STUDY PROTOCOL

THE IMPACT OF CANNABIDIOL (CBD) HEALTH CLAIMS AT POINT-OF-SALE ON CONSUMER PERCEPTIONS AND BEHAVIOR: MINI MART RANDOMIZED CONTROL TRIAL (RCT)

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THE IMPACT OF CANNABIDIOL (CBD) HEALTH CLAIMS AT POINT-OF-SALE ON CONSUMER PERCEPTIONS AND BEHAVIOR: MINI MART RANDOMIZED CONTROL TRIAL (RCT)

Principal Investigator
Kimberly Wagoner, DrPH, MPH

Co-Investigators
Beth Reboussin, Ph.D.
Edgar Alfonso Romero-Sandoval, MD, PhD
Kathleen Egan, PhD

Biostatistician
Cindy Suerken, MS

Programmer
Bobby Amoroso, BS

Research Associate
Olivia Horton, MSW, MPH

Project Manager/Coordinator
Amber Jones, BA

Sponsor
National Institute on Drug Abuse (NIDA)

Background and Purpose

Cannabis sativa contains more than 100 chemical compounds known as cannabiniods.[1] Cannabidiol (CBD), one of the most prevalent compounds in *Cannabis,* has no intoxicating effects to users. Its prevalence is second only to delta-9-tetrahydrocannabinol (THC), the main psychoactive compound in cannabis.[2] Hemp and marijuana are two strains of *Cannabis*. Hemp contains an abundance of CBD, but no more than 0.3% of THC;[3] marijuana contains both, with levels of THC reaching over 30%.[4-6] C*annabis* is illegal federally, and is considered a Schedule 1 drug.[7] Recently, the Agriculture Improvement Act of 2018 removed hemp from this classification, which resulted in an explosion of CBD-infused consumer goods that are under the regulatory authority of the Food and Drug Administration (FDA).[8]

CBD-infused products, available in small specialty shops as well as large mainstream retailers, are predicted to reach over $20 billion in US sales by 2024.[9] An estimated 46 million US adults use CBD despite lacking scientific evidence on its safety, efficacy, and uncertainty about product quality.[10,11] To reduce consumer confusion and product misperceptions, the FDA mandates that products containing CBD cannot be marketed as having *therapeutic benefits* without prior FDA approval.[12] The FDA has approved CBD for one drug (Epidiolex®) to treat specific epilepsy syndromes.[13] Since CBD has been approved as an active ingredient in a drug, it cannot be marketed as a *dietary supplement or food additive*.[12] In addition, CBD marketing cannot be *false or misleading* or imply the product is *approved or endorsed by the FDA,* without such approval.[12]

Recently, the FDA issued warning letters to online retailers for marketing CBD with false claims and illegally promoting it as a drug for a variety of medical conditions, including preventing Alzheimer's disease, curing cancer and relieving chronic pain.[14] This is a public health concern, as these types of claims may be influencing consumers to use CBD, often in combination with other medications and without medical supervision, putting consumers at undue risk. While these claims have been documented online, the point-of-sale at brick and mortar retailers, where the majority of consumers purchase CBD,[10] has been largely ignored. **No studies have documented CBD health claims at the point-of-sale.** Furthermore, there is substantial evidence that retail advertising influences consumer perceptions and behaviors for other substances (e.g. tobacco, food), **but no such evidence exists for how CBD health claims impact consumer behavior.** Therefore, the objective of our study is to inform regulatory science by documenting CBD health claims in brick and mortar retailers, evaluate consumer perceptions of them, and evaluate their impact on consumer purchase behavior.

Objective

We are conducting a two-arm RCT (CBD health claims, no claim control) in the University of North Carolina at Chapel Hill (UNC-CH) Mini Mart to assess the impact of CBD claims on purchase of CBD products (primary outcome), and secondary outcomes (i.e. willingness to try, perceived benefits and product safety).

Methods and Measures

Design

We will conduct an in-person trial with a sample of up to 160 CBD current users (past 30 day use) and 160 susceptible infrequent users (use 12 months ago or more) and 160 susceptible non-users (total n=490; Pilot: n=10; main study: n=480). For both arms, the simulated retail store will be stocked with products from the following categories: 1) food snacks, including a variety of shelf-stable products such as chips, brownies, and beverages such as water and soda; 2) personal products (i.e. oils, lotion, lip-balm, soap) for a realistic retail experience. The store will also offer a variety of CBD-labeled products from the same categories. No items in the Mini-Mart will contain CBD.

