Study Title: Project CheckUP: A Brief Behavioral Intervention for Quitline Callers Who Use Marijuana (MJ) and Tobacco

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Principal Investigator	Kelly Carpenter, PhD
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External Sites/Partners (if applicable)	Denise Walker, PhD (University of Washington, School of Social Work) Beatriz Carlini, PhD (University of Washington, Alcohol and Drug Abuse Institute) Harold Javitz, PhD Independent consultant (previously SRI International) Maryland Marketing Source
Sub-Investigators	Denise Walker, PhD (University of Washington, School of Social Work) Beatriz Carlini, PhD (University of Washington, Alcohol and Drug Abuse Institute)
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1. RESEARCH OVERVIEW / ABSTRACT (LIMIT 500 CHARACTERS)

There is an urgent need to engage co-users of tobacco and cannabis (CB) in evidence-based treatments that lead to better cessation outcomes. A significant number of cigarette smokers who call state quitlines (QL) for help quitting tobacco report using cannabis and are interested in reducing or quitting cannabis. Adding a brief intervention to address cannabis simultaneously

with standard tobacco cessation counseling may lead to improved tobacco cessation outcomes and reduce cannabis use.

2. STUDY PURPOSE & OBJECTIVES

Our specific aims are to:

1) **Develop an integrated tobacco/cannabis (CB) intervention utilizing key components of the Marijuana Check-up (MJCU, a brief behavioral intervention for increasing motivation to reduce or quit using** cannabis**).** We will adapt the MJCU intervention for integration into tobacco cessation counseling; develop the intervention manual and training materials, and pilot test the new treatment with 10 QL callers who use CB. Our team includes an author of the MJCU, Dr. Denise Walker at the University of Washington who will assist with development, training, and implementation of the integrated intervention.
2) **Conduct a small, randomized pilot trial of the integrated intervention compared with the standard QL (treatment as usual; TAU)** to evaluate feasibility, acceptability, and preliminary effectiveness with 100 co-users recruited from 4 participating state QLs. We will assess implementation factors, coach fidelity, treatment engagement, and outcomes at 3 months (satisfaction, tobacco cessation (biochemically verified), and CB use).

We hypothesize that the intervention will: (1) be feasible to deliver (measured by coach treatment fidelity scores); (2) be acceptable to co-users (measured by enrollments and call completion numbers); (3) increase tobacco cessation rates compared with TAU; (4) increase co-users' motivation to change CB use; and (5) will produce greater reduction or cessation of CB.

Significance: This study comes at a critical time to answer key questions posed by state and local health departments who are considering the best methods for reaching CB users and increasing treatment utilization. Nationally, QLs have expressed concerns about the potential growth of co-users calling quitlines and the need to address the impact this has on treatment outcomes.

Public Health Relevance: Smoking cigarettes remains the number one preventable cause of death and disease in the US. Smokers who call QLs and use cannabis may struggle to quit due to the interactive effects of nicotine and CB. The proposed brief behavioral intervention addressing co-use may increase QL callers' chances of achieving and maintaining tobacco abstinence as well as increase their motivation to reduce CB use. As non-medicinal CB use becomes more common and legal in more states, a low touch intervention for co-users of CB and tobacco could improve health outcomes for many. Findings will inform development of scalable public health intervention strategies for co-users easily implemented across QLs.

3. JUSTIFICATION & BACKGROUND

Background and Significance

Tobacco use remains the number one preventable cause of illness and death in the US. Targeted therapies are needed for priority populations. Tobacco use causes more than 480,000 deaths each year and for each of those deaths there are 30 people living with serious smoking-related illnesses. [1] Tobacco use also costs the US economy an estimated $300 billion from health care costs and lost productivity. While smoking rates in recent years have dramatically decreased in the general population, they have remained almost unchanged in people with mental health conditions, including substance use disorders [2].

Cannabis (CB), is the most common illicit substance used today, but is increasingly becoming legal [4]. As of 2018, thirty-three states and the District of Columbia (DC) have legalized CB in some form and 10 states and DC have legalized non-medical CB use (Alaska, California, Colorado, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, and Washington). According to a 2017 survey, 14.6% of US adults used MJ in the past year, 8.7% in the past 30 days [5]. Use appears higher in states with legalized non-medical CB (20%) than in states with only legalized medical CB (14%) or no legal use (12%) and inversely correlated with age, with younger adults using at higher rates than older adults. [5]

Co-users of tobacco and CB have more difficulty quitting either substance and are at higher risk for tobacco-related illnesses. Recent longitudinal research shows that MJ users are more likely to start smoking cigarettes, continue to smoke over time (as opposed to quitting), and to relapse once quit. [18] Indeed, daily use of CB is associated with a 3.6 fold increase in nicotine dependence. [19, 20] Furthermore, nicotine is far more addictive than CB, works on the same neural pathways as CB [21], and cross-sensitization to each substance is likely to occur, with tobacco directly enhancing the subjective effect of CB, [12, 22, 23] leaving co-users more likely to develop a cannabis use disorder. [24]

Optum is the service provider for publicly funded tobacco cessation QL in 20 states and for more than 750 commercial clients with their Quit For Life coaching program. QLs are the primary method of accessing tobacco cessation services in the US and offer free services to any US resident. QL services include phone coaching, nicotine replacement medications (e.g., the nicotine patch), and digital services such as text messaging, a web intervention and a mobile app.

Co-users of tobacco and CB are at risk for continued tobacco dependence and associated serious health consequences of using both substances. CB use hinders smoking cessation efforts and tobacco use is a predictor of poor outcomes of CB dependence treatment. Our understanding of what is effective to reach and help co-users quit tobacco and CB is limited. Within this gap of knowledge is whether co-users who call tobacco cessation quitlines for help with cessation would benefit from an integrated phone-based program with CB elements based on the Marijuana Check-up (MJCU), the most widely used intervention for CB. Accordingly, we propose to develop and test a brief phone-based intervention for co-users of tobacco and CB for delivery in a quitline setting.

