Study Protocol
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Study Title: Project Verdi

Full Study Title: Social Media Intervention for Cannabis Use in Emerging Adults

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Background

Cannabis use is prevalent among emerging adults (EAs)[1], with national trends toward increasing use[2] and shifting cannabis-related attitudes.[3] The National Survey on Drug Use and Health (NSDUH) data show the annual, monthly, and daily prevalence of cannabis use increased in 18-25 year-olds from 2002 to 2014.[4] Similarly, Monitoring the Future (MTF) data show daily cannabis use increased from 2007 to 2014 (from 3.5% to 5.9%) in college students and non-college EAs (5.0% to 6.9%).[5] These increases are reflected in decreasing risk perceptions.[4,6] Among EAs from 2002-2014, perceived risk of monthly and weekly cannabis used declined by 43% and 48%, respectively, with 75% of EAs stating cannabis is easy to obtain and decreases in perceived peer disapproval since 2008.[5] In 2015, 23% of 18 year-olds reported having friends who use cannabis.[7] These trends are consistent with cannabis risk factors among EAs: perceived availability, peer use, and being offered cannabis.[8-14] Furthermore, shifting perceptions and increased prevalence are occurring in the context of changing cannabis policies.[15] Legalization of cannabis for recreational use by adults (ages 21+) in 8 states (WA, NE, ME, MA, CA, OR, AK, CO) and the District of Columbia (D.C.) may impact the availability and use of cannabis by EAs who can purchase it legally, as well as potentially allowing diversion to those under age 21.

The changing legal context and ongoing illegal use of cannabis highlight the urgent need for preventing cannabis-related problems in EAs. Early use promotes greater risk for developing substance use disorders and other problems in adulthood, including potentially increasing mortality risk.[16] For example, early use may affect neuro-maturational changes to the developing brain, resulting in adverse emotional and cognitive changes.[17-19] Decision-making and inhibitory control are critical functions developing in adolescence and emerging adulthood, which can be compromised by cannabis use.[19-21] Although cannabis use is related to long-term health problems (e.g., lung cancer, respiratory issues)[22-24], the short-term effects of cannabis are also alarming.[25-28] After acute use (<6 hours), cannabis can alter executive functions, such as: attention, decision-making, inhibition/impulsivity, risk-taking, working memory, and concentration.[18,29] Daily data suggest that cannabis is associated with increased impulsivity and hostility.[30] Findings on executive functioning suggest increased propensity for risk behaviors, such as risky sex[31,32] or impaired driving[33,34]; 10% of EAs reported past-year drugged driving[1]. Evidence supports adverse relationships between cannabis and psychiatric problems[35], including emerging psychotic disorders.[36,37]

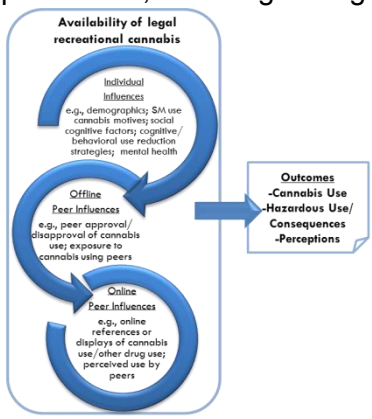

Figure 1. Guiding Conceptual Model

There is an urgent need to reduce cannabis use among EAs, who have the highest prevalence. Given the role of peer influences in EAs' drug use[38], modifying perceived peer norms of cannabis use is a viable strategy. Thus, consistent with NIDA's Strategic Plan for 2016-2020, which calls for researchers to "explore the potential for technology-based methods for delivering prevention interventions, such as…social media," we seek to develop and test a social media (SM) intervention to address legal and illegal recreational cannabis use by EAs, delivered by peer coaches. SM provides the opportunity to intervene in EAs' real-life contexts and to harness peer influences via peer-led interactions within a group-based intervention. The guiding framework for this intervention can be found in Figure 1.