Each participant will participate in 1 visit at the Mini Mart. The 245 square foot store replica allows researchers to experimentally evaluate the influence of retail characteristics on consumer behavior in a controlled, real-world setting. Participants will be randomized to either see 1) non-CBD advertising (control condition) or 2) CBD advertising (experimental condition). Participants will be given a $75 electronic debit card to complete the following shopping task: each participant will be directed to select one item from a blue shelf or refrigerator that contains primarily food/beverage products, one item from a red shelf that contains primarily personal use products and one additional product from either shelf. In total, the participants will purchase 3 products. Each participant will take a computer survey after completing the shopping task. Each participant will receive an incentive valued at $75 for participating in the study.

Setting

The Mini Mart is located at UNC in Chapel Hill, NC. Participants will be recruited from the surrounding area (Chapel Hill, Durham and Raleigh). The Mini Mart visits will occur in person. Visits will be scheduled to allow participants enough time to complete the shopping task and a RA to set up the store for the condition. The RA will also complete any pre-visit items prior to the next participant arriving.

Recruitment

Before public use, all recruitment materials will receive approval from Wake Forest IRB (see Human Subjects section below).

Subjects Selection Criteria

Inclusion Criteria

- Age 18-79
- One of the three use statuses:
    - Current user: past 30 day CBD user;
    - Susceptible Infrequent user: CBD use 12 months ago or more and reporting 3 or 4 to any of the following three items:
        - Are you curious about using CBD? (1. Definitely Not; 2. Probably Not; 3. Probably yes; and 4. Definitely Yes)
        - Do you think you will use CBD in the next six months? (same response options)
        - Would you try CBD if one of your good friends offered it to you? (same response options)

    - Susceptible Never CBD users: never use of CBD and reporting a 3 or 4 to any of the following three items:
        - Are you curious about using CBD? (1. Definitely Not; 2. Probably Not; 3. Probably yes and; 4. Definitely Yes)
        - Do you think you will use CBD in the next six months? (same response options)
        - Would you try CBD if one of your good friends offered it to you? (same response options)
- Able to read and speak English
- Able to complete a survey on a computer or ipad without help
- Willing to complete shopping task at study Mini Mart

Exclusion Criteria
- Non-English speakers
- Age <18 and >79

RCT
Screener for eligibility

- The screener survey will assess demographics (age, sex, gender identity, race/ethnicity, education, and income), and CBD use, including ever and past month use. For those who have never used CBD and for infrequent users we will assess susceptibility to CBD use.

Interventions and Interactions
Interested individuals will link to the screener survey using the QR code on the flyer or email. Everyone completing the screener will be assigned a unique ID. Ineligible individuals will not receive an incentive for completing the screener. Participants who meet eligibility criteria will contacted by the study team and invited to participate in the Mini Mart RCT. Interested individuals will be scheduled for a 60 minute visit to the Mini-Mart in Chapel Hill, NC. The RCT will last approximately 60 minutes. Participants will be assigned to a randomized condition after they arrive at the Mini-Mart and provide informed consent. Participants randomized to the intervention condition will see approximately 20 CBD advertisements posted throughout the Mini-Mart using advertising materials documented during Aim 1 of the study. Participants randomized to the control condition will not see any CBD advertising. The CBD advertising will be replaced with benign marketing (i.e. transportation and password safety).

Participants will be asked to complete a shopping task in the Mini Mart. Within the Mini Mart, we will clearly define shelf space by color-coding shelves and placing eligible products in those designated areas. Participants will be given a $75 electronic debit card and asked to select one item from the blue shelf or refrigerator that contains primarily food/beverage products, one item from the red shelf that contains primarily personal use products and one additional product from either shelf/refrigerator. In total, the participants will select 3 products. After completing the task, the Research Assistant will use a study ipad with the participants unique ID to log the items selected for purchase (CBD-branded or non-CBD-branded items). No products in

the Mini-Mart will contain CBD; products will only be branded as containing CBD. The Research Assistant will record the selected items on the ipad and will upload a photo of all 3 items purchased. Participants will not be able to keep any selected items. Upon completing the task, the Research Assistant will take the participant to an adjacent private room where the participant will complete a short survey to assess secondary outcome measures (described below). At the end of the survey, the participant will be given a debrief document that explains the deception protocol and the Research Assistant will be available to answer any questions. The debrief provides the current scientific evidence for CBD and provides links to the US Food and Drug Administration (FDA) and the Substance Abuse and Mental Health Services Administration (SAMHSA). Upon completion participants will receive an incentive valued at $75 for participating.

