

1. BACKGROUND/SIGNIFICANCE

Increased Marijuana Use and Legalization. Marijuana is the most commonly used federally illicit drug in the US.¹ As of 2014, 22.2 million adults (8.4%) were past 30-day marijuana users, marking an increase from 2002 to 2013.² This increase has coincided with increased state-level decriminalization and legalization of both medical and recreational marijuana use. Currently, 25 states have medical marijuana and/or decriminalization laws.³ Since 2012, 4 states (Colorado, Washington, Oregon, Alaska) and DC have legalized recreational marijuana use for adults (≥ 21 years old). In 2016, California, Maine, Massachusetts, and Nevada voted similarly. Moreover, a majority of US adults now favor legalization of marijuana,⁴ suggesting that marijuana deregulation will increase, even as marijuana's health effects continue to be widely debated.⁵⁻¹¹ In Colorado and Washington, recreational marijuana retailers serve as medical marijuana dispensaries, requiring a separate license to do so. States subsequently legalizing recreational marijuana are likely to follow this practice, and thus, recreational marijuana retail is likely to influence medical marijuana use.

Growth and Diversification in the Marijuana Product Landscape. As policy changes have allowed marijuana retail, the marijuana industry has become one of the fastest growing industries in the US, with the legal marijuana market projected to be over \$7 billion in 2016 and \$22 billion by 2020.¹² This demonstrates astonishingly high growth rates for any industry. Within this new and rapidly growing retail environment, a mass of proliferating marijuana retailers and dispensaries have offered increasingly diverse marijuana products. Although marijuana is thought to be primarily smoked,¹³ marijuana can be consumed in various ways, including smoking or inhaling it in joints, bowls, pipes, bongs, water pipes, hookahs, and blunts; eating or drinking it in foods or beverages/concentrates; vaporizing it; using topicals (e.g., lotions, lip balms); etc. These modes are used to consume different marijuana products, including cannabis herb, resin, and oil, among others.¹⁴ The differing types of products contain variable levels of cannabinoid vs. tetrahydrocannabinol (THC) and yield differing "highs" depending on if it is an indica (e.g., physically sedating), sativa (e.g., mentally energizing), or a hybrid of the two in different proportions.¹⁴ The variety of potential products suggests a rich opportunity for product development and tremendous market expansion. Indeed, a growing percent of marijuana sales are from newer marijuana products, such as edibles.^{15,16} The increasing product variety and greater sophistication in distinguishing the types of 'highs' achieved has implications for both medical and recreational marijuana use.

Indications and Regulations of Medical Marijuana. Marijuana may be helpful in managing a wide range of medical conditions and complications, including AIDS wasting, spasticity from multiple sclerosis, depression, post-traumatic stress disorder, anxiety, chronic pain, and nausea associated with chemotherapy, among others.¹⁷⁻¹⁹ The specific covered conditions and processes for obtaining, possessing, and using medical marijuana vary from state to state. Regardless, some aspects of medical marijuana laws are relatively consistent, such that: a) the individual must have one or more qualifying conditions; b) a physician must document that the patient has a qualifying condition and submit a form to the state; c) the state then provides a verification card to the patient; d) the patient can then either grow a small amount of marijuana or obtain medical marijuana from a "caregiver"; and e) the cards must be renewed on a regular basis to remain valid. However, the oversight of how medical marijuana is overseen and regulated remains relatively unexamined.

Negative Consequences of Marijuana Use. Though medical marijuana use may have medical utility for some conditions,¹⁷⁻¹⁹ marijuana use has been linked to a number of adverse health and psychosocial outcomes, thus raising concerns regarding recreational use.²⁰ In terms of specific health complications, marijuana use is associated with negative effects on almost every organ system in the body. Marijuana use is related to cardiovascular effects (e.g., heart rate, blood pressure changes),²¹ respiratory/pulmonary complications (e.g., chronic cough, emphysema), impaired immune function leading to vulnerability to and increased infections, increased risk of developing head, neck, and/or lung cancer,²² and fetal and developmental consequences.²⁰ Regarding psychosocial and behavioral outcomes, marijuana use is associated with risk for cannabis dependence, other psychiatric conditions (e.g. psychosis), neurocognitive problems, interpersonal violence,²³⁻²⁹ traffic accidents, poorer school and work performance, and lower life-time achievement.¹³ As marijuana is known as the "gateway drug",³⁰ there is concern that marijuana use could also lead to greater utilization of other licit and illicit substances.^{31,32} Thus, marijuana use poses serious risks.