4. STUDY DESIGN

1. Design

D.4. Phase 2: Preliminary effectiveness pilot randomized controlled trial.
Overview. QL registration agents, coaches and/or research staff at Optum will screen for CB use and other study eligibility criteria and enroll participants into their respective state quitline. Once confirmed eligible, consented participants will complete the baseline assessment and be randomized into standard QL treatment as usual (TAU) or the experimental treatment, QL-CBCU. Approximately 3 months after randomization, we will email participants a link to the follow-up survey (with instructions). For those who fail to complete the online survey after two emails, we will send participant contact information via a secure transmission protocol to an external survey group who will attempt to complete the survey by phone, making 11 attempts at

different times of day and on different days. Those who do not complete the interview within 14 days will be emailed a reminder to take the full online survey or an optional brief online survey. Our research team will monitor completed surveys to identify those who reported they had not smoked tobacco in the past 7 days and request a biochemical validation test from participants as explained below (See section D.8.2. Biochemical Validation).

D.4.1. Setting. Participants will primarily be recruited from incoming callers from four state tobacco QLs with fully legalized CB use (Alaska, Washington DC, Oregon, Washington). See letters of support. These four QLs offer four or five proactive coaching calls, mailed support materials, access to text messaging, and web-based programs, plus at least two weeks of free NRT. If recruitment rates are slow, an alternative strategy of recruiting from social media (e.g., Reddit) will be implemented. All eligibility criteria will remain the same.

There will be two behavioral interventions tested in this trial; the standard quitline (treatment as usual: TAU) and the standard QL plus an adapted version of the CBCU (QL-CBCU). Both are phone based, brief, and utilize similar behavior change techniques: motivational interviewing (MI) and cognitive behavioral therapy (CBT). Both interventions include 4-5 proactive counseling calls, mailed materials, and at least 2 weeks of NRT. The new QL-CBCU intervention is being designed to be integrated into the quitline setting and delivered by quitline coaches with minimal training and infrastructure adaptation.

1. Duration

Participation will take about 3 months. The entire duration of the study is approximately 3 years.

2. Metrics and Variables

Table 2. Self-Report Measures	**Screen**	**Baseline**	**3-month follow-up**
Demographics	X	X	
Chronic Conditions and Health Problems	X		
Mental Health (PhQ2, GAD, PSS)		X	
Alcohol Use		X	
TO & E-Cigarette Use	X	X	X
Motivation for Quitting TO		X	
Cessation Medication use			X
CB Use		X	
Marijuana Problem List (MPL) & CUDIT		X	X
Motivation for Quitting/Reducing CB Use	X		X
CB Quit Goals and Impact on TO Use	X		X
Outcomes			
Program satisfaction and acceptability (usefulness, would recommend the program to others)			X
7- and 30-day point prevalence tobacco abstinence			X
Cannabis use (days/ week; occasions/day; hours of intoxication)		X	X

3. **Data**
   The sources of research materials obtained from individual human subjects in the study are limited to records and data, which will be available to the study team. Records include number and duration of counseling calls automatically collected by Optum. Data will be in the form of self-report questionnaires collected on the phone or via the internet and stored in a secure computer assisted telephone interview (CATI) system or via a secure link to a survey collection database. The 3-month follow-up survey may be completed via an online secure survey sent by Optum or telephone survey conducted by an external survey team. For participants who do not respond to the online or phone surveys, the research team will email participants a reminder to complete the full online survey or an brief online survey. There will also be biochemical verification of tobacco use at 3 months post randomization.
4. **Materials**
   Emailed and mailed letters
   An emailed outcomes survey
   Saliva test kit
5. **Devices – N/A**

5. STUDY POPULATIONS

1. Target Population

Quitline callers from participating states who are current smokers interested in quitting smoking cigarettes who also indicated that they use marijuana.

2. Number of Subjects

We will conduct a small randomized controlled study of the new intervention with 100 (up to 230) co-users recruited from the four state quitlines (AK, DC, OR, WA).

3. Eligibility

Eligibility criteria: Inclusion criteria: study participants will be daily tobacco smokers who smoke 5 or more cigarettes per day (CPD), aged 21 and older that are recruited from participating state QLs (or social media sites), screen positive for current use of CB, screen negative for serious mental illness (schizophrenia), and provide an email address (to receive study communications and links to the follow-up (2/3 month) survey). Other eligibility criteria include wanting to quit tobacco in the next 30 days and use of CB on 9 or more of the past 30 days. Exclusion criteria include being unable to speak and read English, limited access to a telephone, use of cannabis in the past 12 months was recommended by a doctor or other health care professional, and those who do not have another member of their household enrolled in the study. Pregnant or post-partum women are also excluded because they are offered a tailored QL protocol that differs from the standard call program).

4. Potentially Vulnerable Populations – [N/A]

5. Subject Identification & Accrual Plan (OR Plan for obtaining data and/or bio specimens if subjects are not directly enrolled)

Participants will be recruited from incoming callers to participating state quitlines or recruited from ads on social media sites (e.g., Reddit) and enrolled into the quitline. State quitlines have given their permission for us to recruit from their callers and to

recruit from external sites if needed. All research personnel have experience working with quitline callers and smokers. Drs. Walker and Carlini have experience working with smokers who also use cannabis.

