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Assessing the Impacts of Marijuana in America



In this edition, our theme is “Assessing the Impact of Marijuana in America.” The contributions include an original paper entitled, *Assessing Physicians’ Perspectives and Knowledge of Medical Marijuana and the Delaware Medical Marijuana Act*, by Barret Michalec, PhD, Laura Rapp, PhD and Tanya Whittle, MA, that examines physicians’ knowledge regarding marijuana as a treatment and how many physicians lack valuable knowledge of the policy.

The other original piece in this issue is authored by Dr. Bertha Madras of Harvard University Medical School and thoughtfully considers the flaws in

a recent study that discusses the risks of marijuana use to adults. Her piece is titled, *20 Flaws in Study Finding No Health Problems in Adult Males Who Were Chronic Marijuana Users as Teens, Young Adults*.

The Journal is also republishing a piece from the *South Dakota Medicine 2015 Special Edition - Preventive Medicine: The Best Medicine for All Time*, courtesy of the South Dakota State Medical Association. With the advent of marijuana legalization efforts across the country, the authors, Shawn Van Gerpen, MD, Tamara Vik, MD, and Timothy J. Soundy, MD sound the alarm about psychiatric health risks to pot users, particularly youth. Diversion of marijuana from “legal” users to youth is a significant problem rendering increased individual and societal risks.

The commentary included in this edition, *A New Era of Reefer Madness*, by Eric Voth, MD, highlights marijuana proponents’ efforts to discredit the scientific approach addressing prohibition of pot by calling it “reefer madness.” He turns it around by suggesting that the highly potent forms of marijuana with 70-80%THC concentration are creating real life “reefer madness” in those that use it and calls for a systematic examination of public health data to address societal impacts and reduce marijuana use



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COMMENTARY

A New Era of Reefer Madness

Assessing Physicians' Perspectives and Knowledge of Medical Marijuana and the Delaware Medical Marijuana Act

*Barret Michalec, PhD; Laura Rapp, PhD; Tanya Whittle, MA
Center for Drug & Health Studies, University of Delaware*

Abstract

Objective: To examine physicians' perspectives and knowledge of medical marijuana.

Data Sources/Study Setting: Primary cross-sectional data was collected from physicians practicing in Delaware (DE).

Study Design: Eighty-five physicians completed a survey assessing their: a.) knowledge of medical marijuana, b.) likelihood and concerns regarding authorizing patients to use medical marijuana, c.) sources of information about medical marijuana, d.) proposed resources to learn more about medical marijuana and Delaware Medical Marijuana Act (DE MMA).

Data Collection: The survey was sent to members of the Medical Society of Delaware. Survey data from close-ended questions were analyzed using a statistical analysis software package. Data from open-ended questions were analyzed by hand through thematic categorization and frequency analysis.

Principle Findings: A majority of participants reported being less than knowledgeable about medical marijuana as a treatment option and about the DE MMA specifically. Lack of Knowledge and Potential Misuse/Abuse were the most cited concerns regarding authorizing medical marijuana, and the majority of participants stressed the desire for educational resources.

Conclusions: Providers play a key role in connecting patients to this therapy option, it is therefore imperative to provide engaging educational resources to providers, patients, and the general public.

Key Words: Medical Marijuana; Health Policy; Physician Attitudes; Physician Knowledge

INTRODUCTION

The Delaware Medical Marijuana Act¹ (DE MMA) became effective July 1st 2012, making Delaware the 15th state in the U.S. to implement a program allowing for the legal use of botanical cannabis[†] for medicinal purposes. As of July 2015, 22 other states, the District of Columbia, and Guam have passed similar legislation. State-based regulatory initiatives began with California's Proposition 215, "The Compassionate Use Act of 1996" - the first to legally allow patients to possess and use cannabis if recommended/approved by a physician. Although numerous state governments have ratified the legal use of botanical cannabis for medicinal purposes, and such use has the support of various reputable scientific/academic societies, the Federal Government still lists marijuana as a Schedule I drug under the Controlled Substances Act (1970)². This Schedule I classification maintains the label that marijuana has "...no currently accepted medical use in treatment in the United States", and, in turn, stifles potential research on the efficacy of

botanical cannabis for various symptoms and afflictions. Furthermore, despite the consistent state-based authorizations for patient utilization of marijuana for medicinal purposes, minimal research has explored physicians' attitudes and perspectives regarding authorizing patients to use medical marijuana, or their knowledge of the nuances of the medical marijuana policy within the state they practice.

This study examines Delawarean physicians' perspectives on enabling patients to obtain and utilize marijuana for medicinal purposes as well as their knowledge of the DE MMA in general. As the medical marijuana program continues to unfold in Delaware (The First State Compassion Center, Delaware's first medical marijuana distribution center, opened its doors on June 26th, 2015), it is necessary to assess practitioners' knowledge of and attitudes towards the program in order to better understand providers' stance on the treatment and policy, promote effective and efficient healthcare policy, and potentially develop and offer quality educational programs for providers and patients alike.

The Current State of Medical Marijuana and an Apparent Lack of Clinical Knowledge

In reviewing the current state of the literature on medical marijuana, specifically that featuring physicians' viewpoints and perspectives of the initiatives, it is evident there is a great deal of confusion regarding state-based medical marijuana programs and the therapeutic use of marijuana in general. The issues and concerns raised by providers include: the "gap" between state and federal laws, the actual medicinal efficacy of cannabis for particular ailments, the potentiality and probability of abuse, the lack of standardized conceptualizations of key terms referenced in policies (i.e. what constitutes a "bona fide" doctor-patient relationship), and

perceived possible legal ramifications related to signing off on a patient's use of marijuana, a severe lack of rigorous scientific clinical research on the endocannabinoid system and botanical cannabis as a therapeutic treatment, among others³⁻¹¹.

Although states have ratified medical marijuana legislation, the Federal Government, including the FDA and Drug Enforcement Agency (DEA), continues to categorize botanical cannabis as a Schedule I drug. The American Medical Association (AMA), the Institute of Medicine (IOM), the American College of Physicians, and other professional health-oriented societies have called for the FDA to reclassify marijuana as a Schedule II drug to open the door for more thorough empirical testing of botanical cannabis in order to establish clinical standards related to dosage, potency, vehicle (e.g. smoking, inhaling vapor, edible-based, pill-form, topical, etc.), the neurological and physiological nuances of various compounds, as well as “best practices” in regards to discussing and authorizing marijuana as a treatment option with patients – yet the classification remains.