Distinguishing Medical Versus Recreational Marijuana Use. Given the medical benefits of marijuana as well as the negative health and psychosocial risks of use, it is important to understand how medical versus recreational marijuana use is distinct. For example, how do medical versus recreational marijuana users differ in terms of use patterns, levels of use, symptoms of addiction, modes of use (e.g., smoked, ingesting), and channels of access. Differences in risk perceptions and motives for marijuana use should also be examined in relation to medical versus recreational use. Understanding these differences may help identify those medical marijuana users who may be at risk for abuse or dependence. Prior research suggests that drug experiences

are learned through an individual's experience in taking the drug (e.g., form of the drug, level of use) and the differing contexts for taking the drug (e.g., in a hospital, at a party).^{33,34} One previous study of individuals using marijuana for medical purposes (multiple sclerosis, Tourette's syndrome, attention deficit disorder, rheumatism) in Norway³⁵ found that those previously using marijuana for recreational purposes needed to change the way they interpreted marijuana's effects in the context of medical use. They indicated that, whereas the main effect sought had previously been pleasure, now the experience of using marijuana had to be relearned as, for example, the 'reduction of pain' or 'reduced spasms'. Such conflicts are not exclusive to marijuana. Prescription drugs such as benzodiazepines or opiates may also result in intoxication and pleasure. However, these effects are usually described as side effects and are accompanied by warnings about drowsiness and an inability to complete complex tasks under their influence. In a similar vein, it has been argued that the high resulting from marijuana use ideally should be considered a side effect or a bad effect.²⁷ Some argue that this effect should be eliminated before medical marijuana can be used.²⁷ Several medical activists share this view; others argue that medical (versus recreational) use should involve taking lower doses of marijuana.^{36,37} The fact is that the notions of 'main effects' and 'side effects' of drugs are not pharmacologically distinct categories.^{33,34} Taken together, identifying some distinctions between medical versus recreational marijuana use or users is important for clinicians in assessing patients who might misuse medical marijuana and to oversee their marijuana use to prevent potential drug addiction.

Young Adults as Vulnerable Marijuana Consumers. Young adults (aged 18-25 years) represent the highest risk group for marijuana use.² As of 2014, 6.8 million or 19.6% of this age group reported current marijuana use; an additional 13.5 million adults aged 26 years and older (6.6%) are current users.² Moreover, our prior research indicates that they represent the largest segment of recreational marijuana retailer consumers.³⁸ In addition, we documented that, in young adults, marijuana is perceived more positively than all tobacco products, having among the lowest perceived risks in relation to harm to health and addictiveness and being perceived as the most socially acceptable.³⁹ Our prior research documented that, among 649 current marijuana users aged 18-34 recruited via Facebook in 2014, the average number of days used in the past 30 was 17.86 (SD=11.29), and 15.5% reported at least one symptom of addiction.⁴⁰ Common ways of accessing marijuana was from friends (29.8%) or buying it from someone in their communities (27.6%) or a dealer (25.8%); 10.8% had a medicinal marijuana card and obtained it from a dispensary. Participants reported most frequently using marijuana in a bowl (77.0%), joint (52.4%), or waterpipe (44.5%). Since this study, patterns and modes of use, as well as access channels, likely have shifted due to changing policies, social norms, and product availability. In addition to the varieties of marijuana products emerging, co-use of marijuana with tobacco and alcohol is a concern, particularly in young adults. Young adults have the highest rates of substance use,⁴¹⁻⁴⁴ as well as high rates of polysubstance use,^{45,46} relative to any other age group. Our team has been highly involved in researching polysubstance use patterns,^{40,47-49} documenting that it not only occurs but that there are distinct clusters of use, such that marijuana use is highly associated with use of hookah and little cigars and cigarillos.⁵⁰⁻⁵² As such, young adults require a specific focus in terms of marijuana use.

