CanCope Micro-Randomized Trial Study Protocol and Statistical Analysis Plan

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Methods

Study Design

The CanCope Study was a micro-randomized trial (MRT) conducted to gather evidence about the feasibility of a mobile intervention to reduce cannabis craving among young adults. The study duration was from August, 2021 to October, 2021. Each participant remained in the study for 29 days including the date of their enrollment.

Study Participants

Participants were recruited from advertisements on social targeting young adults who were interested in reducing their cannabis use and who resided in the United States. Participant screening, informed consent, and study surveys were all conducted electronically, with no staff contact. Interested individuals from the target population who saw the recruitment ads downloaded the MetricWire app by clicking a link (if the participant was already on their phone) or by scanning a QR code (if the participant was browsing on their computer). Assessment, randomization, and intervention content were delivered through a commercially available app (MetricWire). Upon downloading the app, interested individuals were prompted to enter their name and email address. After verifying their email address, participants were given a brief introduction to the study in the app and asked if they consented to be screened for eligibility to participate in the study. Consenting participants continued to complete the initial eligibility screening which asked about the participants' age, whether they were pregnant/breastfeeding, whether they were in treatment for substance use, assessed willingness and readiness to reduce their cannabis use, and gathered information about participant's substance use frequency over the past 30 days including cannabis use. People were excluded from participating if they were outside the ages of 19 – 25 years, pregnant or breastfeeding, currently receiving treatment for

substance use, or used cannabis fewer than 10 out of the past 30 days. Eligible participants were then given additional information about the study and asked if they consented to participate in the intervention phase. Consenting participants who completed the demographics and baseline surveys were enrolled. All enrolled participants automatically began the 28-day intervention period the day following the completion of their baseline survey. This study was approved by the Dartmouth College Institutional Review Board.

CanCope Intervention

The CanCope intervention was delivered through the MetricWire app, which participants downloaded onto their personal mobile phones. CanCope consisted of "push" interventions, comprised of messages sent by the MetricWire system. Messages were either a mindfulness-based strategy for coping with cannabis cravings, a distraction-based strategy for coping with cannabis cravings, or a control message thanking the participant for engaging in the study. A message was randomly delivered (or not delivered) according to a decision rule. All messages were created according to evidence-based interventions (Guarino et al., 2018; Witkiewitz et al., 2014).

<u>Example mindfulness-based coping strategy:</u> *"You may be thinking 'I can't stand this,' or 'this is unbearable and not worth the effort.' Just notice these thoughts of distress then carry them away, letting them come and go. Remember, you can have whatever thoughts and feelings you have and still act differently than what you think or feel."*

<u>Example distraction-based coping strategy:</u> *"We can only pay attention to so many things at one time. To distract yourself from unpleasant thoughts, you can pay attention to your physical surroundings, or events or objects around you. For example, you might look around the room to find all the circular or rectangular objects and count them."*

Study Procedure and Randomization

Baseline

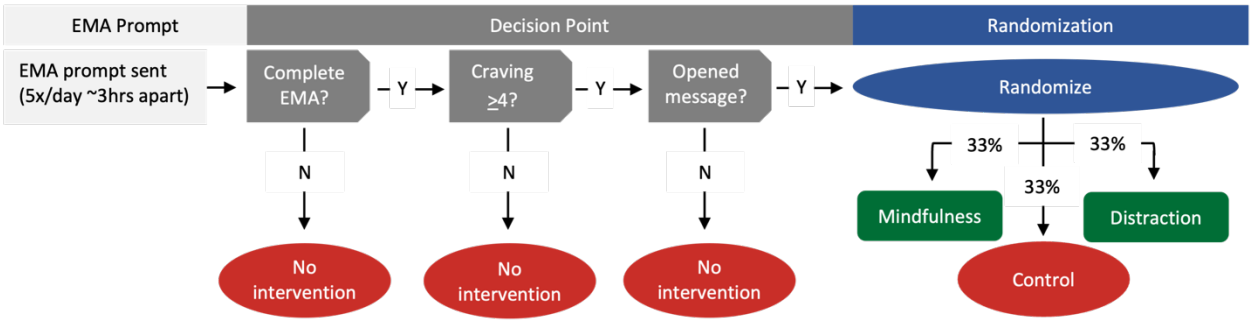
The screening survey administered at baseline assessed participants' age, pregnancy or breastfeeding status, whether they were receiving counseling or treatment for substance use problems, and cannabis use in the past 30 days. Cannabis use in the past 30 days was measured using a scale from 0 to 30 days, where 0 = no days of cannabis use in the past 30 days (SAMHSA, 2015). If eligible based on the screening survey, participants self-reported gender identity, sexual orientation, race, and ethnicity.

