CBD Consumer Survey (Aim 2)

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STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

THE IMPACT OF CANNABIDIOL (CBD) HEALTH CLAIMS AT POINT-OF-SALE ON CONSUMER PERCEPTIONS AND BEHAVIOR: ONLINE SURVEY

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THE IMPACT OF CANNABIDIOL (CBD) HEALTH CLAIMS AT POINT-OF-SALE ON CONSUMER PERCEPTIONS AND BEHAVIOR: ONLINE SURVEY

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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(s)

The overarching goal of this web survey is to assess consumer claim perceptions and claim meanings of CBD advertisements documented in a sample of brick and mortar retailers in North Carolina, Maryland, and Colorado, as well as willingness to try, perceived product safety, perceived benefits, and outcome expectancies.

Online Consumer Perceptions Survey PROTOCOL

Methods and Measures

Design

We will conduct a cross-sectional online survey with a nationally representative probability-based sample of adults (ages 18-65) recruited from the AmeriSpeak panel, funded and operated by NORC at the University of Chicago. All panel members aged 18-65 will be invited to be screened, and those who have used CBD in the past 30 days (current users), those who have ever used CBD (ever), and those who have never used CBD (non-users) will be invited to participate. We will assess consumer perceptions of documented health claims made inside CBD retailers. Given NORC's estimated response rate of 34% and prevalence estimates for CBD use between 14-25%, we estimate a random sample of 22,000 adults will be screened to achieve our goal of 3,000 completed surveys consisting or 1,000 current CBD users, 1,000 ever CBD users, and 1,000 non-users. AmeriSpeak participants will receive points, worth approximately $5, for completing the survey. No incentive will be provided for completing the screener. Although our goal is to have 3000 completed surveys, we anticipate having up to 600 additional completed surveys since this is an online survey and we will allow anyone who is taking the survey to complete it and receive the incentive. We will monitor the number of completed surveys by user status on a daily basis to achieve the targeted goal of 3000 completes and minimize additional surveys over the targeted goal. Thus**, our sample size is n=3525**.
We will assess data quality by ensuring participants meet sufficient completion criteria. Participants must have met both of the following criteria to be included in the study: 1) at least 75% of the outcome variables answered (not skipped) and 2) survey completion time of > 5min. All completed surveys will be used in data analysis.

To assess eligibility, participants will be asked their age and several questions about CBD use. If eligible, participants will be invited to complete the full survey. For the survey, participants will be randomly assigned to a panel consisting of up to 10 CBD advertisements that include FDA prohibited or potentially-prohibited claims. Participants will complete questions while the stimuli are shown on the survey webpage. After the interview, participants will receive a link to electronic resources with up-to-date CBD information based on the literature, guidance documents from the Food and Drug Administration (FDA), and organizations including the Center for Disease Control (CDC) and Substance Abuse and Mental Health Services Administration (SAMHSA).

Setting

Survey participants will complete the online survey in a location of their choosing.

Subjects Selection Criteria

AmeriSpeak is an active panel, funded and operated by NORC at the University of Chicago that is designed to be representative of the U.S. household population. U.S. households are randomly selected within NORC's National Sample Frame and supplemented by address-based sample frames. This is conducted through a two-stage sampling process. The first stage is the primary sampling unit, which is a National Frame Area of an entire metropolitan area or county. The second stage occurs within this sampling unit. Secondary sampling

units are segments defined from Census tracts or block groups. Within these segments, all housing units are listed using the U.S. Postal Service Delivery Sequence File. The final National Frame contains approximately 3 million households. Selected households are invited to join AmeriSpeak™ by telephone or by web, and participate in research studies 2-3 times a month. For this study, all 18-65 year old panel members will be screened by AmeriSpeak™. Individuals who are a current CBD user within the past 30 days will be invited to participate in the study. We will also include a sample of ever-CBD and non-CBD users to understand consumer perceptions from those who do not currently use, as well. We will oversample CBD users so the final respondent sample is comprised of 1/3 current CBD users, 1/3 ever CBD users, and 1/3 never-users. It is expected that AmeriSpeak™ will screen 22,000 adults to obtain the sample size.

(Approximately 1,000 current CBD users; 1,000 ever CBD users, and 1,000 non-users). Therefore, the survey will begin with a short screener survey about CBD use.

Screener
All interested individuals will be able to complete our screener. Interested individuals will click on the link to the survey and be routed to a website to review consent language and complete the survey. Participants will complete a one-minute screener to determine if they are eligible for the full survey based on their age and CBD use. If eligible, they will be consented and then proceed to take the survey.