Objective

The specific aim of this clinical trial is to:

Aim #2: Test the preliminary efficacy of a cannabis intervention delivered by trained e-coaches (versus attention-placebo control; up to N=90 per group with a target enrollment of 72 per group) on primary outcomes of cannabis use (quantity, frequency) and hazardous use (i.e., consequences) and secondary outcomes of perceived risk of cannabis, peer approval/disapproval of cannabis use, cannabis impaired driving, other drug use, and alcohol use (quantity, frequency)

Social Media Intervention Pilot RCT

Enrollment: We will conduct a two-arm pilot RCT of the intervention compared to an attention-placebo control condition *(n = up to 90 per group, target enrollment of 72 per group) for EAs who use cannabis at least 3x/week.* Eligible participants will complete a baseline survey, a post-test at 3-months, and a 6-month follow-up.

Participants and Recruitment Procedure. Study participants will be recruited via sponsored advertisements appearing on social media websites (e.g., Facebook and Instagram). Advertisements will be targeted towards 18-25 year olds in specific regions (e.g., states with legal recreational cannabis vs. not legal). When users click on the advertisement, they will be redirected to an online screening consent (with waiver of documentation). Interested participants will be asked to provide consent in Qualtrics and answer a captcha question (for identity verification). Participants will have the option to print or save a copy of the informed consent before moving on to the online survey.

Following determination of eligibility by completing a 5-minute survey, negative screens will receive a thank you page ending their participation in the study. This page will also include a pdf of a resource list with contact information for national organizations that can provide assistance in the areas of substance use and physical/mental health and well-being. No identifying information will be collected from participants who are not eligible for the study, although the IP address of the device used to complete the survey will be automatically recorded by Qualtrics.

Eligible participants will be notified of their eligibility and asked to provide contact information for verification purposes and to contact them with instructions for baseline procedures completion. After completing the contact information form, participants will see a "Thank You" message that includes a link to the resource list.

Those eligible will be invited to review an RCT consent form, directed to an online baseline survey and priority-mailed a urine drug screen (UDS; uploading a photo of results, as in prior work[137]). Due to the COVID-19 pandemic including the disruptions in work/research and participant concerns' about receiving mailed packages, starting May 2020, baseline procedures will no longer include a UDS (as approved by the study's NIDA Program Officer). Participants will upload a selfie with a timestamp to verify their identity; baseline compensation will be a $35 gift card for completing all procedures. Verified participants (e.g., captcha, verified survey completion time, IP address) will be randomized and join their assigned secret Facebook group (intervention/ control; separated by age [18-20, 21-25] and residence in states with/without legal recreational cannabis).

Inclusion/Exclusion Criteria. Participants will be eligible for the screening survey if they are able to view and click on a social media ad, participants who cannot read English will be informally excluded. Participants will be eligible to participate in the study if they are 18-25 years old, self-report using cannabis at least 3x per week or more often in the past month, and have an active Facebook profile. Participants will be excluded if they fail identity verification based on: 1) IP addresses, 2) survey time completion, 3) repeat attempts, 4) survey responses, and 5) photo identification via a timestamped selfie sent to the RAs. Participants from an earlier intervention content development study used to determine content for this intervention will be excluded.

Randomization and Consideration of Key Biological Variables. Randomization to conditions will be balanced across groups based on sex and cannabis use (<daily vs. daily [~43% estimate]), using urn randomization. Groups will be conducted separately by age (18-20 vs. 21-25) and state residence (legal recreational cannabis vs. not) with 8 groups total (4 intervention; 4 control; *N*~20 per group).