2. SPECIFIC AIMS. Drawing from the Socioecological Model⁵³ and Social Cognitive Theory^{54,55} to inform our conceptual framework, we will examine specific intrapersonal (e.g., use motives/expectancies, other substance use), interpersonal (e.g., social influences), and community-level factors (e.g., availability of dispensaries) to distinguish medical versus recreational marijuana use in young adults. This information will guide clinical practice regarding the oversight of medical marijuana use. Drawing from these perspectives, we aim to:

Aim 1. Examine differences between medical only, recreational only, and both medical and recreational marijuana users in relation to their levels of use, modes of use (e.g., smoking, ingesting), motives for use, other substance use, social influences, and sources of marijuana. We will conduct an online survey of marijuana users recruited via social media to examine differences among marijuana users reporting use for medical purposes only, recreational only, and both medical and recreational purposes.

Aim 2. Qualitatively examine how individuals using marijuana for medical purposes describe, interpret, and rationalize the intoxicating and pleasurable effects of marijuana and distinguish medical versus recreational use. We will recruit survey participants reporting only medical use or both medical and recreational use to participate in phone-based, semi-structured interviews examining these phenomena.

3. INNOVATION. Despite the rapidly increasing trend toward medical marijuana use and legalization, there has been remarkably little research on how medical marijuana users are distinct from recreational marijuana users, particularly those in young adulthood. This is a critical gap in the research that must be addressed. We propose to employ novel recruitment strategies to engage the appropriate population across the US. We also

will use a sequential mixed methods research design,⁵⁶ specifically an explanatory design, with quantitative research preceding qualitative research.⁵⁶ The rationale of using this mixed methods approach is to obtain quantitative data regarding medical versus medical marijuana use that can inform an in-depth assessment of these behaviors and related attitudes, which is appropriate given the dearth of research in this critical area.

4. RELEVANCE. This proposal has significant implications for the healthcare system and for policy. The importance of this research is informed by the literature regarding other drugs used for medical purposes with similar potential for long-term use, abuse, and addiction. For example, while the use of opioid analgesics for the treatment of acute pain is highly effective and appears to be generally benign, long-term use of opioids is associated with increased risk of abuse and addiction. Unfortunately, there has been a marked increase in the abuse of prescription opioids in the US,⁵⁷ creating challenges for healthcare providers who prescribe opioids. Drawing from these prior significant public health problems, research is needed to better inform clinicians, specifically on how to prevent or minimize abuse or addiction related to medical marijuana use.

