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Comparing adult cannabis treatment-seekers enrolled in a clinical trial with national samples of cannabis users in the United States

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ABSTRACT

Background: Cannabis use rates are increasing among adults in the United States (US) while the perception of harm is declining. This may result in an increased prevalence of cannabis use disorder and the need for more clinical trials to evaluate efficacious treatment strategies. Clinical trials are the gold standard for evaluating treatment, yet study samples are rarely representative of the target population. This finding has not yet been established for cannabis treatment trials. This study compared demographic and cannabis use characteristics of a cannabis cessation clinical trial sample (run through National Drug Abuse Treatment Clinical Trials Network) with three nationally representative datasets from the US; 1) National Survey on Drug Use and Health, 2) National Epidemiologic Survey on Alcohol and Related Conditions-III, and 3) Treatment: Episodes Data Set – Admissions.

Methods: Comparisons were made between the clinical trial sample and appropriate cannabis using sub-samples from the national datasets, and propensity scores were calculated to determine the degree of similarity between samples.

Results: showed that the clinical trial sample was significantly different from all three national datasets, with the clinical trial sample having greater representation among older adults, African Americans, Hispanic/Latinos, adults with more education, non-tobacco users, and daily and almost daily cannabis users.

Conclusions: These results are consistent with previous studies of other substance use disorder populations and extend sample representation issues to a cannabis use disorder population. This illustrates the need to ensure representative samples within cannabis treatment clinical trials to improve the generalizability of promising findings.

1. Introduction

Cannabis is the most commonly used illicit substance in the United States (US) (Center for Behavioral Health Statistics and Quality, 2015). Cannabis use rates are increasing among adults (Grucza et al., 2016; Hasin et al., 2016), while the perception of harm associated with cannabis is declining (Berg et al., 2015; Johnston et al., 2015; Pacek et al., 2015; Sinclair et al., 2013). Legislation surrounding cannabis use and possession is rapidly changing in the US, and while the full impact of this change is still largely unknown, it may contribute to an increase in chronic use and cannabis-related harms (Hall and Lynskey, 2016). While the public perception of cannabis is changing, the literature on the adverse health and societal effects of cannabis is growing (Brady and Li, 2014; Compton et al., 2014; Hall, 2009; Hall and Degenhardt, 2009; Lynskey and Hall, 2000; Meier et al., 2012; Volkow et al., 2016). The development of cannabis use disorder (CUD) is a potential adverse effect that may occur among chronic users. Data comparing rates of cannabis use and CUD prevalence from 2001-2002 to 2012-2013 showed a more than doubling of cannabis use rates and prevalence of CUD among adults, with three out of 10 users developing a CUD (Hasin

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et al., 2015). This study found that the risk of developing a CUD did not increase, but CUD rates increased due to the increased prevalence of use in the US.

Given the apparent increased prevalence of cannabis use among adults, healthcare settings and substance use disorder (SUD) treatment centers may encounter more adults seeking treatment for CUD or obtaining court-mandated treatment. While research focused on the treatment of CUD is needed, the generalizability of results from clinical trials does not always translate well to real-world practice settings (Humphreys, 2016; Rothwell, 2005). Clinical trials often employ stringent exclusion criteria and tend to recruit small and unrepresentative sub-samples of the target population. A recent analysis explored the representativeness of study samples within the National Drug Abuse Treatment Clinical Trials Network (CTN) compared to national US datasets (Susukida et al., 2016). The 10 CTN studies used in this analysis varied with respect to the intervention being tested and particular substance of abuse being targeted by the intervention, though none were focused specifically on cannabis use. This study found notable differences in the demographics of those participating in research studies versus those entering SUD treatment, specifically in the areas of education and employment. It is unknown, however, if similar differences exist among those with CUD when compared to nationally representative samples. One study found that the majority of adults meeting criteria for cannabis dependence through a household survey would have been excluded from a clinical trial using common exclusion criteria (Okuda et al., 2010). Therefore, the representativeness of CUD clinical trial samples is a timely issue given that novel therapeutics and treatment strategies are needed for CUD and more treatment trials are likely in the near future. It is important to identify differences, should they exist, among those who volunteer for randomized clinical trials compared to other cannabis users in order to improve sample representativeness and the generalizability of promising clinical trial results.