Intervention condition. Content will be posted daily in secret Facebook groups where participants are randomly assigned at enrollment (N~20 per group for this feasibility pilot). Secret group members are kept private; groups cannot be identified in a web or Facebook search and can only be joined via a personal Facebook invitation from study staff. Groups will be closed; with enrollment in the group within approximately 1 month of baseline assessment. Peer e-coaches will post intervention content 6 times per day, 7 days per week, for 8 weeks, mostly during late afternoon and into evening/night to capture time after school or work. E-coaches will also private message participants via other SM accounts (e.g., Twitter, Snapchat, Instagram) to notify them of trending posts and prompt them to visit the group. E-coaches will encourage discussion of content by utilizing open-ended questions and reflections, consistent with Motivational Interviewing (MI). They will reply to comments with MI strategies (e.g., reflection, affirmation), including managing sustain talk (e.g., come alongside, agree with a twist), tagging other participants' or the original commenter to encourage discussion and engagement. Based on our ongoing Alcohol social media intervention on Facebook, we have developed an e-coach manual outlining basic MI principles, protocols for posting, risk assessment (e.g., how to

respond if a participant posts about self-harm/suicidality), and e-coach professionalism (e.g., how to respond if a participant contacts the e-coach on their personal SM profile). The group process, although conducted online by peer e-coaches, is analogous to group therapy in a treatment setting where therapists introduce rules and guidelines for the group and share intervention content, eliciting feedback, and calling on group members to react or to share their own ideas. "Tagging" a participant on a post functions like calling on a group member. To harness the presence of peers, e-coaches will tag multiple participants to encourage interaction. Use of "likes" and reactions (e.g., "haha," "sad,") allow for members and coaches to provide support and affirmation. We have also revised the User Safety Agreement from our current alcohol-SMI RCT for use in this study which outlines guidelines for participation (e.g., privacy, no posting opportunities to buy or receive drugs; no racial or political slurs; respect and confidentiality). Participants must signify their agreement with the User Safety Agreement before receiving the group invitation. Groups will be monitored multiple times/day (including weekends, holidays) during the 8-week period by scheduled e-coaches and rotating on-call supervisors (all highly experienced in MI) who include the investigators, study coordinator, and our lab network of clinical post-docs and clinical social workers, who work as a team across studies in our Center. We will note in the group cover photo, that we cannot monitor groups 24/7, and include crisis numbers.

Attention-Control condition. Control participants will be assigned to secret Facebook groups where the e-coaches (RAs) will post daily content (e.g., news, videos) unrelated to intervention topics for 8 weeks, using the same schedule as the intervention. Participants must agree to the User Safety Agreement; groups will be monitored.

Follow-Up Procedures. Self-report data will be collected online via Qualtrics ($35 for 3-month post-test; $40 for 6-month follow-up). Participants will be reminded to complete post-test and follow-up measures via e-mail, private Facebook messaging, text message, and phone calls. Participants will be mailed UDSs and return time-stamped photos of their results through Qualtrics, to encourage accurate reporting of cannabis use. Due to the COVID-19 pandemic, including the disruptions in work/research and participant concerns' about receiving mailed packages, follow-up procedures will no longer include UDS starting May 2020 (as approved by the NIDA Program Officer).

Measures.

We will use reliable and valid measures from prior studies with adolescents and EAs.

Screening Survey. To assess study eligibility and characterize the study sample, participants will be asked about their demographics[41], social media involvement[39,42-44], and health behaviors, including cannabis use[45].

Baseline and Follow-Up Assessments. Participants will be asked to self-report measures including: demographics; SM involvement; cannabis use, motives, consequences, and protective strategies*; perceptions of peer approval, cannabis risk perceptions,* etc. Primary dependent measures are cannabis quantity and frequency assessed in the Timeline Follow-back (TLFB[170-172]), *hazardous use/consequences, risk perceptions and perceived peer approval.* In May 2020 as approved by the study's NIDA Program Official, all assessments will include questions pertaining to the impacts of the COVID-19 pandemic in order to provide important contextual information about substance use and psychosocial factors that may be related to study findings. If there is incomplete/inconsistent timeline follow back answers study staff will contact participants by phone to clarify data. We will ask participants to self-administer UDSs at baseline and follow-ups, sending a timestamped photo of results to the study staff, since in-person UDSs are not possible in a national study. As described the recruitment and follow-up procedures above, as a result of the COVID-19 pandemic, participants will no longer receive a mailed UDS. The 3- and 6-month surveys will mirror the baseline survey measures with the inclusion of acceptability measures at 3-months and engagement with other group members measures at 3 and 6-months.