5. APPROACH. Below we describe our team, the study design, and the methods mapping onto each Aim.

Project Leadership. Our research team is comprised of professionals in public health, medicine, psychology, and law. **Carla J. Berg, PhD, (mentor)** is an Associate Professor in the Dept. of Behavioral Sciences and Health Education in Emory's Rollins School of Public Health and Associate Director for Population Sciences in Emory's Winship Cancer Institute. Her expertise includes examining consumer behavior in the context of tobacco policy and marketing;^{58,59} tobacco control policy implementation;⁶⁰⁻⁶³ young adult alternative tobacco use;^{51,64} marijuana use and co-use with tobacco;^{47,51,65-71} social marketing and health communications;⁷²⁻⁷⁶ and market research to identify high-risk populations for tobacco and marijuana use.^{72-74,76} Methodologically, she has expertise in conducting large web-based surveys,^{64,77} longitudinal studies,^{51,64} and qualitative research.^{65,78,79} She recently lead the development and testing of a marijuana retail assessment tool that will be leveraged in the current study.⁶⁸ She will oversee all aspects of the proposed study. **Jingjing Li, MBBS, MPH, (co-PI)** is a doctoral student in the Dept. of Behavioral Sciences and Health Education in Emory's Rollins School of Public Health. With her previous clinical medicine training, she is able to integrate her professional medical knowledge and expertise to resolve public health issues in vulnerable populations. She is particularly strong in survey research⁸⁰⁻⁸³ and has received extensive conceptual and technical training on substance use from her advisor Prof. Carla Berg. Her role in the proposed study is to design, disseminate and collect online questionnaire; as well as to generate in-depth analyses of the raw data and write manuscripts for Aim 1. She will also participate in qualitative data collection and analyses for Aim 2, and is responsible for all relevant research administration and coordination. **Milkie Vu, MA, (co-PI)**, is a doctoral student in the Department of Behavioral Sciences and Health Education in Emory's Rollins School of Public Health. Her research focuses on determinants of preventive care-seeking, cancer screening behaviors, and substance use in diverse populations. Her relevant methodological expertise includes quantitative and qualitative data collection and analyses and data management of large-scale surveys. She will lead interview guide development, conduct of interviews, and qualitative data analyses for Aim 2. She will also participate in survey development and quantitative analyses for Aim 1 and contribute to all other aspects of the proposed study. **Roberto España, BS, (co-I)** is a doctoral student in the clinical psychology program at Emory University. His research and clinical interests focus on neurodevelopmental factors behind psychosis, especially as they pertain to the effects of exogenous substances like marijuana. He will contribute to developing the survey and interview guides. **Tariq Farah, BA, BS, (co-I)** is a student at Emory's School of Law who is interested in the neurological and behavioral aspects of marijuana and the moral and societal lenses through which marijuana-related policies are developed and implemented. He will contribute to interpreting results.

Preliminary Work. The increasing use of the Internet among the entire US population provides a great opportunity for reaching vulnerable populations to inform research and policy. Roughly 80% of US residents have access either to broadband internet in their home or to the internet via smartphones, with slightly lower access rates in Blacks or those with lower education or income or living in rural areas.⁸⁴ Second, 86% of internet-using adults have a Facebook account, with virtually no racial/ethnic differences but lower rates in those with lower education or income or living in rural areas.⁸⁵ Third, prior research documented that survey data derived from participants recruited through traditional venue-based recruitment versus social media documented limited differences in sociodemographics or health behaviors.⁸⁶

The proposed team has considerable experience recruiting participants into online research studies. Dr. Berg's K07 research included a cross-sectional survey of 1,567 young adults conducted over a 3-week period in Aug 2014 using recruitment via Facebook,^{67,87} modeled after prior research.^{86,88} With minimal targeting of

marijuana users, we were able to obtain survey responses from 649 participants (41.4% of the sample). This will inform our proposed recruitment methods. Dr. Berg has also conducted extensive research regarding market segments (i.e., segments similar in values, attitudes, lifestyle) of young adults and has conducted message testing to determine the appeal of different messaging among the segments.^{72,73,76,89} Collectively, the proposed methods are built on Dr. Berg's prior research and the experiences of the team of students.

Phase 1. Survey Examining Differences in Medical vs. Recreational vs. Medical/Recreational Users Procedures. Three hundred current young adult marijuana users will be recruited via social media using methods based on Dr. Berg's prior work^{67,87} to participate in an online survey. This recruitment approach is justified based on 1) the extensive research regarding Facebook as a successful recruitment strategy; and 2) limited alternative viable options. Regarding our first point, outside of our own success using Facebook to recruit,^{67,87} a recent systematic review indicated the success of using Facebook recruitment.⁹⁰ This review found that researchers were able to target their ads to their intended audiences and that the cost per click was between \$0.39 and \$0.67 per click. In addition, other research has documented that, despite variety in individual ad success and potential concerns about sample representativeness, Facebook is a useful, cost-effective recruitment source for young adults.^{86,88} In terms of the latter, using panels such as GfK, SurveyMonkey, Qualtrics, etc. is not viable because they lack sufficient sample size of young adults using marijuana in various states with differing marijuana policy environments.