In order to address the question of sample representativeness in CUD clinical trials, this study aimed to compare the demographics and cannabis use characteristics of adult participants with CUD enrolled in a multi-site treatment trial for cannabis cessation with a comparable population from national datasets. This clinical trial was conducted within the CTN and recruited a geographically diverse sample through six study sites in the US. The study sample was compared with two unique national samples of adults; 1) meeting criteria for CUD (or cannabis dependence) through household surveys, and 2) entering publically funded SUD treatment programs for CUD.

2. Methods

2.1. Participants and study procedures

This multi-site clinical trial evaluated a pharmacotherapy added to a behavioral intervention for cannabis cessation among US adults (Achieving Cannabis Cessation: Evaluating *N*-Acetylcysteine Treatment [ACCENT]). Methodological details for this study can be found elsewhere (McClure et al., 2014). Briefly, participants were adult men and women (N = 302) between the ages of 18–50 years who met criteria for cannabis dependence (based on Diagnostic and Statistical Manual of Mental Disorders (DSM IV (First et al., 2002)), were interested in quitting, and had a positive urine cannabinoid test during the screening assessment. Exclusion criteria were focused on safety concerns and aimed to appropriately characterize the sample. The following exclusion criteria were employed: known allergy to *N*-Acetylcysteine (NAC), pregnant or lactating, use of NAC-containing supplements or hazardous concurrent medications, current enrollment in treatment for cannabis dependence, use of synthetic cannabinoids, current substance dependence other than nicotine or caffeine and/or positive urine drug screen (other than cannabis), on opioid-replacement therapy, recent history of asthma, uncontrolled medical or psychiatric illness that could put the participant at risk, and risk of homicide or suicide.

Eligible participants were randomized to receive NAC or matched placebo for 12 weeks. Contingency management procedures were used for both experimental groups to reinforce abstinence from cannabis during twice weekly study visits, in addition to a separate compensation schedule targeting attendance at study visits. Six study sites across the US participated in the ACCENT trial (Behavioral Health Services of Pickens County [Pickens, SC], The APT Foundation [New Haven, CT], University of Kentucky Medical Center [Lexington, KY], University of California, Los Angeles Integrated Substance Abuse Programs [Los Angeles, CA], The University of Texas Health Science Center at San Antonio [San Antonio, TX], and CODA, Inc. [Portland, OR]). This trial was registered with Clinicaltrials.gov (NCT01675661), and completed study procedures in August 2015. The institutional review boards at participating centers approved the study protocol, which was overseen by an independent National Institute on Drug Abuse-appointed Data and Safety Monitoring Board. Cannabis abstinence outcomes from this trial are described elsewhere (Gray et al., Under Review).

2.2. Measures

2.2.1. Sources of data

Data from the ACCENT study were compared to three nationally representative datasets. Due to some constraints introduced by the national datasets, six ACCENT participants were excluded from this analysis. Four participants were 50 years of age (national datasets include 50 as the lower limit of a larger range). Two participants had less than an eighth grade education, leading to an insufficient comparator group. This resulted in a final sample of 296 participants being included from the ACCENT study in the current analysis.

Three national datasets were compared with the ACCENT study sample: the National Survey on Drug Use and Health (NSDUH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA) 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III), and the Treatment Episodes Data Set – Admissions (TEDS-A). The NSDUH is a publicly available dataset that measures the prevalence of drug use in the US among a representative community dwelling population. NSDUH 2014 data were used for this analysis (United States Department of Health and Human Services Substance Abuse and Mental Health Services Administration, 2016). Weighting variables were used for this dataset as recommended for the NSDUH. The NESARC-III includes data from non-institutionalized, civilian adults (18 years or older) in the US. This survey employed multistage probability sampling to choose respondents. A limited dataset from the NESARC-III was used for the current analysis. Additional details regarding the NESARC-III are available elsewhere (Grant et al., 2014). Weighting variables were used for this dataset. The TEDS-A includes data on treatment admissions (including court-mandated admissions) to SUD programs that are publicly funded. We used the most recent TEDS-A data available at the time, which was from 2013 (Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, 2015). Since the ACCENT study only enrolled those who were cannabis dependent, had used cannabis in the past 30 days, and were between the ages of 18–50; appropriate sub-samples were selected from the national samples based on those variables (i.e., meeting criteria for cannabis dependence or CUD [based on DSM-IV or DSM-5 criteria] of any severity level and past 30 day use of cannabis [estimated based on past year use for the NESARC-III dataset] and within the age of inclusion). The sample sizes from each data source are shown in Table 1 for weighted and unweighted samples of the total records available and the cannabis use sub-samples.

2.2.2. Demographics

Basic demographic information was obtained for all datasets. Response options were collapsed for consistency across datasets, mostly