We will use software we developed to analyze user engagement with content posted in groups, tallying reactions (e.g., reactions, likes) and comments on a post. Our software also uses automated linguistic coding for text posts to categorize content (e.g., cannabis-related); we have developed a list of drug terms, including slang, that will be used in this coding. This automated process will be supplemented by RAs who will hand-code non-text posts (e.g., videos) for topic and content.

Pilot Verbal TLFB Collection
For the final 6-month follow-up survey, starting Nov 2020, participants will be asked to indicate at the end of the survey if they are interested in participating in an additional follow-up interview. Of those who indicate they are willing to be re-contacted, we will randomly select and schedule a phone or video call with up to 20 participants. On the call a member of the study team will complete a pilot verbal Timeline Follow Back semi-structured interview (analogous to the Timeline Follow Back online survey measure they have completed at each study assessment) where participants will answer questions about their substance use in the past 30 days. Participants will be paid $30 (online gift card) for completing this procedure. This pilot procedure is not part of the formal clinical trial analysis.

Data analysis
To assess changes in the primary dependent measures *(perceptions of risk and peer approval, quantity/frequency of consumption, cannabis consequences)* while controlling for the fact that this is an individually randomized group-treatment trial (IRGT), we will use we will use generalized linear mixed models (GLMMs). We will account for correlations between individual within the same Facebook group using random intercepts. To assess treatment effects at 3M and 6M outcomes, we will fit separate models for each follow-up that control for baseline measurement, as well as age, sex, recreational cannabis status, and will quantify the treatment effect using the coefficient for the treatment/control indicator. Controlling for the baseline outcome is critical for guarding against regression to the mean in treatment effect estimation. We will convert the treatment effects to effect sizes (Cohen's D) by dividing the mean difference by the (square root of) the total variation unaccounted for by the fixed effects in the model (i.e., the residual variance + the random effect variance). Confidence intervals for the effect sizes will be derived using estimated marginal means (averaged across sex) and the confidence intervals are produced from the estimated variance of the estimate, and the estimated residual degrees of freedom from the random effects model. Overall, this approach is effectively the same as ANCOVA, but accounting for the IRGT design, and controlling for sex and the strata used in the randomization (age and recreational cannabis status). Our initial specification will be a linear mixed effects model (i.e. Gaussian error distribution) with only a random intercept to capture within-group dependence. As the need is ascertained through model diagnostics, we will examine other distributional choices (e.g., Poisson, Negative Binomial) and more complex random effects structures (e.g., autoregressive).

Human Use Considerations and Protections

Eligibility and study informed consent will be administered online (**a waiver of documentation of consent is requested**) as the first pages of the screening and baseline surveys, respectively. The consent document will include information on the general nature of the study, privacy rights, expectations for participation, the voluntary nature of participation, and that participation can be withdrawn at any time. Participants will also be assured that data will not be shared with anyone outside of the study team. Because of the sensitive nature of the information collected, as an added protection for subjects, this research is covered by a Certificate of Confidentiality from NIH. Study documents will make explicit the voluntary nature of the subjects' participation as well as potential situations for breaking confidentiality (see below for more information about limitations to confidentiality). Participants will be informed that their answers to the screening questions will be used to determine their eligibility for a research study. No identifying information will be collected from those who complete the screen and are ineligible or choose not to participate in the study, although the IP address of the device used to complete the screening survey will be automatically recorded in Qualtrics.