6. Recruitment Plan and Materials

Recruitment

Recruitment for the study will have two methods. The primary method begins by screening for CB use during enrollment with the quitline and assessing eligibility and interest in the study. Optum's computer system will provide initial pre-screening so that only callers from participating quitlines who are 21+ years old are screened for the study. Registration agents will ask additional screening questions including CB use for at least 9 days in the last 30, interest in quitting smoking within 30 days, ready access to phone and email, screen negative for serious mental illness (schizophrenia), and whether they have an interest in study participation. The secondary recruitment method will be recruiting from ads on location specific social media sites (e.g., the r/Washington site on Reddit). Interested participants will email the study research assistant who will screen participants over the phone and enroll them into their respective state quitline if eligible. All participants will be contacted by phone by research-trained coaches who will describe the study in more detail, obtain informed consent, and deliver the baseline assessment and the post-randomization script.

Additionally, after the baseline assessment participants will be randomly assigned to receive the standard QL intervention (TAU) or the integrated intervention (QL-CBCU). All participants will receive the follow-up assessment (outcomes) survey at 3 months.

7. Enrollment / Consent Plan and Materials

Research-trained coaches will describe the study in more detail, read the information/consent document verbatims- and obtain verbal informed consent.

8. Compensation/Remuneration/Reimbursement

Incentives

Participants will receive $30 after completing call 1 (for the baseline assessment and call 1 participation), $20 for completing the second coaching call, $50 for completing the follow-up survey or $25 for a partially completed follow-up survey or a brief survey in lieu of the full follow-up survey, and $20 for completing the biochemical validation test. Participants will also have an option to complete the online survey within 48 hours of the email informing them to complete the survey for an additional $25 bonus. These incentives will be provided to all participants and both study groups (TAU and QL-CBCU). A randomly selected group of participants in the experimental group will be invited to complete a post intervention interview with the PI or the Co-I and receive $25 upon completion.

6. STUDY PROCEDURES

1. Procedures

Quitline registration agents at Optum will screen incoming callers from participating QLs for CB use and other study eligibility criteria or the study research assistant will screen interested participants recruited from social media ads. Specially trained QL (RIU Check-UP) coaches deliver the informed consent script. They complete the baseline assessment over the phone with participants who give their verbal consent to participate in the study. Participants are randomized to the standard QL treatment as usual (TAU) or the experimental treatment (QL-CBCU), which is provided by the RIU Check-UP coaches.

We will email participants a link to the follow-up survey (with instructions) at 3 months post enrollment. For those who do not complete the online survey after two emails, we will send participant contact information via a secure transmission protocol to an external survey group, Maryland Marketing Source (MMS; blind to study condition) who will attempt to complete the survey by phone, making up to 11 attempts at different times of day and on different days. Those who do not complete the interview within 14 days may be emailed a reminder to complete the full online follow-up survey or an optional brief survey in lieu of the full follow-up survey. Our research team will monitor completed surveys to identify those who reported they had not smoked tobacco in the past 7 days and request a biochemical validation test from participants as explained below. Selected participants will be contacted after completing the follow-up survey for an interview via Microsoft Teams or Zoom about their experience with the intervention. Participants will be provided with the link and dial in number for Teams or Zoom to access the interview and be notified the call may be recorded or transcribed. If the participant objects to a Zoom or Teams interview, they may be offered a phone interview as an alternative. If a participant engages in inappropriate or abusive behavior towards the study team, they may be terminated from the study by the Principal Investigator.

Biochemical verification:

Participants self-reporting tobacco abstinence 7 or more days at follow-up will be sent a test to confirm their abstinence by biochemical verification (saliva). Before sending the biochemical verification kit, study staff may contact the participant via email with an alert that a biochemical verification kit with instructions will be mailed to them and can be tracked with the provided USPS tracking number. A cover letter will be included in the kit explaining how to complete the test, instructions for returning the results via a photo to the study team's email box, and 14 day requested timeline for submitting the results. Instructions in the kit will inform participants to not eat or drink 10 minutes prior to taking the saliva test. Participants will be directed to refrain from including any PII in this email. If the results are not received within 7 days of delivery, a follow up email reminder may be sent. If the test outcome is returned by the participant, study staff will send the participant a $20 gift card for their participation (regardless of test outcome).

2. Subject Participation

Participant experience in the study:

Day 1.

SCREENING- Participant will answer questions if interested in study participation.

- **INFORMED CONSENT** – If interested and eligible, participant will hear the consent form read to them by the Quit Coach. The participant may ask questions before giving their consent. The Quit Coach will note the participant has provided their verbal informed consent. The participant will be mailed a copy of the consent.
- **BASELINE SURVEY** – Participant will spend approximately 20 minutes answering baseline assessment questions.
- **FIRST COACHING CALL** – Participant will engage in coaching call about quitting smoking with some discussion of how cannabis use will affect their quit attempt. Afterwards they will be sent a gift card for $30.
- ***EMAIL PFR*** Participant will be sent a feedback report based on their answers to the assessment questionnaire.
- **COACHING CALL 2** – Participant will be contacted by phone second coaching call which will focus on interaction of tobacco and cannabis and the feedback report. Participant will be paid $20 following this call.

FOLLOW UP COACHING CALLS. Participants will be contacted for 2-3 more calls to discuss how their smoking quit is going and follow up on cannabis use and goals. *2/3 months following enrollment:*

- **Survey**: Participant will be emailed follow up survey which will take about 5 minutes for the brief and 20-30 minutes for the full to complete online. If participant does not complete online, a phone survey company will call and deliver the survey by phone. If not reached by phone, participants may be mailed a reminder to complete the full online survey or a brief online survey. Participants will receive a $50 gift card for completing the full survey or $25 for a partially completed full survey or the brief survey. If participants complete the outcomes survey within 48 hours of the email sent informing them about the survey, they will receive an additional $25 bonus for completion.
- **Biochemical Verification**: If participant reports being quit from tobacco at follow up, a saliva test will be sent for confirmation. Participants will receive a small package containing all materials and instructions. After completing the test, they will take a picture of the test strip and send to the study team via email. They will receive a $20 gift card for completing the test and sending a picture within 14 days
- **Interview**: Selected participants may agree to a phone interview. The research team will call selected participants to schedule an interview via Teams or Zoom. Questions will concern the participants experience and opinions about the intervention. This will take less than an hour, and they will receive a $25 gift card for the interview.