Although the 1999 IOM report¹² provided evidence for the therapeutic benefit of marijuana in combating symptoms such as nausea/vomiting, pain, and significant loss of appetite, there are still mixed findings regarding the actual effectiveness of medicinal marijuana as a treatment option for ailments and illnesses^{13,14}. Furthermore, there are conflicting stances on the actual potentiality of abuse/addictive nature of marijuana, with some physicians citing the troublingly addictive nature of marijuana and specific reports indicating that marijuana is no more addictive than anti-anxiety medication, and far less addictive than alcohol and tobacco^{12,15}. There is also discussion regarding medical marijuana diversion, especially among adolescents, and the impact

of the availability of and societal-level norms associated with marijuana, as well as if the legalization of medical marijuana actually lends to increased overall marijuana use among populations¹⁶⁻¹⁹.

From the literature, it appears physicians may feel somewhat confused, frustrated, and/or unaware regarding their state's medical marijuana policies and programs, especially concerning the lack of research/clinical knowledge and their own responsibilities/duties (treatment-wise, legal, and interpersonal) concerning patient care. Yet, there has been minimal research exploring physicians' perspectives and attitudes regarding medical marijuana, questions or concerns they may have, or even their knowledge of their state's medical marijuana policy. If state officials are interested in implementing effective, efficient, and beneficial medical marijuana policies and programs, it is essential to assess where their practitioners "stand" on this debate, their proclivity and potential determinants to approve patients for the use of medical marijuana, and their understanding of the state and federal laws (including their own rights as physicians) associated with medical marijuana. Put simply, physicians are key agents in the realization of these policies – yet their voice has been somewhat muted in the current research. This study explores Delawarean physicians' attitudes and perspectives of the state's unfolding policy and their possible concerns regarding the use of marijuana as a medical treatment option.

Methods

Two members of the author team worked closely with representatives from the Medical Society of Delaware (MSD) and the Delaware Department of Health and Social Services (DHSS) (Division of Public Health (DPH)), to construct a brief survey to assess physicians': a.)

knowledge of the DE MMA, b.) likelihood (and reasoning) of authorizing *qualified* patients to use medical marijuana, c.) sources of knowledge of medical marijuana in general, d.) concerns regarding authorizing medical marijuana as a treatment option for qualified patients, and e.) suggestions of what would be helpful in learning more about the Delaware Medical Marijuana Act and medical marijuana as a treatment option. Demographic questions such as gender, age, years of practice, and primary specialty were also included in the survey.

The survey (hardcopy and a link to an e-version) was included in the November 2014 issue of the Delaware Medical Journal, which is sent to all physicians who are members of the MSD. The survey included a brief description of the study, noted that respondents' identity would remain confidential, and provided the contact information for the Delaware DPH if respondents had any questions related to the survey or the state's medical marijuana program. Institutional Review Board (IRB) approval for the use of human subjects was obtained by the authors' institution.

Measures

Knowledge: To assess physicians' knowledge of medical marijuana as a treatment option, as well as their state's medical marijuana policy, they were asked: a.) *At this time, how would you rate your knowledge about medical marijuana as a treatment option?*, and b.) *At this time, how would you rate your knowledge about the Delaware Medical Marijuana Act, which became effective July 1, 2012?* Participants were provided response categories ranging from *Little/No knowledge* to *Very knowledgeable* (i.e., Likert-scale). Physicians were also asked to indicate any and all of their sources of information regarding medical marijuana; they were provided a list of various resources to choose from (e.g., medical literature, news media, DHSS, lectures/seminars,

among others) but allowed to list others as well – and were able to select more than more source of information.

Likelihood/Comfort to Authorize: In order to better understand physicians’ proclivity to authorize their patients to attain marijuana as a treatment option, respondents were asked, *At this time, how comfortable do you feel authorizing patients to use medical marijuana?* The question included a list of all the qualifying debilitating conditions (as outlined by DE MMA). Answer categories ranged from *Very Unlikely* to *Very Likely* (respondents were also allowed to select, *I would not see patients with any of these conditions*). In the question that followed, participants were asked to elaborate on their answer (i.e., *why* they selected the answer category they did). Respondents were also asked to list and describe any specific concerns they had regarding authorizing patients to attain marijuana as a treatment option.

Sample

Eighty-five physicians responded (out of over 1,600 members of the MSD). Using the qualifying debilitating medical conditions outlined by the DE MMA, primary specialties listed by the respondents (the question was open-ended) were categorized on the basis of: (1) specialties that are likely to encounter/manage patients with these conditions either directly or as a referral source (e.g., “Hematology/Oncology”, “Hospice and Palliative Care”, “Rheumatology”), (2) specialties which are not likely to encounter/manage patients with these conditions given their scope of practice (e.g., “Surgery”, “Pulmonary”, “Gynecology”, “Reproductive Health”, (3) primary care/generalists (e.g., “Family Practice”, “General Practice”, “Internal Medicine”) – the highest percentage of respondents - this specialty group is likely to encounter patients with these

conditions, and may in turn authorize patients, (4) Emergency Medicine, and (5) Pediatricians. Although Pediatricians could be included in the Primary Care/Generalist group, given the controversy and debates surrounding allowing children and young adults to utilize medical marijuana as a treatment option, we thought it best to extract them from the primary care/generalist group so as not to possibly impact the results.

Of the entire sample, there were 66 men and 19 women. A majority of respondents were between the ages of 56-65 (37%), yet 22% were 66 or over, 22% were 46-55, 16% were 36-45, and only 2% of the sample was between the ages of 25 and 35. Whereas most participants reporting having practiced medicine between 31 and 40 years (31%), 29% reported practicing for 21-30 years, 22% reported practicing for 11-20 years, 10% reporting practicing for 1-10 years, and 8% reported practicing for 41 or more years

Analyses

Basic modes and frequencies were calculated for each close-ended question. A series of cross-tabulations and bivariate correlations were constructed to investigate potential significant relationships between demographic information and variables measuring likelihood and degree of knowledge. Table 1 presents the most frequently reported answer (by age, years of practice, and specialty group) for *Knowledge of Medical Marijuana*, *Likelihood to Authorize*, and *Sources of Information*. Regarding the open-ended questions, the author team read through all responses and identified prominent, reoccurring thematic categories. The responses were then grouped into these categories and frequency analyses were then conducted - counting the number of responses within each category. This was done for each open-ended question to identify the most common

“type” of response to each question. Given the sample size of each specialty, comparisons were not made between groups. Rather, prominent categories among *all* participants’ statements were identified. These answer categories, their frequencies, and exemplary representative data (participants’ statements) are featured in Table 2.