Since the age of majority varies across states (i.e., age 18 in most states, age 19 in Alabama and Nebraska, and age 21 in Mississippi), **a waiver of parental consent is also requested** for those participants who are in the study's target age group but are under the legal age of consent in their state of residence (i.e., AL, NE, MS). The same consent document described previously will be used for minors and adults. According to the Federal regulations governing research (45 CFR 46),163 Section 116(d) allows a waiver of the parental permission requirement for informed consent when (a) the research involves no more than minimal risk, (b) the waiver would not adversely affect the rights and welfare of the participants, (c) the research could not

practicably be carried out without a waiver, and (d) whenever appropriate, the participants will be provided with additional pertinent information after participation.

a) This study involves no more than minimal risk. Every effort will be made to ensure that study participants are protected from risk. For screening eligibility, we will not collect any identifiers from participants unless they screen eligible for and are interested in enrolling in the main study. Screening data will be anonymous for those participants who are not eligible or interested in the main study. Participants will be informed in the consent document about the procedures taken to maintain and protect their confidentiality, including assigning unique ID, securing data on secure, password protected UM servers and that this study is covered by a Certificate of Confidentiality.

b) The waiver of parental consent does not adversely affect the rights and welfare of the subjects (age 18-20 in certain states). Screening data will be anonymous for those participants who are not eligible for the main Aim 1 baseline study, as well as those who are eligible but choose not to enroll in the main study. To the extent possible given legal requirements on information required in the informed consent, the consent form is written in simple terms that should be understandable to individuals of varying ages and education levels. Participants will be able to download a copy of the consent form which contains contact information for research study staff should questions arise following enrollment. Participants who are eligible for the study and are interested in continuing will provide contact information and can indicate the method they prefer for being contacted.

c) The research could not practicably be carried out without a waiver: This research could not be practicably conducted without a waiver of parental consent because we would not be able to ensure confidentiality around the participant's substance use if parental consent were required for participants under the age of majority in their state (age 18-20 in certain states). Lack of a waiver of parental consent would hinder recruitment, particularly of young adults engaging in high-risk behaviors, and more importantly, have the potential to severely limit the generalizability of the findings. Research shows lower rates of young adult enrollment when parental consent is required, and that participants with lower risk (less substance use) are disproportionally enrolled (higher risk/ greater use less likely to participate).

d) Whenever appropriate, the participants will be provided with additional pertinent information. After completing the screening and baseline surveys, participants will receive a pdf of an electronic resource brochure with contact information for national and community resources, including suicide hotlines, mental health and substance use treatment, etc.

We also request a waiver of consent for re-consent of minors (in states where the age of majority is greater than 18) who reach the age of majority in their state while participating in the study (between screening completion and baseline invitation). As described above, this study involves no more than minimal risk to subjects. Given the brief length of time in which a participant is part of this study, it will not be feasible to obtain immediate consent for any minors (age 18-20 in certain states) who reach the age of majority during the study. Furthermore, we anticipate that all study assessments will be completed online.

Every effort will be made to ensure that study participants are protected from risks. Although it is not expected that there will be any risks to participants because of online screening and baseline assessment procedures, the risk of violation of confidentiality exists because human participants are giving personal information. Consent documents will contain a statement explaining mandatory reporting requirements for information regarding child abuse and intention to harm self or others. We do not expect that participants will disclose such information in the context of this study, since our assessments do not inquire about these behaviors. However, we will notify participants when/if we must make any mandatory reports based on information they disclose and we will only disclose the minimum information necessary. Participants will be informed in the consent about the procedures taken to maintain and protect their confidentiality.

To minimize the risk of violating confidentiality, RAs will make every effort to ensure that study data are always kept confidential. Staff training procedures will include information about the importance of confidentiality and techniques to maintain confidentiality of all information reported by research participants. Staff will maintain human subjects and confidentiality certifications through the U-M Program for Education and Evaluation in Responsible Research and Scholarship system.