Intervention

During the intervention, participants received five EMA push notifications via the study app daily at a set window to assess their cannabis craving level. Those who self-reported elevated cannabis craving ($\geq$4 on a scale from 0 – 10 where 0 = no urge to use and 10 = extreme urge to use) received a second push notification prompting them to click on a new message. If they clicked on that new message, they were eligible for micro-randomization. The new message contained either one of the two intervention messages (mindfulness or distraction coping strategy) or a control message. Study participants received $1 for each EMA completed, with an additional $10 per week if they completed >80% of their EMA prompts for the week.

At each decision point, the randomization was independent of previous randomizations. During the 28-day intervention period, messages were randomized up to 140 (5x28) times for each participant. We used a probability of .66 for receiving a message and a probability of .34 for receiving a control message at each decision point when participants were available for the intervention.

Figure 1. Intervention flow



Outcomes and Measures

The aim of this study was to identify which strategies were most effective in helping participants cope with their cannabis cravings.

Proximal Outcome Measure

Cannabis craving has been positively correlated with cannabis use. Therefore, this study's primary proximal, or short-term, outcome was the effect of messaging on cannabis craving, determined by assessing the level of craving at the next EMA after the decision point for sending a coping strategy or control message.

Distal Outcome Measure

The distal, or long-term, exploratory outcome was the frequency of cannabis use over the past 30 days. The conceptual model underlying this MRT is that if the proposed intervention improves participants' ability to cope with cannabis cravings, they will be less likely to use cannabis. Given the exploratory nature of this objective, results are not presented for this outcome.

Statistical Analysis

We used a centered and weighted least squares (CWLS) method to analyze all available data (Boruvka et al., 2018; Klasnja et al., 2019; Qian et al., 2022). This method accommodates

within-participant correlation across time which results from the MRT design with decision points nested within participants. Furthermore, this method accounts for the endogeneity inherent in the MRT design due to the fact participant availability for intervention and covariates (e.g., pre-intervention craving level) are likely impacted by prior intervention. By capitalizing on the sequential randomization to estimate causal treatment effects, the CWLS method accounts for endogeneity in the data analyses (Klasnja et al., 2019; Qian et al., 2020).

We conducted a power analysis using the MRT sample size calculator to identify the needed sample size for 80% power to detect a small effect size of 0.2, assuming a 0.05 type 1 error rate, and 20% eligibility for randomization (3 out of 5 EMAs completed per day; craving level ≥4 on 1 out of the 3 submitted EMAs; and clicking on the delivered message every time craving was elevated). To meet this assumption, the desired sample size was 47. To allow for 15% attrition defined by failure to complete any EMAs, we recruited 8 additional participants.

Results

Study Participants

A total of 93 individuals downloaded the app which housed the intervention (MetricWire; www.metricwire.com). Of those, 74 individuals verified their email address used to register for the app and were assessed for eligibility to participate in the study. Of the 74 individuals assessed, 13 were ineligible because they met exclusion criteria: 4 did not complete the screening; 1 did not consent to be screened; 4 were not between the ages of 19 and 25 years; 1 was pregnant or breastfeeding; 1 was currently in treatment for a substance use disorder; and 3 did not use cannabis ≥10 out of the past 30 days. One person met two exclusion criteria and is reflected twice in the reason counts. Of the 61 individuals eligible to participate 8 did not enter the study: 1 did not complete the consent form; 1 did not consent to participate; 4 did not

complete the baseline assessments; and 2 did not complete any EMA. During the course of the study, 4 participants were lost to follow-up. We used all available data in the analyses, so all 53 participants who submitted at least one EMA during the course of the study are included in the analyses.

Outcomes

Decision Points, Participant Availability, and Message Delivered

For the 53 study participants, there were 140 possible decision points per person during the 28 days of the intervention period, for a total of 7420 possible person-decision points among all participants. Participants were eligible for the intervention during 1321 of the 7420 decision points (18%). A total of 406 mindfulness messages were delivered, 461 distraction messages, and 454 control messages when participants were eligible to be randomized to an intervention condition.

Effect of Coping Strategy Messages on Cannabis Craving in the Next EMA after a Decision Point

Our primary analysis showed that among all the decision points for which participants were eligible to receive an intervention throughout the 28-day intervention period, the average craving level after receiving a control message was 4.74 (SD = 2.82) and average craving level after receiving an intervention message was 4.63 (SD = 2.78). There was no statistically significant intervention effect ($z = -0.54$, $p = .589$).

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