Control group only

Participant experience in the study - the control group participants will receive standard QL services and are eligible for the same gift cards but will not receive the marijuana use-related materials (PFR) or treatment (coaching call content). They will not be invited to participate in any qualitative interviews.

3. Participant Engagement & Results

All counseling calls will be attempted at least five times over different days. We will increase retention at the 3 month follow up survey by reminding participants during coaching calls, notifying participants by email that their survey is due, and offering the survey first via email with a link to the online survey. For those who do not complete the online survey, we will have an external survey company attempt to reach participants by phone, making 11 attempts to reach them on different days and at different times. Finally, if participants have not responded to the phone survey, we may email participants a reminder via email containing links to take the full online survey or optional brief survey. We may follow up with participants who only partially

completed the survey online to troubleshoot any issues completing the survey online offer opportunity to complete survey by phone. Participants will receive an invitation for a post intervention interview with the PI or Co-I and receive $25 upon completion, for a total of up to $145 in incentives. Strategies such as these have proven to be effective in our quitline research studies resulting in higher recruitment and retention rates.

4. Data Collection

The sources of research materials obtained from individual human subjects in the study are limited to records and data, which will be available to the study team. Records include number and duration of counseling calls automatically collected by Optum. Data will be in the form of self-report questionnaires collected on the phone or via the internet and stored in a secure computer assisted telephone interview (CATI) system or via a secure link to a survey collection database. The follow-up survey may be completed via an online secure survey sent by Optum or telephone survey conducted by an external survey team. There will also be biochemical verification of tobacco use at 3 months post randomization. Documentation of verification will be provided to the study team by the participant in the form of a de-identified picture of the test result.

5. Data Analysis

For the proposed pilot study we plan to use summary statistics (means and proportions) with confidence intervals (CIs), and standard errors (SE), and graphical displays (histograms, pie charts, Box plots, etc.), as appropriate, to describe participant self-reported demographic characteristics, use of tobacco and cannabis, and other tobacco and cannabis variables measured at baseline and/or at each coaching call and at 3-months. We will use Fisher's exact tests, t-tests, and Wilcoxon rank sum tests to compare intervention and control groups. Comparisons including mean number of calls completed, mean satisfaction ratings, mean change in cigarettes per day (CPD), and mean change in days of cannabis use will be completed. We also will compare groups on changes over time on other cannabis measures, including hazardous cannabis use. We will address the effect of missing values on estimated smoking cessation rates using sensitivity analyses for outcome measures: 1) we will analyze responders only, and 2) we will impute missing tobacco use as 'smoking'.

We will have sufficient power with 100 participants (50 per group) and a 70% response to the follow-up interview to detect significant effects of the integrated intervention (vs. standard treatment controls) on feasibility and acceptability of the QL-CBCU intervention as measured by calls completed and treatment satisfaction at 3 months. This sample size is also sufficient for estimating QL-CBCU's potential impact (compared with the standard quitline) measured at 3 months on tobacco abstinence and CB outcomes (motivation to reduce days using CB, confidence in avoiding CB over-use, decreased problems associated with CB use, and decreased frequency of use). The sample sizes for this feasibility study are sufficient for the conduct and reporting of stage I pilot studies and were not selected for purposes of detecting statistically significant group differences at the alpha .05 level on outcomes. Our sample size is sufficient for documenting what power is available. For ordinal measurements that can statistically be treated in a similar manner to "continuous" measures (such as the number of QL calls completed and days used CB), we have 80% power to detect an effect size of 0.68. For proportions, we are powered to detect a difference in proportions of 0.22 to 0.34 (depending on the proportions in the two groups).

7. RISKS AND BENEFITS

1. Risks and Risk Mitigation

STUDY RISKS

- The primary risk of participating in this study is the risk of breach of confidentiality. A breach could potentially occur, for example, if an unauthorized individual accesses the study's database records. Data that the participant sends to the study team via email for biochemical verification could potentially be intercepted or viewed by others, as this data may be transmitted by the participant from an insecure phone or computer. Additionally, some participants may experience emotional discomfort that might occur during discussion of smoking, cannabis use, and impacts on their own health. Persons who quit smoking may experience temporary discomfort associated with nicotine withdrawal symptoms such as irritability, mood changes, headaches, trouble sleeping, and cravings to smoke. Similarly, those who use CB daily or nearly daily and choose to reduce their CB use may experience temporary discomfort associated with withdrawal such as irritability, anxiety, and sleep disturbances.
- Risks of NRT. **These are standard QL protocol and not specific to the study. These are detailed by the quit coach during coaching calls, and so are not listed in the consent form.** As part of standard service offerings from their state or district quitline, nicotine replacement therapy (NRT) in the form of the nicotine patch, gum, or lozenge will be offered to participants in this trial. The study will follow standard NRT protocols as provided through the quitlines. For each participant who opts to use NRT, Optum coaches will assess their medical safety to use NRT and then determine the appropriate dose according to clinical practice guidelines. Optum will then mail the NRT to the participant along with instructions on how to use the medications. The NRT in this trial is being used for its FDA-approved purpose and will be offered to all participants, and therefore, the effect of NRT is not being evaluated as part of the trial, although use of NRT will be assessed at follow-up. As part of standard quitline services, coaches ask about possible side-effects of its use during telephone counseling sessions. According to the FDA-approved product insert, possible side effects associated with the patch include headache, dizziness, lightheadedness, drowsiness, stomach upset, nausea, or flushing the first few days as a user adjusts to the medication. The area around the patch may become red, itchy, or irritated. Rarely, users may experience breathing difficulties, chest pain, irregular heartbeat, nervousness, anxiety, or tremors. Very rarely, a user of the patch may experience an allergic reaction such as a rash, itching, swelling, dizziness, or trouble breathing. Side effects will be disclosed in the study consent form. Optum distributes NRT to 65,000 of its 250,000 callers per year and has established protocols for addressing side effects with callers.
  Alternatives to these risks include not participating in the study.
  Protections against Risk
- **Protection against breach of confidentiality: security at Optum.** Optum's quitline business is a HIPAA-covered entity and complies with all HIPAA regulations regarding data security. The Optum offices provide physical and electronic access security, automated backup power for the servers, isolated environmental controls, and fault-warning systems to maintain a stable production environment for their quitline services. Servers, storage appliances, and network components are housed in a dedicated server