Inclusion Criteria
- Age 18-65
- US Residents

Exclusion Criteria
- Non-English speakers
- Younger than 18 or older than 65
- Not US residents

Full Survey
Inclusion Criteria
- Age 18-65
- US Residents
- Satisfies one of the following categories:
    - 1. Current CBD users
    - 2. Ever CBD users
    - 3. Non-CBD users
- Members of the AmeriSpeak™ panel

Exclusion Criteria
- Non-English speakers
- Younger than 18 or older than 65
- Not members of the AmeriSpeak™ panel

Sample Size
- Based on a response rate of 34% and prevalence estimates for CBD use between 14-25%, we estimate a random sample of about 22,000 adults will be invited to complete the screener survey to achieve our goal of 3,525 completed surveys.

Interventions and Interactions
Individuals will be contacted by AmeriSpeak™ to participate in the survey, and if interested, will complete a screener to determine eligibility. After completing the screener, participants who are ineligible will be thanked for their time and will exit the survey. They will not receive an incentive for completing the screener. Participants who meet eligibility criteria will be invited to complete the full survey. The full survey will last

approximately 15-20 minutes. After completing the survey, participants will receive a small incentive in the form that they've agreed to with their panel (approximately $5).

Outcome Measure(s)

Outcome Measure

This is a post-test only experimental design. The primary outcome is *claim perception* by CBD use status. We will determine if advertisements are interpreted by consumers in one or more ways that the FDA has determined are prohibited (i.e. drug effect; FDA approved/endorsed; dietary supplement; food additive; false/misleading-youth; false/misleading-science). We will assess this using the following items, all of which will use a 5-point response scale, (1) Not at all to (5) Extremely.

To assess drug effect claims, all participants will be asked "**How much does this ad suggest that CBD can cure, prevent, or treat a health condition?"**
To assess FDA endorsement claims, participants will be asked **"How much does this ad suggest that the advertised CBD is approved or endorsed by the US Food and Drug administration (FDA)?"**
To assess dietary supplement or vitamin claims, participants will be asked **"How much does this ad suggest that CBD is a dietary supplement or vitamin?"**
To assess food additive claims, participants will be asked **"How much does this ad suggest CBD is a main ingredient in a food or beverage?**
To assess if a claim is false and misleading participants will be asked **"How much does this ad suggest the information shown is based on scientific evidence?"** and **"How much would this ad appeal to youth under the age of 18?"**

We will also assess perceived product safety, appealand perceived 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 goals of the analysis are to 1) determine if CBD use status is associated with interpreting our main outcome and secondary outcomes (main = claim perception as one of the prohibited claim types, secondary = appeal of advertisements and perceived product safety); 2) identify which claims are interpreted by consumers in ways that the FDA has determined are prohibited; and 3) explore participant characteristics (beyond use status) that are associated with interpreting a claim as one of the prohibited claim types.

First, analyzing all claims together, we will assess the mean score for each claim type (i.e. drug effect; FDA approved/endorsed; dietary supplement; food additive; false/misleading-youth; false/misleading-science) to determine if CBD use status is associated with interpreting ads as containing one of the prohibited claim types. We will also assess the mean for perceived product safety and appeal by use status. For each of the advertisements, we will then estimate the proportion of participants that interpret the claim as one or more of the prohibited claim types (i.e. drug effect, FDA approved/endorsed; dietary supplement; food additive; false and misleading). Chi-squared tests will compare proportions between CBD users and non-users. Next, analyzing all claims together, we will model the likelihood of interpreting a claim as a prohibited claim type as a function of CBD use status, sex, race/ethnicity, claim meaning score, and chronic health conditions using random-effects logistic regression modeling to account for the repeated measures within an individual. Odds ratios from the models will be used to identify differences between groups in their perceptions of claims. 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

Participants will be recruited and screened by AmeriSpeak™ according to age (18-65) and CBD use status (current CBD (users within the last 30 days), ever CBD users, and non-users). All panel members who are 18-65 years old will be screened for the survey, and those who are classified as a CBD user, ever user, or non-user will be invited to participate in the study. Eligible participants will continue to review the informed consent and complete the full survey.

Informed Consent
A waiver of signed consent/assent s requested. This is an online survey and individual participation involves providing voluntary responses to survey questionnaires. The research presents no more than minimal risk of harm to subjects. Consent language will be included in the survey and participants will be asked to check a box to indicate that they agree to participate.

Confidentiality and Privacy
Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. Data will be collected and housed on the secure NORC server and the Wake Forest University School of Medicine server. De-identified data will be provided to the Wake Forest team.
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. It will also be monitored closely by the Wake Forest School of Medicine IRB.

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 PI or designated member of the study team to the IRB and sponsor or appropriate government agency if appropriate.

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