Unique identification numbers will be assigned to participants. All computerized databases with survey data will identify participants by this number and will be saved on a secure, encrypted, password-protected server. For participant tracking, one electronic document will be maintained linking participants' ID numbers to their names. This document will be kept in a restricted-access folder on a password-protected computer within a secure research server. This document will be deleted as soon as the study is completed. All data will be collected specifically for use on this project.

For the online surveys, participants will be reminded that they may refuse to answer any questions that make them uncomfortable and that they may terminate the assessment at any time. As described above, all participants will also receive substance use and mental health resources after completing the screening and baseline surveys. Participants' confidentiality will be breached by the research study only to protect the safety and welfare of research participants and only in accordance with state and federal law.

Potential Benefits of the Proposed Research to Human Subjects and Others

Participation in this study may not directly benefit participants. However, in previous studies conducted by our team, participants have expressed that they enjoy being a part of research that will directly help other young adults around their age. The assessments themselves could also benefit participants by asking them to review their substance use. Furthermore, all participants will receive a resource list with referral information including the suicide hotline and text line, substance use, and mental health treatment.

Rationale for Including Special Vulnerable Populations. Although our participants are aged 18-25 and are not children per NIH definitions, this research will involve individuals considered children ages 18-20 in states where the age of majority is greater than 18. This age range is critical for this research because rates of cannabis use reach peak prevalence during this developmental period, and interventions targeting this age group can potentially prevent future escalation and consequences associated with use, which could have enormous public health impact. It is important to include this vulnerable population because their feedback can enhance the acceptability of our intervention to other young adults between the ages of 18-20. All ethnicities and races will be included in the proposed studies, to the extent that they agree to participate in screening and meet eligibility criteria.

Importance of the Knowledge to be Gained

Given that cannabis use behaviors often peak in emerging adulthood, as well as the correlation with other substance use, the individual and societal cost of these behaviors, and the fact that many emerging adults are not in settings where they may receive traditional preventive services, the development of effective targeted prevention programs are clearly needed. Given the current penetration of social media into the lives of young people, the potential reach for interventions using this medium, and the ability to harness peer influences to create behavior change within a social network, the knowledge to be gained from this research is significant. The risks to participants are reasonable in relation to the importance of this knowledge to be gained and potential public health impact of developing an effective program to reduce the use of and consequences associated with cannabis use among emerging adults.