room at the corporate headquarters. All electronic and paper records that contain identifiable health information are secured and their use is limited to persons with a direct business-related need for access to this information. All hardware is handled as if it contains protected health information (PHI). Hardware that is no longer used is electronically and physically destroyed. The same security standards that apply to Optum normal business practices will be used to secure data collected for this study. Paper measures will be stored in locked file cabinets. All Service Delivery and Research Staff Members receive biannual Human Subjects training, yearly HIPAA training, sign a confidentiality statement, and are required to adhere to confidentiality and security policies and procedures.

- **Distress due to participation in the study intervention or assessment.** It is possible that some participants may be upset or embarrassed by participating in the study intervention. Consent scripts will advise potential participants about the study intervention and their right to terminate participation at any time without risk or penalty. Participants are free to refuse to participate in any element of the study or treatment and to refuse to answer any question during the assessments. Expert clinicians are available to counsel any participant who becomes distressed, including Drs. Carpenter and Walker, who are licensed clinical psychologists, and the clinical supervisory team at Optum.
- **Nicotine and CB withdrawal**. Nicotine and CB withdrawal symptoms are temporary and balanced by long term improvements in health. NRT can help mitigate nicotine withdrawal. Coaches are trained to help participants cope with short-term effects of quitting/reducing tobacco and/or adjust their dose of NRT. Study coaches will be educated about withdrawal symptoms associated with CB reduction or cessation. Although most of these symptoms are similar to nicotine withdrawal, coaches will receive additional training on best ways to help CB users cope with symptoms.
- **NRT side effects.** Participants enrolled in state quitlines have access to nicotine replacement therapy (NRT). Before recommending any medication or dosage, a participant's health condition is assessed with a series of screening questions. Coaches assess medical safety for NRT use by screening for Use Exclusion (UE) factors. Use Exclusions include: diagnoses of heart attack, stroke, or TIA within the past two weeks; being told by a health care provider within the past 6 months of a rapid or irregular heartbeat that required a change in activities or medication; being told by a health care provider in the past 6 months that they have serious or worsening angina; or a previous reaction to patch medication or adhesive tape that caused a rash or hives over the body, swelling of face or throat, wheezing or shortness of breath, or high fever, or that required the participant to discontinue use, or caused irritation that continued after rotating the patch and/or using hydrocortisone cream. If a participant is not eligible for NRT due to a UE, then a Medical Doctor (MD) Override Letter is sent to the participant. Once Optum receives the completed MD Override form from the participants MD and confirms NRT dosing with the participant, Optum sends the participant's NRT shipment. The screening questions were designed by Optum's medical team, and they are intended for use by non-clinical staff to exclude any individuals with specific conditions. Quit Coaches will also educate participants on the utilization of the products and related side effects. Manufacturers' information about side effects is given to the participant in written form and via a 1-800 number that has recorded information. Quit coaches help participants

problem solve around minor side effects (such as minor rash at site of the patch) and recommend that participants seek medical help for more serious side effects.
- There is a six-month delay for participants to re-enroll in quitline services after study involvement to ensure all study data is collected.

2. Benefits

Please describe the benefits of conducting the project.

- All participants may receive some satisfaction or indirect benefit from contributing to this trial. Participation in this research could increase health and quality of life if participants quit smoking and reduce or quit cannabis use. Participants will gain knowledge about quitting and reducing harmful substance use regardless of their quit status. Others may benefit by reduced exposure to second-hand smoke from tobacco or CB products if the participant reduces or quits either substance. If successful, this study could lead to improved tobacco cessation outcomes for those who also use cannabis, which would lead to improved health and longer lives.

8. DATA HANDLING

1. Data Protection, Storage and Transfer Plan

See mitigations of risk above for Optum data handling processes. In addition:

- Any personal information will be stored as electronic data in password-protected secure computer files, secured from unauthorized access. Data will be kept for at least 6 years after the study ends and related reports are published. Data will be completely destroyed once it is no longer needed.
- Any published results will take the form of summary results; they will not report anything that would identify a specific person.
- The research team at Optum will have access to the study data Only the minimal data required to complete the research will be accessed and analyzed.

- Some study data may be shared with research partners and regulatory bodies. This includes:
    - Researchers at University of Washington
    - Maryland Marketing Source (MMS) who may call you to complete your follow up survey;
    - Office of Human Research Affairs (OHRA) at United Health Group, who oversees our research, and;
    - National Institutes of Health, National Institute of Drug Abuse, who funds our research.
- The parties named above may need to look at study records for this research study and related quality assurance, survey completion, or data analysis. In particular:
    - Co-Investigators at the University of Washington (Drs. Carlini and Walker will have access to recordings of study calls to assist with treatment fidelity monitoring. These recordings will be sent via Optum-approved secure file transfer processes following recommendations from Optum Compliance, Privacy and Legal (CPL). Recordings will be deleted following fidelity coding procedures.

- Dr. Beatriz Carlini will assist with interviewing participants at the end of their treatment. Interview recordings and notes will be stored on a password protected laptop and transferred to Optum via secure file transfer processes as required by CPL and deleted following study completion.