Results

Table 1: Most Frequently Reported Category (and %) for Knowledge of Medical Marijuana, Likelihood to Authorize, & Sources of Information by Age, Years of Practice, & Specialty Grouping

Group (n)	Knowledge about Medical Marijuana	Knowledge about DE Medical Marijuana Act	Likelihood to Authorize	Sources of Information*
25-35 (2)	Minimal Knowledge (50%), Knowledgeable (50%)	Minimal Knowledge (50%), Knowledgeable (50%)	Very Unlikely (50%), Possibly (50%)	Medical Literature (50%), News Media (50%), Other Physicians (50%), Lecture/Seminars (50%), DHSS (50%)
36-45 (14)	Knowledgeable (46.2%)	Somewhat Knowledgeable (38.5%)	Very Unlikely (33.3%)	Medical Literature (64.3%)
46-55 (19)	Somewhat Knowledgeable (37.5%)	Somewhat Knowledgeable (56.3%)	Very Unlikely (42.9%)	Medical Literature (73.7%)
56-65 (31)	Somewhat Knowledgeable (43.3%)	Knowledgeable (30%)	Very Unlikely (25%), Possibly (25%)	Medical Literature (75%)
66+ (19)	Knowledgeable (38.9%)	Somewhat Knowledgeable (42.1%)	Very Unlikely (41.2%)	Lectures/Seminars (73.7%)
1-10 (9)	Knowledgeable (62.5%)	Knowledgeable (37.5%)	Very Unlikely (25%), Possibly (25%), Very Likely (25%)	Lectures/Seminars (66.7%)
11-20 (18)	Somewhat Knowledgeable (44.4%)	Somewhat Knowledgeable (50%)	Very Unlikely (46.7%)	Medical Literature (78.9%)
21-30 (24)	Somewhat Knowledgeable (45.5%)	Somewhat Knowledgeable (39.1%)	Very Unlikely (28.6%)	Medical Literature (76%)
31-40 (27)	Somewhat Knowledgeable (44%)	Minimal Knowledge (32%), Knowledgeable (32%)	Very Unlikely (26.1%), Likely (26.1%)	Medical Literature (77.8%)
41+ (7)	Knowledgeable (71.4%)	Somewhat Knowledgeable (42.9%)	Very Unlikely (57.1%)	Lecture/Seminars (100%)
Specialties Likely to Encounter (22)	Knowledgeable (40.9%)	Somewhat Knowledgeable (50%)	Very Unlikely (38.9%)	Medical Literature (90.9%)
Specialties Unlikely to Encounter (17)	Somewhat Knowledgeable (41.7%)	Somewhat Knowledgeable (46.2%)	Very Unlikely (40%)	Medical Literature (58.8%)
Primary Care / Generalists (36)	Somewhat Knowledgeable (40%)	Minimal Knowledge (31.4%)	Very Unlikely (34.3%)	Medical Literature (64.9%)
Emerg. Med (6)	Knowledgeable (50%)	Somewhat Knowledgeable (75%)	Very Unlikely (25%), Unlikely (25%), Possibly (25%), Likely (25%)	Medical Literature (100%)
Pediatricians (4)	Knowledgeable (50%)	Knowledgeable (50%)	Possibly (33.3%), Very Likely (33.3%)	Medical Literature (66.7%)

*Respondents were able to select more than one Source of Information.

Knowledge of Medical Marijuana as a Treatment:

Of the physicians who responded to the survey, 8.8% reported having “little or no knowledge” about medical marijuana as treatment compared to 16.3% who felt they possessed “minimal knowledge”, 36.3% who felt “somewhat knowledgeable”, 35% who felt “knowledgeable”, and 3.8% who felt “very knowledgeable”. Interestingly, those with the least and most time practicing reported greater knowledge than others: The majority of respondents with 1-10 and 41 or more

years of experience were more likely to consider themselves “knowledgeable” about marijuana’s use as a medical treatment (62.5% and 71.4% respectively) compared to respondents with 11-20, 21-30, and 31-40 years of experience who considered themselves to be “somewhat knowledgeable” (44.4%, 45.5%, and 44% respectively).

Respondents from specialty areas that were considered likely to encounter eligible patients generally reported feeling “somewhat knowledgeable” (31.8%) or “knowledgeable” (40.9%) about medical marijuana as a treatment. Similarly, primary care physicians, who are also likely to encounter eligible patients, reported feeling “somewhat knowledgeable” (40%) or “knowledgeable” (25.7%). Pediatricians reported feeling “somewhat knowledgeable” (33.3%) or “knowledgeable” (50%). Specialists considered not likely to encounter eligible patients reported feeling “somewhat knowledgeable” (41.7%) or “knowledgeable” (33.3%). A minimal number of respondents reported feeling “very knowledgeable,” including 4.5% of specialists that are very likely to encounter eligible patients and 5.7% primary care physicians. No pediatricians or physicians who specialize in fields unlikely to encounter eligible patients reported feeling “very knowledgeable”.

Knowledge of DE MMA:

Overall, respondents reported less knowledge of DE MMA than of marijuana as a treatment option. Of the total sample, 9.9% reported “little or no knowledge” and 23.5% reported “minimal knowledge”. In contrast, 38.3% reported “somewhat knowledgeable” while only 21% and 7.4% reported feeling “knowledgeable” and “very knowledgeable” respectively. There were no

discernible differences in regards to age or years of practice and reported knowledge of DE MMA.

The majority of specialists likely to encounter eligible patients reported feeling “somewhat knowledgeable” (50%) or “knowledgeable” (18.2%) about the DE MMA. Primary care physicians reported “minimal knowledge” (31.4%), “somewhat knowledgeable” (28.6%), or “knowledgeable” (22.9%). Interestingly, pediatricians and specialists not likely to encounter eligible patients reported greater knowledge of the DE MMA (16.7% and 15.4%, respectively) compared to specialists likely to see eligible patients (4.5%) and those in primary care (5.7%).

Comfort with Likelihood of Authorization:

Half (50%) of the participants reported that they were uncomfortable with authorizing medical marijuana: 16.2% said they were “unlikely”, and 33.8% said they were “very unlikely” to authorize medical marijuana use for eligible patients. However, half (50%) of respondents reported they were “possibly likely” (16.2%), “likely” (16.2%), or even “very likely” (17.6%) to authorize medical marijuana use for patients that present eligible conditions. There were no discernible differences between age groups, however, there were noticeable differences between groups of years practicing. Practitioners with 41 or more years of experience reported being “very unlikely” (57.1%) to authorize medical marijuana use compared to respondents with 1-10 years (25%), 11-20 years (46.7%), 21-30 years (28.6%), or 31-40 years (26.1%) of experience.

