participant. Any AE will be reported to the PI immediately, and the PI will make the determination if the event is an AE or SAE and related or unrelated to the study. Any SAE that is related to the study will be reported within 24 hours of the determination to the IRB as well as funding agency. AE/SAEs that are unrelated to the study will be reported during regular reporting intervals.

3. If a participant has an adverse experience during the study, study participation will be discontinued for the participant.

## III. Subject Participation

**A. Recruitment:** Participants will be recruited through the KUMC's collaborator site (Swope Health Services), via posted fliers, Craigslist fliers, announcements, and word-of-mouth referrals. Once participants contact the study team, the project coordinator will reply with a brief description of the study procedures and try to schedule the individual's baseline session.

**B. Screening Interview/questionnaire:** Participants will be screened out using questionnaires if they indicate a severe substance use disorder according to the DSM-V with any substance other than tobacco or have any significant medical or psychiatric condition. Such conditions could include traumatic brain injury, dementia, significant learning disability, or psychotic symptoms. Participants will be consented prior to screening procedures.

**C. Informed consent process and timing of obtaining of consent:**

1. The project coordinator (Sergej Grunevski) will give subjects detailed and comprehensive information about the study and obtain their written consent.

2. The project coordinator (Sergej Grunevski) will summarize study procedures, risks, compensations, and other relevant information to the participant. Then, the participant will be allowed to fully read the ICF in as much time as they need. The participant may ask questions at any point before or after reading the ICF, after which they will have the chance to sign the document. Participants will be given a copy for their records and will be able to withdraw their consent at any point without penalty.

3. Individuals who are cognitively or decisionally impaired (e.g., dementia, psychosis) will be screened out over a phone call prior to consent procedures. The project coordinator (Sergej) will screen interested individuals over the phone.

**D. Alternatives to Participation:** The alternative to participation is to not participate.

**E. Costs to Subjects:** There will be no costs to participants during this study.

**F. How latest information will be conveyed to the study subject and how it will be documented:** Latest information regarding the participants in the study will be conveyed via email. This will be documented in a spreadsheet to ensure that all participants received all necessary information for the study.

**Payment, including a prorated plan for payment:** Participants will be compensated using a prepaid debit card (ClinCard) for their participation in this study. They will receive $25.00 for completing all assessments at the baseline session. For the weekly training sessions, they will be receive a minimum of $17.50 for every session they complete. If they complete at least 5 computer training sessions, they will receive $10.00, and if they complete an additional 5 (i.e., all 10 session), they will be given an additional $20.00. They will receive $35.00 for completing the post-training session, $30.00 for completing the 1-week post-quit date session, and $30.00 for completing the 1-month post-quit date session. The payment for each of the assessment sessions reflects a $10 amount to compensate individuals for transportation to the study site.

**A. Payment for a research-related injury:** N/A

## IV. Data Collection and Protection

**A. Data Management and Security:** Data will primarily be collected using Qualtrics. Digital data files that contain identifiable information will be kept on a KU SharePoint site. Pictures of saliva sample test results will also be kept on the SharePoint.

1. The research team, including Dr. Anahi Collado, Sergej Grunevski, and Archana Sundar will have access for study data.

2. Data will be stored on a KU-owned SharePoint site. Only study staff will have access to the data for this study. All study data will be de-identified and given a numerical identification number.
3. Study staff will maintain a database with identifiable information of participants, but participants will be identified using a unique identifier throughout study participation.
4. All study team members will have access to the key code for de-identified data.
5. Each subject will get one numerical identification code that will be used only for this subject.
6. Data files will be maintained in a secure KU-owned SharePoint site.
7. Mobile devices will not be used for data collection or storage.
8. N/A.

**B. Sample / Specimen Collection:** Saliva samples will be collected using mouth swab tests, after which a picture will be taken of the test and the test will be discarded. The sample will be identified only by unique participant identifiers.

**C. Tissue Banking Considerations:** N/A

**D. Procedures to protect subject confidentiality**: Participant data will be coded with a numerical identification code and all data, including subject identifiers, ICFs, and contact information will be digitally stored on a KU-operated SharePoint folder (in addition to storage on Qualtrics). The data will be accessible only to study staff who are involved with the study. The data will be held for a maximum of 10 years after the primary results are published. After said period, all data will be erased.

**E. Quality Assurance / Monitoring**

1. The data will be updated every time a new participant is added to the study. Data collected and added will be checked using documents that the participant filled out to ensure that all data is correctly entered. All data will be checked weekly to ensure that the data is consistent and complete. Following any contact with a participant, additional information from the meeting will be added to the data.

2. There are no plans to have an ongoing third-party monitoring.

## V. Data Analysis and Reporting

**A. Statistical and Data Analysis:** Hypotheses encompassed within Aim 1 will be tested using Hierarchical Linear Modeling (HLM; Raudenbusch & Bryk, 2002), which allows the analysis of repeated measures and has been recommended because of its ability to: 1) accommodate missing data, 2) examine individual change over time in outcomes, and 3) include the average change and the individual variation around this average change which is especially important in a small sample (Raudenbusch & Bryk, 2002; Singer. & Willett, 2003), even in smaller samples (Collado et al., 2019).

**B. Outcome:** The study will conclude once we collect full data from 10 participants. It is expected that study hypotheses will be supported, with success/failure determined by results from WM training on cigarette use over time.

**C. Study results to participants:** Participants will be given information on their breath/saliva samples results immediately following testing if they are interested.

**D. Publication Plan:** Data will be used to support a subsequent NIH grant application. Attempts to publish in relevant peer-reviewed journal will made if hypotheses are sufficiently supported.

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## APPENDIX I: VULNERABLE POPULATIONS

I. **Cognitively or decisionally impaired individuals**: Cognitively or decisionally impaired individuals will be excluded from the study.

II. **Children**: Children (below 18 years of age) will be excluded from the study.

III. **Pregnant women:** Pregnant women will will not be targeted for inclusion.

IV. **Prisoners:** Prisoners will not be targeted for inclusion.

V. **Students and/or Employees**: Students and employees will not be targeted for inclusion.