2. **Statistical Analysis**
   See data analysis section above.
3. **Future Utilization**
   Research findings will be:
   1. Used to inform product development if found to be effective at helping participants quit tobacco and/or decrease cannabis use.
   2. Disseminated via peer-reviewed publications and presentations at national conferences.

4. **Publication Plan**

   Research findings will be disseminated as peer-reviewed publications and conference presentations. If applicable, findings may be used to secure funding for additional research and a fully powered randomized trial.

9. QUALITY CONTROL, MONITORING AND REPORTING

Service Delivery registration staff, Quit Coaches, and all study staff are required to complete the appropriate version of the CITI Human Subjects Research Training. Select coaches in the Research Implementation Unit (RIU) will be utilized for this project. RIU quit coaches have received additional training in research methods and have delivered QL interventions for multiple studies. They are also the coaches who deliver tailored clinical content to participants enrolled in the mental health QL program and other programs for special populations (e.g., youth, pregnant women). Study coaches are trained Tobacco Specialists. In addition, they will attend a study-specific training lasting approximately 8 hours, with content on study procedures, the study intervention, and supplemental content around cannabis.

In addition, the grant project manager (Helena Berlin) and Principal Investigator (Dr. Kelly Carpenter) have attended the NIH-required Good Clinical Practices (GCP) training (with refresher training every 3 years). Our research team follows GCP guidelines for documenting research procedures, including the development of a Standard Operating Procedures (SOP) manual to document standard practices and daily processes conducted to assure execution of research tasks in accordance with institutional, state, and federal guidelines. During the course of a study, all changes in procedures and deviations are documented in the SOP.

References Cited

1. National Center for Chronic Disease, P., S. Health Promotion Office on, and Health, *Reports of the Surgeon General*, in *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General*. 2014, Centers for Disease Control and Prevention (US): Atlanta (GA).
2. Cook, B.L., et al., *Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation.* JAMA, 2014. **311**(2): p. 172-82.
3. Williams, J.M., et al., *Smokers with behavioral health comorbidity should be designated a tobacco use disparity group.* American Journal of Public Health, 2013. **103**(9): p. 1549-1555.
4. *Drug Facts: Nationwide Trends*. 2015 [cited 2019; Available from: https://www.drugabuse.gov/publications/drugfacts/nationwide-trends.
5. Steigerwald, S., et al., *Smoking, Vaping, and Use of Edibles and Other Forms of Marijuana Among U.S. Adults.* Ann Intern Med, 2018. **169**(12): p. 890-892.
6. Hasin, D.S., et al., *Prevalence of Marijuana Use Disorders in the United States Between 2001-2002 and 2012-2013.* JAMA Psychiatry, 2015. **72**(12): p. 1235-1242.
7. ElSohly, M.A., et al., *Changes in Cannabis Potency Over the Last 2 Decades (1995-2014): Analysis of Current Data in the United States.* Biological Psychiatry, 2016. **79**(7): p. 613-619.
8. Chandra, S., et al., *New trends in cannabis potency in USA and Europe during the last decade (2008-2017).* Eur Arch Psychiatry Clin Neurosci, 2019. **269**(1): p. 5-15.
9. Volkow, N.D. and R. Baler, *Emergency Department Visits From Edible Versus Inhalable Cannabis.* Ann Intern Med, 2019.
10. Zehra, A., et al., *Cannabis Addiction and the Brain: a Review.* J Neuroimmune Pharmacol, 2018. **13**(4): p. 438-452.
11. Schauer, G.L., et al., *Assessing the overlap between tobacco and marijuana: Trends in patterns of co-use of tobacco and marijuana in adults from 2003-2012.* Addict Behav, 2015. **49**: p. 26-32.
12. Agrawal, A. and M.T. Lynskey, *Tobacco and cannabis co-occurrence: does route of administration matter?* Drug and Alcohol Dependence, 2009. **99**(1-3): p. 240-247.
13. Agrawal, A., et al., *Do early experiences with cannabis vary in cigarette smokers?* Drug Alcohol Depend, 2013. **128**(3): p. 255-9.
14. Schauer, G.L., et al., *Differences in Tobacco Product Use Among Past Month Adult Marijuana Users and Nonusers: Findings From the 2003-2012 National Survey on Drug Use and Health.* Nicotine Tob Res, 2016. **18**(3): p. 281-8.
15. Goodwin, R.D., et al., *Trends in Daily Cannabis Use Among Cigarette Smokers: United States, 2002-2014.* Am J Public Health, 2018. **108**(1): p. 137-142.
16. Richter, K.P., et al., *Cigarette smoking among marijuana users in the United States.* Subst Abus, 2004. **25**(2): p. 35-43.
17. McClure, E.A., et al., *Tobacco and cannabis co-use: Drug substitution, quit interest, and cessation preferences.* Exp Clin Psychopharmacol, 2019. **27**(3): p. 265-275.
18. Weinberger, A.H., et al., *Is Cannabis Use Associated With Increased Risk of Cigarette Smoking Initiation, Persistence, and Relapse? Longitudinal Data From a Representative Sample of US Adults.* J Clin Psychiatry, 2018. **79**(2).
19. Akbar, S.A., et al., *Tobacco and cannabis co-use and interrelatedness among adults.* Addict Behav, 2019. **90**: p. 354-361.