References

1. Center for Behavioral Health Statistics and Quality. *2015 National Survey on Drug Use and Health: Detailed Tables.* Rockville, MD: Substance Abuse and Mental Health Services Administration;2016.
2. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of marijuana use disorders in the United States between 2001-2002 and 2012-2013. *JAMA psychiatry.* 2015;72(12):1235-1242.
3. Salas-Wright CP, Vaughn MG, Perron BE, Gonzalez JM, Goings TC. Changing perspectives on marijuana use during early adolescence and young adulthood: Evidence from a panel of cross-sectional surveys. *Drug Alcohol Depend.* 2016;169:5-10.
4. Azofeifa A, Mattson ME, Schauer G, McAfee T, Grant A, Lyerla R. National estimates of marijuana use and related indicators - National Survey on Drug Use and Health, United States, 2002-2014. *MMWR Surveill Summ.* 2016;65(11):1-25.
5. Johnston LD, O'Malley P M, Bachman JG, Schulenberg JE, Miech RA. *Monitoring the Future national survey results on drug use, 1975-2014: Volume 2, College students and adults ages 19-55.* Ann Arbor: Institute for Social Research, The University of Michigan 2015.
6. Carliner H, Brown QL, Sarvet AL, Hasin DS. Cannabis use, attitudes, and legal status in the U.S.: A review. *Prev Med.* 2017.
7. Johnston LD, O'Malley P M, Bachman JG, Schulenberg JE, Miech RA. *Monitoring the Future national survey results on drug use, 1975-2015: Volume 2, College students and adults ages 19-55.* Ann Arbor: Institute for Social Research, The University of Michigan 2016.
8. Patrick ME, Kloska DD, Vasilenko SA, Lanza ST. Perceived friends' use as a risk factor for marijuana use across young adulthood. *Psychol Addict Behav.* 2016;30(8):904-914.
9. Abadi MH, Shamblen SR, Thompson K, Collins DA, Johnson K. Influence of risk and protective factors on substance use outcomes across developmental periods: A comparison of youth and young adults. *Subst Use Misuse.* 2011;46(13):1604-1612.
10. Tang Z, Orwin RG. Marijuana initiation among American youth and its risks as dynamic processes: prospective findings from a national longitudinal study. *Subst Use Misuse.* 2009;44(2):195-211.
11. Poudel A, Gautam S. Age of onset of substance use and psychosocial problems among individuals with substance use disorders. *BMC Psychiatry.* 2017;17(1):10.
12. Moss HB, Chen CM, Yi HY. Early adolescent patterns of alcohol, cigarettes, and marijuana polysubstance use and young adult substance use outcomes in a nationally representative sample. *Drug Alcohol Depend.* 2014;136:51-62.
13. Green KM, Doherty EE, Ensminger ME. Long-term consequences of adolescent cannabis use: Examining intermediary processes. *Am J Drug Alcohol Abuse.* 2016;43(5):567-575.
14. Few LR, Grant JD, Nelson EC, et al. Cannabis involvement and nonsuicidal self-injury: A discordant twin approach. *J Stud Alcohol Drugs.* 2016;77(6):873-880.
15. Hasin DS. U.S. Epidemiology of Cannabis Use and Associated Problems [Epub ahead of print] *Neuropsychopharmacology.* 2017.
16. Manrique-Garcia E, Ponce de Leon A, Dalman C, Andreasson S, Allebeck P. Cannabis, psychosis, and mortality: A cohort study of 50,373 Swedish men. *Am J Psychiatry.* 2016;173(8):790-798.
17. Castellanos-Ryan N, Pingault JB, Parent S, Vitaro F, Tremblay RE, Seguin JR. Adolescent cannabis use, change in neurocognitive function, and high-school graduation: A longitudinal study from early adolescence to young adulthood. *Dev Psychopathol.* 2016;29:1253-1266.
18. Crean RD, Crane NA, Mason BJ. An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *J Addict Med.* 2011;5(1):1-8.
19. Gruber SA, Dahlgren MK, Sagar KA, Gonenc A, Killgore WD. Age of onset of marijuana use impacts inhibitory processing. *Neurosci Lett.* 2012;511(2):89-94.
20. Gruber S, Sagar K, Dahlgren M, Racine M, Smith R, Lukas S. Splendor in the grass? A pilot study assessing the impact of medical marijuana on executive function. *Front Pharmacol.* 2016;7.
21. Lopez-Larson MP, Bogorodzki P, Rogowska J, et al. Altered prefrontal and insular cortical thickness in adolescent marijuana users. *Behav Brain Res.* 2011;220(1):164-172.
22. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med.* 2014;370(23):2219-2227.
23. Rumalla K, Reddy AY, Mittal MK. Association of recreational marijuana use with aneurysmal subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis.* 2016;25(2):452-460.