Although 33.3% of specialists likely to see eligible patients reported they are “very likely” to authorize medical marijuana, 38.9% reported they are “very unlikely”. Among primary care

physicians, 34.3% were “very unlikely” to authorize while 20% were “likely”. Of pediatricians, 33.3% were “very likely” and 33.3% would “possibly” authorize, compared to only 16.7% who were “likely” and 16.7% who reported “very unlikely” to authorize.

The relationship between physicians’ level of knowledge about medical marijuana and their level of comfort authorizing its use was statistically significant ($r=.400$, $p=.000$). There was also a significant relationship between knowledge of the DE MMA and one’s comfortability with authorizing its use ($r=.277$, $p=.017$). Put simply, it was found that the more knowledgeable about medical marijuana in general, and the DE MMA in particular, the more comfortable physicians are with authorizing its use.

Source(s) of Information:

Respondents’ sources for information on medical marijuana treatment and policy varied considerably. The most frequently cited sources of information included medical literature (72.4%), lectures and seminars (52.9%), news media (43.5%), other physicians (36.5%), and experiences with patients (36%). Less frequently cited sources were Department of Health and Social Services (DHSS) (14.9%), family and friends (11.5%), and practice policy (3.4%).

Age was found to correspond with certain information sources. Although approximately 75% of the physicians that were 46 and older cited medical literature as an information source, only 64.3% of respondents 36-45 years of age and 50% of the respondents 25-35 years old reported the same source. Similarly, whereas about half of respondents 25-35, 36-45 years old and 56-65 years old cited lectures and seminars as an information source, the percentage was much higher

for respondents 66 years and older (78.9%). Also, younger respondents were more likely to cite other physicians as a source of information.

Years of practice also appears to relate to preferred information sources: 75% of respondents with 11-40 years of experience reported using medical literature as a source of information whereas 55.6% of respondents with 1-10 years of experience and 42.9% of respondents with 41+ or more years in the field reported the same source. About two-thirds of respondents with 1-10 and 31 or more years of experiences reported lectures and seminars as information sources, but only 31.6% of physicians with 11-20 years cited the same source. Similar to age, those respondents with the least years of experience (1-10 years) were likely to cite other physicians as a source of information.

Medical literature was cited as a source of information by 90.9% of specialists likely to encounter eligible patients, 64.9% of primary care physicians, 58.8% of specialists not likely to encounter, 100% of those in emergency medicine, and 66.7% of pediatricians. Prior experience with patients was reported as a source by 45.5% of specialists likely to encounter eligible patients and 43.2% of primary care physicians, 50% of physicians in emergency medicine, and 33.3% of pediatricians, but only 6.3% of physicians who are in a specialty area unlikely to encounter eligible patients. Half of specialists likely to encounter eligible patients and 41.7% of primary care doctors cited news media as a source of information, whereas 66.7% of the pediatricians, 25% of those in emergency medicine, and 37.5% of specialists unlikely to see eligible patients cited the same source. Although about half of pediatricians and half of those in emergency medicine cited other physicians as an information source, only about 25-40% of

respondents in other specialty groups cited the same source. Seminars and lectures were reported as sources of information by 54.5% of specialists likely to encounter eligible patients, 51.4% of primary care physicians, 47.1% of specialists who are unlikely to encounter eligible patients, 75% of those in emergency medicine, and 66.7% of pediatricians. Emergency medicine physicians were the most likely to cite DHSS as a source of information (25%), whereas pediatricians were the least likely (0%). Although only 11.5% of respondents reported using friends/family as a source, 33.3% of pediatricians and 25% of emergency medicine physicians cited friends/family.

Among respondents who reported “little or no knowledge” about medical marijuana as a treatment, 85.7% did *not* cite medical literature, other physicians, or DHSS as an important source of information; none (0%) relied on prior experiences with patients, and 71.4% did *not* cite lectures and seminars for information. However, over two-thirds of these respondents reported relying on news media. In contrast, 100% of physicians who considered themselves “very knowledgeable” about medical marijuana treatments cited medical literature and lectures and seminars, and about 66% cited experience with patients, other physicians, media, and DHSS as sources of information. Respondents’ knowledge of DE MMA did not generally correspond to information sources. There was one exception: respondents who cited lectures and seminars as sources of information reported having a much higher degree of knowledge of the Act than did respondents who did not cite lectures and seminars.

Interestingly, medical literature, experience with patients, and lectures and seminars were commonly cited by respondents that reported being likely or highly likely to authorize medical

marijuana for treatment. In contrast, news media was cited more commonly among respondents who are unlikely to or will possibly authorize medical marijuana for treatment.

Open-Ended Questions

Table 2: Frequency of Categorized Responses

DOMAIN	CATEGORY	FREQ.	PARTICIPANT'S STATEMENTS
Comfort w/ Authorizing (would not)	<i>Lack of knowledge</i>	18	<p>"Not comfortable with prescribing something about which I have virtually no knowledge."</p> <p>"Would need to know more about law and indications."</p>
	<i>Not "prescriber"/ unlikely to see pts</i>	13	<p>"I would not consider myself knowledgeable enough about the medication to prescribe or educate patients."</p> <p>"Not a prescribing care giver."</p> <p>"I typically do not treat any patients with those disease."</p> <p>"Unlikely to see patients in this stage of illness."</p>
	<i>Potential for abuse/misuse</i>	8	<p>"Liberalizing it's use will only open the door to more serious drug abuse!"</p> <p>"Increased odds of being abused and shared with someone else. I have already had an incident where the patient suffered from one of the listed ailments and their caregiver wanted to sign that they indeed had this ailment. It was obvious to me that the caregiver actually wanted it for themselves and the patient was not interest in it."</p> <p>"I cannot imagine myself giving or facilitating a 'prescription' to smoke."</p>
Comfort w/ Authorizing (would)	<i>When other Rx fail</i>	18	<p>"As a hospice physician, I am certain to run into patients with the qualifying conditions whose symptoms are not being relieved with more standard therapies. At that point, I am OK with a pt trying medical marijuana."</p> <p>"I often care for patients with chronic cancer pain or other chronic pain syndromes for which I feel they may ultimately benefit from medical marijuana, if other treatments have failed or have been maximized."</p>
	<i>Effectiveness/benefits/humane treatment</i>	16	<p>"I see patients with diseases that I do not have a treatment for. If there is research suggesting that Med Marijuana may be effective for these patients I am likely to offer that as a treatment option."</p> <p>"These are serious, chronic diseases, many that are fatal. These are legitimate reasons for marijuana usage and humane."</p> <p>"There is no question in my mind that marijuana is beneficial for patients which chronic/debilitating illnesses. It should be should be administered via a vaporizer as a supplement to other medication. Indeed, it would probably be more effective, less expensive, and less addicting than the more traditional medications."</p> <p>"For the right patient, medical marijuana can provide relief from pain. Patients should be given an alternative to the usual medications presently available."</p>