Pilot test

Prior to conducting the main trial, we will pilot the trial with approximately 10-15 participants to 1) optimize the timing and flow of the protocol, 2) ensure participants understand the directions and color-coding of the product categories, and 3) conduct a final test of the product documentation and survey programming. We will also ask some questions related to the deception protocol to ensure participants are not upset about 1) not being able to take the products with them and 2) receiving the full amount of the incentive as cash. Assuming no problems, we will use the same procedures outlined in this protocol for recruitment, scheduling and conducting the trial.

Outcome Measures

This is a post-test only experimental design. The primary outcome is purchase of a CBD product.

We will also assess claim recognition, perceived product safety and benefits, outcome expectancies, and willingness to try CBD (non-CBD users only). For CBD users, we will ask additional questions about their use of CBD (i.e. frequency, product type, reasons for use, and use with other cannabinoids). All participants will be asked about their demographic and health status.

Analytic Plan

The primary outcome is purchase of a CBD product. Our hypothesis is that CBD health claims displayed in the advertising will increase the probability of purchasing at least one CBD product during the shopping task. First, we will look at the percent of participants who purchase a CBD product in each group (control vs experimental). Logistic regression models will be used to test differences in the probability of purchasing at least one CBD product between participants that were randomized to the CBD claims condition compared to those in the no CBD claims condition. Models will adjust for age, sex, race/ethnicity, chronic medical conditions and use of CBD and marijuana products. We also hypothesize that chronic medical conditions and sex may modify effects. Secondary analyses will test these hypotheses by including an interaction between these factors and the randomized condition. Our secondary hypothesis is that CBD claims displayed in the retail setting will lead to increased perceived benefits, product safety, and willingness to try CBD. For perceived benefits, we will look at the mean number of selected benefits for each group (CBD ads vs non-CBD ads). For perceived product safety, we will look at the mean and response option frequencies for all products combined for each group (CBD ads vs non-CBD ads). For willing to try CBD, we will look at the mean score and response option frequencies of each group (CBD ads vs non-CBD ads). Both linear and logistic regression models will be used to test for differences in these measures between participants assigned to the randomized CBD claims condition and those to the no CBD claims condition. All statistical tests will be two-sided with a 0.05 significance level and all analyses will be performed using SAS V9.4.

Human Subjects Protection

Subject Recruitment Methods

To recruit participants, we will post flyers at public locations likely to reach potential participants, such as YMCAs, public libraries, CBD shops, the bus station, and local restaurants. Permission to post these flyers will

be obtained where necessary. In addition, we will send out non-paid advertisements viaplatforms like NextDoor, Facebook and Reddit). We will send out informational emails to appropriate listservs, such as WFUSM PHS listserv (phs_sshp-core_dl@wakehealth.edu) and UNC-Chapel Hill's Informational listserve (no_reply@massemail.unc.edu). In addition, we will post it on BeInvolved at AtriumHealth/WFUSM website (WakeHealth.edu/BeInvolved) and UNC-Chapel Hill's research opportunity website (Research For Me https://researchforme.unc.edu/index.php/en/). We will post paid social media ads and will work with the institution's communication and marketing team to design and post them on Facebook and other approved platforms. Paid ads will also be posted on Craigslist. We will also contact previous Minimart participants who indicated they would like to be contacted about future Minimart studies by their preferred method of communication (i.e. email, phone). The materials will contain a QR code and/or hyperlink that will direct participants to a screener survey to see if they are eligible. If eligible, participant will be contacted by study staff to schedule them.

Informed Consent

Electronic informed consent will be obtained from participants when they arrive to the Mini-Mart and prior to starting the shopping task. The Research Assistant will review the consent documents and explain the study to the participant. The participant will click a box indicating they have read the consent documents and agree to participate in the study. The informed consent document for the pilot will be the same as the main study's informed consent document.

Confidentiality and Privacy

Confidentiality will be protected by maintaining all study information in a secure manner. Data will be collected at the UNC Mini Mart in Chapel Hill on a study ipad that will have a secure survey link for each individual participant. We will link all study data (e.g. screener, consent, randomization assignment, products purchased, and post shopping task survey) using the participant ID which will be assigned when the screener is completed. Data will be housed on the secure Wake Forest University School of Medicine server. The pilot study will be conducted solely at the UNC-Mini Mart in Chapel Hill.

Access to de-identified data will be limited to study staff. Data and records will be kept locked and secured with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The Principal Investigator, Dr. Wagoner will be responsible for the overall monitoring of the data and safety of study participants. Dr. Wagoner will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

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