Ads and strategies will be employed to recruit marijuana users. The ads will be posted on Facebook (mobile/desktop news feeds, right column ads). Ads will target marijuana users by using imagery and text appealing to marijuana users and targeting individuals following political/social groups regarding marijuana or marijuana retailers. Ad content and placement will be informed by Dr. Berg's prior work identifying young adult market segments^{72,73,76,89} and targeted message testing.⁷² Once potential participants click the ads, they will be directed to a page with a study description (i.e., health-related study) and consent form. Consenting individuals will be screened for eligibility; those eligible will be sent to the online survey, administered via SurveyGizmo. To limit duplicate responses, one response per IP address will be permitted. The survey will take ~20 minutes.

Participants. Inclusion criteria will include: 1) speaks English; 2) residing in a state with medical marijuana legalized; 3) reporting marijuana use on at least 1 day of the prior 30 days; and 4) aged 18-29 years, as this age range is at the highest risk for use of marijuana.^{2,91} We will use stratified sampling to obtain roughly equal sample sizes of men and women and representative proportions of racial/ethnic minorities. Given our pilot data,^{67,87} we estimate a conservative period of 3 months to establish our survey sample of n=300.

Measures. Our survey instrument will assess the following:

- **Self-reported Reason(s) for Use:** Participants will report if they use marijuana: for medical purposes only; for recreational purposes only; or for medical and recreational purposes.
- **Intrapersonal Factors:** To assess **level of marijuana use**, we will ask participants to report the number of days of marijuana use in the past 30 days, the number of times used per day, and age at initiation per standard measures.^{92,93} To assess **modes of use**, we will ask about lifetime use of marijuana in various forms (e.g., joint; bowl; water pipe; vaporized), what form they most commonly use, and the number of days they used each form in the past 30 days, as well as number of times per day used.⁴⁰ To assess **motives for use**, we will administer the Drinking Motives Measure,⁹⁴ a 25-item questionnaire assessing five motives which has previously been adapted to assess marijuana use motives.⁹⁴ The five motives include: social (e.g., "to be sociable"), enhancement (e.g., "to get high"), coping (e.g., "to forget my worries"), conformity (e.g., "so that others won't kid me about not using"), and expansion (e.g., "to be more open to experiences"). Participants indicate how often they have used marijuana for each reason (1=almost never/never to 5=almost always/always).⁹⁴ To assess **other substance use**, we will ask participants to report lifetime and current (past 30-day) use of tobacco (i.e., cigarettes, little cigars/cigarillos, e-cigarettes, hookah, smokeless),⁹⁵ alcohol,^{92,93} and a range of other drugs (e.g., cocaine, heroin), deriving the list from the National Survey on Drug Use and Health.² We will also assess use per day and age of initiation of each substance used.^{2,92,93} These variables will be operationalized both continuously and dichotomously.
- **Interpersonal Factors: Social influences** will be assessed by asking participants to report marijuana, tobacco, alcohol, and other substance use among parents, friends, and other household members.³⁹
- **Community and Policy Context:** We will ask participants to report their state of residence to obtain **state-level marijuana policy** information (i.e., medical legalized, recreational legalized). We will also assess how they **access** marijuana (e.g., from friends, dealer, retailer, etc.). Assuming type of community might impact access, we will also assess **type of community** (i.e., rural, urban, suburban).
- **Covariates:** We will assess sociodemographics (e.g., age, sex, race/ethnicity, education, employment).

Data Analysis. First, descriptive analyses will be conducted to examine distributional characteristics of the data.⁹⁶ We will also investigate missing data and employ appropriate methods such as multiple imputations. Next, bivariate analyses will examine associations between independent and dependent variables. Finally, we will conduct a multinomial logistic regression examining correlates of being a medical only, recreational only, or both medical and recreational user, using medical only users as the referent group to determine specifically how this group differs from the other two groups. Data analyses will be conducted in SAS 9.4.