Table 2 Con't: Frequency of Categorized Responses

DOMAIN	CATEGORY	FREQ.	PARTICIPANT'S STATEMENTS
Specific Concerns w/ Authorizing	<i>Potential for abuse/misuse / diversion</i>	25	<p>"My concern would be that people, other than the intended person, would use the drug. It should not be used for recreational purposes."</p> <p>"As with any other controlled substance, diversion is an area to be aware of."</p> <p>"Patients coming in requesting medical marijuana for abuse purposes under the guise of vague conditions like intractable nausea that I cannot prove is occurring."</p>
	<i>Legality issues (for pt and provider)</i>	8	<p>"legal related to state and federal prosecution for supplier and pt."</p> <p>"Concern is what can the patient do if questioned by police."</p> <p>"Marijuana is still illegal in the United States of America, of which Delaware remains a part. The DEA a federal agency, gives us our licenses to prescribe controlled substances. Marijuana is still considered a 'category one' narcotic, meaning there is no legitimate medical use. Thus, I am concerned that recommending a schedule one narcotic to my patients, could in theory, put my DEA license at risk and possibly subject me to federal criminal sanctions."</p>
	<i>Lack of standardization (quantity & quality)</i>	7	<p>"How to ensure that the marijuana isn't tainted. How to rate one's response to it. How to quantify usage."</p> <p>"Will not authorize. No standard dosing."</p> <p>"It is a mind altering substance, and the quality control varies from batch to batch."</p>
Helpful to Learn More	<i>Education: Courses (online and CME-sponsored), seminars, lectures, pamphlets, reviews of DE Law</i>	27	<p>"Concise written educational material."</p> <p>"Online course sponsored by the State and MSD."</p> <p>"A review of the law, as to how the dispensaries will work, how patients will be able to fill and refill, RX limits, and a review of the literature about medical marijuana."</p>
	<i>Clinical/Empirical research</i>	12	<p>"Clinical studies indicating effectiveness, rage of use as a treatment modality."</p> <p>"Well-designed studies to show safety and efficacy and give dosing and strain information."</p> <p>"More independent research on the effects of Med marijuana in specific disease states."</p>

In response to *why* participants reported their degree of likelihood to authorize patients to utilize medical marijuana as a treatment option, *Lack of Knowledge* (about medical marijuana as a treatment option in general, as well as the DE MMA specifically) was the most frequently stated concern. However, it is important to note that a number of participants reported their willingness to authorize patients *When other Prescription Drugs Fail*, and many noted the perceived potential *Effectiveness/Benefits* for their patients. The *Potential for Abuse/Misuse* was also a commonly reported issue that impacted participants' comfort-level with authorizing patients to attain medical marijuana.

Participants were also asked to offer specific concerns (if any) with authorizing patients to attain medical marijuana as treatment option. Again, *Potential for Abuse/Misuse* was a very common response (the most frequently expressed concern by participants for this specific question). This category also included concerns regarding *Diversion* and statements referring to medical marijuana as a “gateway drug”. *Legality Issues* were the second most frequently stated concern. Interestingly, participants often expressed worry about the legal issues surrounding authorizing and maintaining their licenses and own practice, yet many also expressed concern for their patients' rights. *Lack of Standardization* regarding potency, strain, dosage, and quality, was the third most frequently stated concern with authorizing.

Regarding what would be helpful in learning more about medical marijuana as a treatment option and the DE MMA, participants stressed the importance and desire for more *Education*. This category included responses referring to Continuing Medical Education (CME) sponsored courses, online courses, seminars, lectures, pamphlets, and reviews for the DE MMA

specifically. Participants also frequently expressed the need for more *Clinical/Empirical Research* examining the effectiveness of medical marijuana as a treatment for various diseases/ailments and appropriate strains and dosage.

Discussion & Conclusion

With 23 states and DC and Guam enacting laws providing marijuana as a viable medical treatment option for certain patients it is essential to explore providers' (i.e. those granting authorization to attain medical marijuana) perspectives and knowledge regarding state-specific medical marijuana laws and medical marijuana in general. Providers play a (if not *the*) key role in connecting patients to this potential therapy, yet very little is known regarding how physicians' feel about medical marijuana and what they understand about the processes and procedures of authorizing their patients as well as their own and their patients' rights.

This study found that the majority of physicians that participated in this study feel less than knowledgeable about medical marijuana as a treatment option, and know even less about their state's medical marijuana law specifically. Furthermore, only about half of the participants in this study would "possibly" consider authorizing patients with qualifying conditions to attain medical marijuana (with only about 34% reporting being "likely" or "very likely" to authorize), and there was notable variation within specialty groups regarding the likelihood to authorize patients. These findings are somewhat concerning - not that it is imperative to increase the number of physicians likely to authorize, but if state governments are implying that medical marijuana is a legitimate medical treatment option for specific ailments and symptoms by enacting the law, it would appear problematic, if not detrimental to the full potential of the policy

and even possibly patient well-being, that many physicians: a.) lack valuable knowledge of the policy and the treatment option, and b.) are unwilling to even consider discussing it with their (qualified) patients as an option.

Participants cited *Lack of Knowledge* and *Potential for Abuse/Misuse/Diversion* as the most significant concerns regarding authorizing patients. As discussed earlier, the literature concerning potential abuse and diversion is somewhat mixed and therefore, given this relative “grey” area of research, there is not a black/white or yes/no response. However, increasing, enhancing, and maintaining knowledge of medical marijuana and state-specific medical marijuana laws is a promising and manageable directive. As suggested by the participants, particular organizations/institutions (e.g. DHSS, DPH, MSD, AMA, perhaps even prominent state universities) could provide courses, seminars, and other various educational materials and resources for providers to become more acquainted with this “new” treatment option, the law, as well as their own and their patients’ rights.