20. Rubinstein, M.L., M.A. Rait, and J.J. Prochaska, *Frequent marijuana use is associated with greater nicotine addiction in adolescent smokers.* Drug and Alcohol Dependence, 2014. **141**: p. 159-162.
21. Pierce, R.C. and V. Kumaresan, *The mesolimbic dopamine system: the final common pathway for the reinforcing effect of drugs of abuse?* Neurosci Biobehav Rev, 2006. **30**(2): p. 215-38.
22. Baggio, S., et al., *Routes of administration of cannabis used for nonmedical purposes and associations with patterns of drug use.* J Adolesc Health, 2014. **54**(2): p. 235-40.
23. Ream, G.L., et al., *Smoking tobacco along with marijuana increases symptoms of cannabis dependence.* Drug Alcohol Depend, 2008. **95**(3): p. 199-208.
24. Hindocha, C., et al., *Associations between cigarette smoking and cannabis dependence: a longitudinal study of young cannabis users in the United Kingdom.* Drug and alcohol dependence, 2015. **148**: p. 165-171.
25. Molnar, D.S., et al., *Prenatal and postnatal cigarette and cannabis exposure: Effects on Secretory Immunoglobulin A in early childhood.* Neurotoxicol Teratol, 2018. **67**: p. 31-36.
26. Meier, E. and D.K. Hatsukami, *A review of the additive health risk of cannabis and tobacco co-use.* Drug Alcohol Depend, 2016. **166**: p. 6-12.
27. Becker, J., et al., *Feasibility of a group cessation program for co-smokers of cannabis and tobacco.* Drug Alcohol Rev, 2015. **34**(4): p. 418-26.
28. Akre, C., et al., *Cannabis and tobacco use: where are the boundaries? A qualitative study on cannabis consumption modes among adolescents.* Health Educ Res, 2010. **25**(1): p. 74-82.
29. Copersino, M.L., et al., *Quitting among non-treatment-seeking marijuana users: reasons and changes in other substance use.* Am J Addict, 2006. **15**(4): p. 297-302.
30. Lee, D.C., et al., *Outcomes from a computer-assisted intervention simultaneously targeting cannabis and tobacco use.* Drug Alcohol Depend, 2015. **155**: p. 134-40.
31. Bush, T., Torres, A., Salmon, E., Carlini, B., *Marijuana/cannabis use and tobacco cessation treatment adherence among smokers calling tobacco quitlines.* Under Review.
32. Cummins, S.E., et al., *Tobacco cessation quitlines in North America: a descriptive study.* Tobacco Control, 2007. **16**(Suppl 1): p. i9-i15.
33. Fiore M, J.C., Baker T, Bailey W, Benowitz N, Curry S, Dorfman S, Froelicher E, Goldstein M, Healton C, et al. , *Treating Tobacco Use and Dependence:2008 Update.* 2008, US Department of Health and Human Services: Rockville (MD).
34. Fiore, M.C., et al., *Preventing 3 million premature deaths and helping 5 million smokers quit: a national action plan for tobacco cessation.* Am J Public Health, 2004. **94**(2): p. 205-10.
35. Stead, L.F., et al., *Telephone counselling for smoking cessation.* Cochrane Database Syst Rev, 2013(8): p. Cd002850.
36. Zhu, S.H., et al., *Telephone counseling for smoking cessation: effects of single-session and multiple-session interventions.* J Consult Clin Psychol, 1996. **64**(1): p. 202-11.
37. Bush, T.M., et al., *The impact of a free nicotine patch starter kit on quit rates in a state quit line.* Nicotine Tob Res, 2008. **10**(9): p. 1511-6.
38. Zhu, S.H., et al., *Evidence of real-world effectiveness of a telephone quitline for smokers.* N Engl J Med, 2002. **347**(14): p. 1087-93.
39. Carpenter, K.M., et al., *Feasibility and Early Outcomes of a Tailored Quitline Protocol for Smokers With Mental Health Conditions.* Nicotine Tob Res, 2019. **21**(5): p. 584-591.
40. Webb Hooper, M., et al., *Effects of a culturally specific tobacco cessation intervention among African American Quitline enrollees: a randomized controlled trial.* BMC Public Health, 2018. **18**(1): p. 123.
41. Gates, P.J., et al., *Randomized controlled trial of a novel cannabis use intervention delivered by telephone.* Addiction, 2012. **107**(12): p. 2149-58.

42. Gates, P.J., et al., *Psychosocial interventions for cannabis use disorder.* Cochrane Database Syst Rev, 2016(5): p. Cd005336.
43. Rooke, S., et al., *Effectiveness of a self-guided web-based cannabis treatment program: randomized controlled trial.* J Med Internet Res, 2013. **15**(2): p. e26.
44. Stephens, R.S., R.A. Roffman, and L. Curtin, *Comparison of extended versus brief treatments for marijuana use.* J Consult Clin Psychol, 2000. **68**(5): p. 898-908.
45. Stephens, R.S., et al., *The Marijuana Check-up: promoting change in ambivalent marijuana users.* Addiction, 2007. **102**(6): p. 947-57.
46. Tait, R.J., R. Spijkerman, and H. Riper, *Internet and computer based interventions for cannabis use: a meta-analysis.* Drug Alcohol Depend, 2013. **133**(2): p. 295-304.
47. Knudsen, H.K., C.R. Studts, and J.L. Studts, *The implementation of smoking cessation counseling in substance abuse treatment.* J Behav Health Serv Res, 2012. **39**(1): p. 28-41.
48. Lee, D.C., et al., *Sequential and simultaneous treatment approaches to cannabis use disorder and tobacco use.* J Subst Abuse Treat, 2019. **98**: p. 39-46.
49. *2014 National Survey on Drug Use and Health: Detailed Tables.* 2015 [cited 2019; Available from: https://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.pdf.
50. Becker, J., et al., *Effectiveness of different Web-based interventions to prepare co-smokers of cigarettes and cannabis for double cessation: a three-arm randomized controlled trial.* J Med Internet Res, 2014. **16**(12): p. e273.
51. Beckham, J.C., et al., *Mobile contingency management as an adjunctive treatment for co-morbid cannabis use disorder and cigarette smoking.* Addict Behav, 2018. **79**: p. 86-92.
52. Hasin, D.S., et al., *Prevalence and Correlates of DSM-5 Cannabis Use Disorder, 2012-2013: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions-III.* Am J Psychiatry, 2016. **173**(6): p. 588-99.
53. Montgomery, L., et al., *A scoping review and meta-analysis of psychosocial and pharmacological treatments for cannabis and tobacco use among African Americans.* Psychol Addict Behav, 2017. **31**(8): p. 922-943.
54. Walker, D.D., et al., *Motivational enhancement therapy for adolescent marijuana users: a preliminary randomized controlled trial.* J Consult Clin Psychol, 2006. **74**(3): p. 628-32.
55. Walker, D.D., et al., *Augmenting brief interventions for adolescent marijuana users: The impact of motivational check-ins.* J Consult Clin Psychol, 2016. **84**(11): p. 983-992.
56. Walker, D.D., et al., *The check-up: in-person, computerized, and telephone adaptations of motivational enhancement treatment to elicit voluntary participation by the contemplator.* Subst Abuse Treat Prev Policy, 2007. **2**: p. 2.
57. Walker, D.D., et al., *Maintenance Check-ups Following Treatment for Cannabis Dependence.* J Subst Abuse Treat, 2015. **56**: p. 11-5.
58. NAQC, *The use of quitlines among priority populations in the US: Lessons from the scientific evidence*, L. Baezconde-Garbanati, eta l., Editor. 2011: Oakland, CA.
59. Force, C.P.S.T., *Reducing Tobacco Use and Secondhand Smoke Exposure: Quitline Interventions.* 2010.
60. Deprey, M., et al., *Using free patches to improve reach of the Oregon Quit Line.* J Public Health Manag Pract, 2009. **15**(5): p. 401-8.
61. Morris, Z.S., S. Wooding, and J. Grant, *The answer is 17 years, what is the question: understanding time lags in translational research.* Journal of the Royal Society of Medicine, 2011. **104**(12): p. 510-520.
62. Smith, S.S., et al., *Enhancing tobacco quitline effectiveness: identifying a superior pharmacotherapy adjuvant.* Nicotine Tob Res, 2013. **15**(3): p. 718-28.