24. Franz CA, Frishman WH. Marijuana use and cardiovascular disease. *Cardiol Rev.* 2016;24(4):158-162.
25. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet.* 2009;374:1383-1391.
26. Desrosiers NA, Ramaekers JG, Chauchard E, Gorelick DA, Huestis MA. Smoked cannabis' psychomotor and neurocognitive effects in occasional and frequent smokers. *J Anal Toxicol.* 2015;39(4):251-261.
27. Simons JS, Dvorak RD, Merrill JE, Read JP. Dimensions and severity of marijuana consequences: development and validation of the Marijuana Consequences Questionnaire (MACQ). *Addict Behav.* 2012;37(5):613-621.
28. Lane SD, Cherek DR, Tcheremissine OV, Lieving LM, Pietras CJ. Acute marijuana effects on human risk taking. *Neuropsychopharmacology.* 2005;30(4):800-809.
29. Gilman JM, Calderon V, Curran MT, Evins AE. Young adult cannabis users report greater propensity for risk-taking only in non-monetary domains. *Drug Alcohol Depend.* 2015;147:26-31.
30. Ansell EB, Laws HB, Roche MJ, Sinha R. Effects of marijuana use on impulsivity and hostility in daily life. *Drug Alcohol Depend.* 2015;148:136-142.
31. Schuster RM, Crane NA, Mermelstein R, Gonzalez R. The influence of inhibitory control and episodic memory on the risky sexual behavior of young adult cannabis users. *J Int Neuropsychol Soc.* 2012;18(5):827-833.
32. Bonar EE, Cunningham RM, Chermack ST, et al. Prescription drug misuse and sexual risk behaviors among adolescents and emerging adults. *J Stud Alcohol Drugs.* 2014;75(2):259-268.
33. Cook S, Shank D, Bruno T, Turner NE, Mann RE. Self-reported driving under the influence of alcohol and cannabis among Ontario students: Associations with graduated licensing, risk taking and substance abuse *Traffic Inj Prev.* 2017;18(5):449-455.
34. Bondallaz P, Favrat B, Chtioui H, Fornari E, Maeder P, Giroud C. Cannabis and its effects on driving skills. *Forensic Sci Int.* 2016;268:92-102.
35. Hanna RC, Perez JM, Ghose S. Cannabis and development of dual diagnoses: A literature review. *Am J Drug Alcohol Abuse.* 2016;43(44):442-455.
36. Radhakrishnan R, Wilkinson ST, D'Souza DC. Gone to pot - A review of the association between cannabis and psychosis. *Front Psychiatry.* 2014;5:54.
37. Carney R, Yung AR, Amminger GP, et al. Substance use in youth at risk for psychosis *Schizophr Res.* 2017;181:23-29.
38. Marschall-Lévesque S, Castellanos-Ryan N, Vitaro F, Séguin JR. Moderators of the association between peer and target adolescent substance use. *Addict Behav.* 2014;39(1):48-70.
39. Bauermeister JA, Zimmerman MA, Johns MM, Glowacki P, Stoddard S, Volz E. Innovative recruitment using online networks: Lessons learned from an online study of alcohol and other drug use utilizing a web-based, respondent-driven sampling (webRDS) strategy. *J Stud Alcohol Drugs.* 2012;73(5):834-838.
40. Teitcher JE, Bockting WO, Bauermeister JA, Hoefer CJ, Miner MH, Klitzman RL. Detecting, preventing, and responding to “fraudsters” in internet research: Ethics and tradeoffs. *J Law Med Ethics.* 2015;43(1):116-133.
41. Centers for Disease Control and Prevention. 2015 State and Local Youth Risk Behavior Survey [questionnaire]. Retrieved from: ftp://ftp.cdc.gov/pub/data/yrbs/2015/2015_hs_questionnaire.pdf2016.
42. Stoddard SA, Bauermeister JA, Gordon-Messer D, Johns M, Zimmerman MA. Permissive norms and young adults' alcohol and marijuana use: the role of online communities. *J Stud Alcohol Drugs.* 2012;73(6):968-975.
43. Duggan M. *Mobile messaging and social media 2015.* Available at: http://www.pewinternet.org/2015/08/19/mobile-messaging-and-social-media-2015.
44. Perrin A. *Social media usage: 2005–2015.* Available at: http://www.pewinternet.org/2015/10/08/social-networking-usage-2005-2015/.
45. Cuttler C, Spradlin A. Measuring cannabis consumption: Psychometric properties of the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU). *PLoS One.* 2017;12(5):e0178194.