In a recent Canadian study featuring over 400 providers, Ziemianski et al.¹¹ found similar knowledge gaps among their participants regarding medical marijuana as a treatment option and medical marijuana policy, and much like this specific study, the strong majority of participants desired more education (about the treatment and policy). Moreover, the concerns and barriers expressed by physicians regarding medical marijuana as a treatment option featured in this specific study echo those found by Ziemianski and colleagues (e.g. misuse, lack of standardization, liability issues). It is important to note, however, that whereas Delawarean physicians and patients have only had about three years with the medical marijuana law,

Canadian physicians and patients have had access to medical marijuana as a treatment option since 1999. It is notable that the findings from this specific study mirror those where the law has been in existence for over 15 years - specifically the reported lack of knowledge among participants. Unfortunately, although Ziemianski et al. do present their participants' preferred formats of educational information (many of which mirror those offered by the participants of this specific study), they do not speak to any specific educational efforts or initiatives regarding medical marijuana provided by any levels of Canadian government or medical institutions/organizations. Similarly, in their study of over five hundred Coloradan family physicians, Kondrad and Reid⁴ found a strong desire among participants for more educational opportunities about medical marijuana, but the authors offer no specific examples of state- or federally-sponsored educational programs for physicians or the public. In fact, at that time (2013), their study of physician attitudes regarding medical marijuana was the first (and only) conducted in a state where medical marijuana had been legalized, and Kondrad and Reid even explicitly call for CME resources to be developed for physicians to learn more about the treatment and the law. Yet, it would appear that this call (and others that followed) has gone unheeded despite state after state enacting and approving medical marijuana policies increasing the number of physicians legally able to authorize patients to attain marijuana as a treatment option. In short, it seems as though the laws are in place but few providers actually know about them. These gaps could have significant impact on best practices concerning medical marijuana, authorization rates (i.e., under- and over-authorization), patients' knowledge of their treatment options and rights, patient satisfaction, doctor-patient communication, and the longevity and livelihood of the policy itself. States that have enacted medical marijuana policies provide specific information about the law on the state government website. However, one could argue

that these sites are not the most user-friendly or likely-to-be-accessed resource. Therefore, given this apparent absence of engaging educational resources for patients and providers, future research should explore the location and availability of any and all educational materials and resources, and examine if and how patients and providers access and utilize these resources.

The physicians featured in this study also desired more empirical evidence (such as that provided by clinical studies) to help shape their understanding of the effectiveness and best practices of medical marijuana as a treatment option. However, the future of marijuana research is somewhat hindered by the current FDA classification of marijuana as a Schedule I substance. Because of this significant barrier to research, it is imperative that state governments and medical organizations (e.g., AMA) offer providers and patients educational programs to increase awareness of and adherence to policy guidelines. Regarding Delaware specifically, clear and shared understandings of all aspects of the Delaware medical marijuana program will be essential for the healthcare workforce, as well as patients and the general public. Educational initiatives should include discussions on state and federal policies, the science of botanical cannabis, and even “best practices” (for doctors and patients) associated with discussing marijuana as a treatment option. Furthermore, more attention should be given to evaluative efforts, which may include: a.) assessing various aspects of the state medical marijuana program and policies, b.) the development and implementation of educational programs, and c.) evaluating doctor-patient interactions concerning medical marijuana as a treatment option. As states continue to move forward in this new (yet old) frontier of patient care, more collaboration between academia, medicine, and government is needed to provide essential translational education and research to healthcare providers, patients, and the general public.

This study has several potential limitations, most notably is the small sample size. Not only does this low number of responses suggest selection bias and a lack of representatives of even Delawarean physicians, but also negatively impacts the generalizability of the findings and the scope of our analysis. However, given that we found lack of knowledge (of medical marijuana and the DE MMA) to be prevalent among the participants, perhaps the lack of response among MSD members could be reflective of an overarching cloud of uncertainty among physicians. Furthermore, because many of our key findings mirror those featured in similar studies with much larger sample sizes, we are confident that our findings do suggest prominent attitudes and knowledge “gaps” among practicing physicians regarding medical marijuana as a treatment and medical marijuana policy.

Notes

[†] For the sake of clarity, within this paper, the terms medical marijuana, marijuana, and botanical cannabis will be used synonymously (and are to be considered distinct from pharmaceutical cannabinoids – synthetic cannabinoid-based medications)

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About the Authors

Barret Michalec, PhD is an Associate Professor of Sociology and the Assistant Director of Health Research in the Center for Drug & Health Studies (CDHS) at the University of Delaware. His research interests include team-based care, interactions within health care settings, and disparities in health and health care. He received his PhD in sociology from Emory University.

Laura Rapp, PhD is an Associate Scientist in the Center for Drug & Health Studies (CDHS) at the University of Delaware. She began working in the area of evaluation, prevention, and substance abuse as a graduate student and continued that work during a post doctorate position. She continues to expand on her work in those areas as an Associate Scientist at the Center. Dr. Rapp is a PI on a contract with a Delaware state agency that funds community groups to implement substance use prevention activities and leads efforts on community level evaluation.

Additionally, she provides training and technical assistance in the areas of data collection, interpretation, assessment, and evaluation to state and community groups. Dr. Rapp also has a background in working for non-profits, specifically in the area of providing support services to those impacted by sexual assault.

Tanya Whittle, MA is a doctoral candidate in the Sociology and Criminal Justice Department at the University of Delaware. She is an Inside-Out Prisoner Exchange Program facilitator and a Graduate Research Assistant at the Center for Drug & Health Studies (CDHS). Her research interests include corrections and prisoner reentry, collateral consequences of felony convictions, drug policy, and street-level bureaucrats' legal consciousness and discretionary decisions within the criminal justice system. Additionally, she has contributed to community substance use prevention program evaluations, youth behavior and health surveys, and evaluations of correctional-and community-based substance abuse and reentry programs.

Conflict of Interest

I declare that I have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled: "Assessing Physicians' Perspectives and Knowledge of Medical Marijuana and the Delaware Medical Marijuana Act."



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Medicinal and Recreational Marijuana: What are the Risks?

By Shawn Van Gerpen, MD, Tamara Vik, MD;
and Timothy J. Soundy, MD

Abstract

With the recent legalization of recreational marijuana in Colorado, Washington, Alaska, the District of Columbia and legislation pending for both medical and recreational marijuana in several other states, it is important for the facts regarding its potential for serious mental health consequences to be known. Little has been said about the psychiatric risks of this substance, particularly in youth. Several studies have shown increased rates of depression, anxiety and schizophrenia among those who use marijuana on a regular basis. In addition, permanent loss of IQ and structural changes in the brain have been demonstrated with habitual use. Legalization of marijuana for recreational use can influence an adolescent's perception of this substance as "safe." In states that have legalized marijuana for medical purposes, there is the very real problem of "diversion." As many as 34 percent of 12th-graders who use marijuana in states with legalized marijuana had obtained it from a person who had received it through a prescription.