63. Bush, T., et al., *Addressing weight gain in smoking cessation treatment: a randomized controlled trial.* Am J Health Promot, 2012. **27**(2): p. 94-102.
64. McClure, J.B., et al., *Impact of a novel oral health promotion program on routine oral hygiene among socioeconomically disadvantaged smokers: results from a randomized semi-pragmatic trial.* Transl Behav Med, 2019.
65. McClure, J.B., et al., *Oral Health Promotion and Smoking Cessation Program Delivered via Tobacco Quitlines: The Oral Health 4 Life Trial.* Am J Public Health, 2018. **108**(5): p. 689-695.
66. Bowen, D.J., et al., *How we design feasibility studies.* American journal of preventive medicine, 2009. **36**(5): p. 452-457.
67. Czajkowski, S.M., et al., *From ideas to efficacy: The ORBIT model for developing behavioral treatments for chronic diseases.* Health Psychol, 2015. **34**(10): p. 971-82.
68. Rounsaville, B.J., K.M. Carroll, and L.S. Onken, *A Stage Model of Behavioral Therapies Research: Getting Started and Moving on From Stage I.* Clinical Psychology: Science and Practice, 2001. **8**(2): p. 133-142.
69. Onken, L.S., et al., *Reenvisioning Clinical Science: Unifying the Discipline to Improve the Public Health.* Clin Psychol Sci, 2014. **2**(1): p. 22-34.
70. Bandura, A., *Social Foundations of Thought and Action: A Social Cognitive Theory*. 1986, Englewood Cliffs, NJ: Prentice-Hall.
71. Fiore M, J.C., Baker T, Bailey W, Benowitz N, Curry S, Dorfman S, Froelicher E, Goldstein M, Healton C, et al., *A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report.* Am J Prev Med, 2008. **35**(2): p. 158-76.
72. Stephens, R.S., J.S. Wertz, and R.A. Roffman, *Self-efficacy and marijuana cessation: a construct validity analysis.* J Consult Clin Psychol, 1995. **63**(6): p. 1022-31.
73. Hollis, J.F., et al., *The effectiveness and cost effectiveness of telephone counselling and the nicotine patch in a state tobacco quitline.* Tob Control, 2007. **16 Suppl 1**: p. i53-9.
74. Orleans, C.T., et al., *Self-help quit smoking interventions: effects of self-help materials, social support instructions, and telephone counseling.* J Consult Clin Psychol, 1991. **59**(3): p. 439-48.
75. Bonn-Miller, M.O. and R.H. Moos, *Marijuana discontinuation, anxiety symptoms, and relapse to marijuana.* Addict Behav, 2009. **34**(9): p. 782-5.
76. Bush, T., et al., *Simultaneous vs. sequential treatment for smoking and weight management in tobacco quitlines: 6 and 12 month outcomes from a randomized trial.* BMC Public Health, 2018. **18**(1): p. 678.
77. Campbell, H.S., et al., *Minimal dataset for quitlines: a best practice.* Tob Control, 2007. **16 Suppl 1**: p. i16-20.
78. Gorelick, D.A., et al., *Diagnostic criteria for cannabis withdrawal syndrome.* Drug and Alcohol Dependence, 2012. **123**(1-3): p. 141-147.
79. *NYMOX. NicAlert®: A simple and cost effective way to monitor exposure to tobacco products.* 2018; Available from: https://nymox.com/products#nicalert.
80. Kistin, C. and M. Silverstein, *Pilot Studies: A Critical but Potentially Misused Component of Interventional Research.* JAMA, 2015. **314**(15): p. 1561-2.
81. Kraemer, H.C., et al., *Caution regarding the use of pilot studies to guide power calculations for study proposals.* Arch Gen Psychiatry, 2006. **63**(5): p. 484-9.
82. Volkow, N.D., W.M. Compton, and E.M. Wargo, *The Risks of Marijuana Use During Pregnancy.* JAMA, 2017. **317**(2): p. 129-130.