Sample Size Justification. Given our sample size (n=300), we have adequate power to detect small differences across the three marijuana user categories.⁹⁷

Phase 2: Semi-structured Interviews Among Medical Marijuana Users

Procedures and Participant Selection. To address Aim 2, we will conduct semi-structured interviews among participants from the Phase 1 survey who report current use of marijuana for either medical purposes only or for both medical and recreational purposes. Semi-structured interviews are an important way to obtain comprehensive, in-depth qualitative data, which is particularly important when concepts are new or novel. We will conduct interviews with 20 users (i.e., 10 medical only; 10 medical and recreational). We will identify 8-10 participants per gender per group to ensure successful recruitment of each gender in each user category. Selected participants will be emailed an invitation to participate in the interviews, which will outline the process, purpose, and incentive to participate (\$50 gift card). If we are unsuccessful at reaching those selected, we will revisit our survey data to identify additional participants meeting our criteria. Research staff will schedule the phone-based interview at times convenient to participants. Participants will be sent email reminders the day before and day of the interview. Each interview will be conducted via phone to minimize participant burden, ~60 minutes long, audio-taped, and guided by standard principles of qualitative methods.⁹⁸ Two interviewers currently serving as graduate research assistants in Dr. Berg's lab are trained to conduct the interviews.

Measures. The interview guide will focus on how participants 1) distinguish medical versus recreational use; and 2) describe and interpret marijuana's intoxicating or pleasurable effects in the context of medical use.

Data Analysis. The interviews will be transcribed by a professional transcription service. Qualitative data will be analyzed using standard principles of qualitative methods⁹⁸ and NVivo (QSR International, Cambridge, MA), a qualitative data analysis tool. The highest level of validity and reliability will be attained attending to concepts outlined by Maxwell.⁹⁹ Three coders (the students on the team) will independently review transcripts, generate preliminary codes, meet to refine primary and secondary code definitions, then independently code transcripts, applying the agreed upon codes. Independently coded transcripts will be compared for discrepancies; a consensus will be reached. Transcripts will be recoded using the final consensus outline. We will compare and contrast medical versus both medical and recreational marijuana users.

6. TIMELINE. In the first quarter, we will develop/pilot measures; develop/pilot facebook ads; and launch Facebook recruitment. The second quarter will focus on administering the survey. In the third quarter, we will identify and recruit interview participants; begin transcription; and begin survey data analysis. In the fourth quarter, we will contract for interview transcription and complete survey and interview data analyses.

7. CONSIDERATIONS. Study Design: The sample of young adult marijuana users recruited via social media may not be representative of young adult marijuana users, and we have outlined above our rationale for using this approach. **Rigor and Transparency:** First, the resulting data provides opportunities for a large number of analyses, potentially allowing for spurious findings. To mitigate this risk, we have clearly articulated a priori hypotheses. In reports based on the proposed analyses, we will identify significant *and* non-significant effects. Any post-hoc analyses or paths added to models will be identified as such. Regarding replicability, we will use widely used standardized survey measures, aimed at ensuring comparisons across studies in different contexts and at different times. We will make available to other researchers limited data sets from the larger project to facilitate verification of our findings and examination of effects of alternative analytic approaches. **Implications, Relevance, and Impact:** This proposal addresses a timely and critical public health issue coinciding with increasing marijuana use, legalization, retail environments, and product offerings. This shift in the regulatory landscape presents a critical period for examining how these factors impact the population at highest risk for marijuana use – young adults. This information will help to inform clinical practice by identifying factors associated with use for medical versus recreational purposes in young adults, which will be critical in identifying patients who may require additional assessment and oversight of their marijuana use. We will disseminate findings to these state health departments and more broadly, as well as to other stakeholders, to provide an evidence base for subsequent regulatory and legislative action related to medical marijuana.

8. REFERENCES

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