Introduction

With the recent legalization of recreational marijuana in Colorado and Washington and the legal use of medical marijuana in 23 states, South Dakota will likely face another concerted effort to legalize marijuana for both medical and recreational purposes. Proponents of marijuana legalization state that marijuana is no different than alcohol and would increase tax revenues and lower the expense of prosecuting users. However, there are significant deleterious effects to the use of this substance that weigh heavily in favor of keeping the laws in South Dakota as they are.

Background

While known by a variety of different names (cannabis, pot, Mary Jane, weed, etc.) marijuana is a drug that is familiar to most people. Research into the use of this drug is bringing to light a number of very serious concerns, especially within the adolescent population, that many familiar with the drug have failed to recognize in the past. The legalization of marijuana, compounded with the continued illegal use of cannabis, continues to have a major impact on the lives of the youth that we treat in our

medical practices and interact with in our communities. Many users of the drug consider it to be a "safe" alternative to "hard core" drugs or alcohol; however, this belief is in stark contrast to the reputable research findings being published on this topic.

Review

According to data published by the Centers for Disease Control and Prevention's (CDC) Youth Risk Behavior Surveillance (YRBS) survey in 2013 which surveyed ninth through 12th grade students in public and private schools throughout the U.S., 40.7 percent of ninth through 12th grade students reported that they had used marijuana one or more times during their lifetime – 8.6 percent of which indicated that they had tried marijuana for the first time prior to age 13. These percentages were noted to be slightly lower in South Dakota's adolescent population with 29.6 percent of ninth through 12th grade students reporting having used cannabis one or more times in their life, and 7.2 percent of those indicating that they had first used marijuana prior to age 13.¹

One of the leading arguments of proponents for legalized marijuana is that the regulated, legal use of cannabis

obtained through legal channels will result in a decrease in the overall amount of marijuana being used due to the disruption of the underground market by which people currently obtain the drug. One study, published between 2002 and 2008, which looked at adolescent marijuana use, showed that the use was lower and the perception of its riskiness was higher in states where medical marijuana was not legal. On the other hand, adolescent marijuana use was noted to be “higher and perception of its riskiness lower” in states where medical marijuana was legal.² Gil Kerlikowske, director of the White House Office of National Drug Control Policy stated, “Today...there is evidence suggesting that regulation schemes that have been promoted by the marijuana legalization lobby are not succeeding in preventing the diversion of marijuana into the hands of young people, as was promised to the voters.” Of interest, it should be noted that “34 percent of the 12th-graders who used marijuana and lived in states with medical marijuana laws reported that they obtained the drug through someone else’s prescription – and 6 percent said they had their own prescription.”³

Not only are there a growing number of adolescents reporting cannabis use, but the perceived dangers of this drug are shifting as well. According to a Feb. 6, 2013 article in *JAMA*, adolescent attitudes toward marijuana use seem to be changing. When looking at adolescent attitudes towards marijuana use, this article indicated that only 41.7 percent of eighth-graders felt that occasional marijuana use was dangerous.⁴ One of the greatest misconceptions surrounding marijuana safety is a false belief that the marijuana of the boomer generation is the same marijuana that is being used by our youth today. According to a report by the National Institute on Drug Abuse, “The amount of tetrahydrocannabinol (THC) in marijuana samples confiscated by police has been increasing steadily over the past few decades. In 2012, THC concentrations in marijuana averaged close to 15 percent, compared to around 4 percent in the 1980s.”⁵

Marijuana, or cannabis, is a derivative of the plant *cannabis sativa*.⁶ Cannabis exists in many forms and levels of potency with herbal cannabis being the most commonly used form.⁷ The active ingredient in cannabis is Δ^9 -tetrahydrocannabinol.⁷ Research has demonstrated that the effects of cannabis on the human body are related to the agonistic effects at the cannabinoid receptors (CB1 and CB2).⁸ The CB1 receptor is a pre-synaptic receptor that is found in large quantities in the striatum, hippocampus and cerebellum and also in lesser amounts in peripheral tissues, liver adipocytes, the pancreas, the gastrointestinal

tract, skeletal muscle and in immune cells.⁸ In contrast, CB2 receptors are located mainly in the immune cells in tissues such as the spleen and liver.⁸

Cannabinoid receptors found in neurons are activated by the neurotransmitter anandamide.⁷ It is the endocannabinoid system that has been identified as one of the key components “for cortical development, neuronal migration, connectivity and synaptogenesis. During adolescence, many brain regions undergo dramatic levels of growth and synaptic remodeling,” particularly in the prefrontal cortex.⁹ THC, the active ingredient in cannabis, acts like anandamide and leads to activation of the neuron. It is activation of the CB1 receptor that leads to the psychoactive effects of cannabis.⁷ One theory that explains how this occurs is that by stimulating the cannabinoid receptors, the glutamate and gamma-aminobutyric acid functioning is altered. This in turn leads to structural changes within the brain of adolescent patients using marijuana.¹⁰ It is these changes in neuronal structure that may account for many of the very serious neurological effects that can accompany adolescent marijuana use. It is also the large number of CB receptors in the striatum, amygdale, hippocampus, cerebellum, and prefrontal cortex that give rise to the brain’s pleasure and reward centers, contributing to the addictive potential of the drug.⁷ It is worth noting that there exists an abundance of cannabinoid receptors in the prefrontal cortex, a region of the brain that has been identified in the development of schizophrenia.⁹

Research looking at the effects of marijuana use on the developing brain support the theory noted above. In a recent study at Northwestern University, it was reported that teens who smoked marijuana daily for a three year period had abnormal changes in the structure of their brain compared to teens in the control group. Brain abnormalities and memory problems were observed in these individuals in their early twenties, two years after they had stopped using marijuana. The cannabis users were noted to have striatal, globus pallidus, and thalamus changes showing these brain regions appearing to shrink and collapse inward. These individuals also had poorer working memory. The earlier the age of cannabis use, the more dramatic the brain changes and memory deficits were noted to be.¹¹

Although many proponents of cannabis legalization have refuted the claim that cannabis is a “gateway drug” to using even more dangerous and addictive substances of abuse, studies that have looked at substance use trends

among cannabis users seem to support the “gateway drug” theory. Not only does it appear that cannabis use itself is a potential precursor to future drug use, but the age of first use of cannabis and the frequency of cannabis use seem to also be predictors of future substance abuse issues. Studies have shown that over two-thirds of those under the age of 18 who have been admitted to a drug treatment program identify cannabis as their substance of choice. It is estimated that the “risk for illicit drug initiation appeared 21 times higher among cannabis experimenters and 124 times higher among daily cannabis users than among nonusers.”⁷

Data from the Treatment Episode Data Set (TEDS), which is a national data base of annual admissions to substance abuse treatment facilities in the U.S., shows that among adults who first used marijuana at the age of 14 or younger, 13.2 percent went on to develop drug dependence or abuse. This rate was noted to be six times higher than that of adults who first used marijuana starting after the age of 18. A 2011 review of demographic data looking at age showed that 74 percent of those surveyed in drug treatment facilities across the U.S. reported that they had first started to use substances of abuse at the age of 17 or younger, with 34.1 percent reporting they had first used substances of abuse between that ages of 15-17 and 29.7 percent reporting their first use between the ages of 12-14. Another 10.2 percent reported that they had first begun using substances of abuse before they were 11 years of age. Of those surveyed, only 26 percent reported that they began using substances of abuse at the age of 18 or older.¹²

Another claim that is often made by those in favor of marijuana legalization is that cannabis is not an addictive drug. Popular belief is that cannabis use is safe and does not carry any long term addictive potential. Credible research contradicts this belief. According to *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, the current criteria for a substance use disorder is a “cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance related problems.” One important characteristic that defines a substance use disorder is “an underlying change in brain circuits that may persist beyond detoxification, particularly in individuals with severe disorder.” These brain changes may be demonstrated by “the repeated relapses and intense drug craving when the individuals are exposed to drug-related stimuli.” As indicated earlier in this article, the activation by THC of

the CB receptors in the striatum, amygdala, hippocampus, cerebellum and prefrontal cortex areas, which are known to give rise to the brain’s pleasure and reward center, contribute to the addictive potential of the drug.¹³

DSM-5 has defined cannabis-related disorders by the following diagnostic criteria:

A. A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
4. Craving, or a strong desire or urge to use cannabis.
5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school or home.
6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
8. Recurrent cannabis use in situations in which it is physically hazardous.
9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
 - b. Markedly diminished effect with continued use of the same amount of cannabis.
11. Withdrawal, as manifested by either of the following:
 - a. The characteristic withdrawal syndrome from cannabis.

- b. Cannabis is taken to relieve or avoid withdrawal.¹³

While many of the acute effects of cannabis tend to be reversible (increased heart rate, blood shot eyes, euphoria and relaxation) proponents and opponents of marijuana legalization tend to disagree on cannabis's ability to cause withdrawal symptoms once the drug has been discontinued. Research has identified a number of symptoms related to cannabis withdrawal such as irritability, anger, aggression, anxiety, depressed mood, restlessness, sleep difficulty and decreased appetite or weight loss. These withdrawal symptoms typically begin within 24-48 hours after discontinuation of the drug and typically last between one and three weeks. These symptoms may cause the user of the drug significant distress and contribute to relapse among those trying to abstain.⁷

For those who do choose to use cannabis, the use of this drug does not come without the potential for serious health risks. Research has shown that there is nearly a five time increased risk of myocardial infarction in the hour after one uses marijuana. Cannabis smokers are also exposed to many of the same harmful chemicals that cigarette smokers are exposed to. This exposure to chemicals puts one at a greater risk for developing cancer, bronchitis and recurrent lung infections.⁷

Marijuana has also been shown to affect one's level of cognition and motivation. Consider for a moment the image that comes to mind when you think of the term "pot head," a slang term often used to describe someone that frequently smokes marijuana. This phrase, often used as a comedic portrayal of a marijuana user, depicts these frequent users of the drug as being extremely laid back, unmotivated, lazy, excessively hungry and as having poor memory.¹⁴ Research shows that there is a connection between marijuana use and one's motivation. Many experts agree that excessive use of marijuana, as well as a number of other "psychoactive" drugs, can lead to amotivational syndrome, a term used to describe the "variety of changes in personality, emotions and cognitive functions such as lack of activity, inward-turning, avolition, apathy, incoherence, blunted affect, inability to concentrate and memory disturbance" that is noted in chronic users of these drugs.¹⁵

Not only does marijuana affect one's motivation, but also one's cognitive ability. Marijuana use has been shown to affect adolescent academic performance. Results from the U.S. National Survey on Drug Use and Health showed

that "youth with poor academic results were more than four times likely to have used cannabis in the past year than youth with average or higher grades." Cannabis use has also been shown to lead to decreased attention span, slower reaction times and motor/coordination deficits. Studies have also demonstrated that the use of cannabis may result in a decrease in adolescent IQ. It has also been shown that adolescents who are heavy users of marijuana have "poorer complex attention functioning, as well as poor sequencing ability, slower psychomotor speed, and difficulties in verbal story memory."⁷

The motivation and cognitive affects of cannabis are also seen in adults who use marijuana. Studies indicate that a strong correlation exists between chronic cannabis use and unemployment, increased dependency on social welfare programs, and a decrease in life satisfaction rates.⁷ The National Institute on Drug Abuse has also released studies showing that employees who used cannabis were more likely to have increased absences, accidents, worker's compensation claims and job turnover when compared to non-cannabis users.⁷

In recent years there has been more research into the role that marijuana plays in the development of mood disorders, anxiety disorders and psychosis. In one study of over 50,000 Swedish patients published by Zammit et al., a link was identified between marijuana use and the development of schizophrenia, a risk that was notably greater with increased marijuana use.¹⁶ In fact, in one published article, it was noted that of the research subjects who used cannabis over 50 times, there was a sevenfold increase in the risk for developing schizophrenia.¹⁶ In another study, performed by Arseneault et al., it was demonstrated that in those subjects who used marijuana prior to the age of 15, there was a four times increased risk of developing schizophrenia by age 26.¹⁶

Not only has marijuana been linked to increased rates of psychosis and schizophrenia, but more evidence is being reported on the link between cannabis and other mental health conditions. A study in Australia demonstrated that there was a relationship that existed in adolescent males and females with regard to the daily use of marijuana and the development of depression.⁸ This relationship was found to be the most profound in adolescent girls. In fact, in girls under the age of 15, it was found that there was a significant increase in suicidal ideation or attempts over the course of the next 15 years of their life.⁸ Another research study performed in Australia found that in teens ages 13-17 who had used marijuana, there was a three

times increased risk of developing depression when compared to those teenagers who had never used the drug.⁸ Increased levels of anxiety have also been linked to marijuana use. For those adolescents who used cannabis on a weekly basis and who continued to use until the age of 29, there was a significantly increased likelihood of developing an anxiety disorder.⁷

From a cognition standpoint, cannabis is known to slow a person's ability to react, decrease their motor coordination, and decrease one's ability to concentrate and focus. This increased level of distractibility, along with slower reaction times, has been shown to be a contributing factor in motor vehicle accidents when users of the drug attempted to drive while under the influence of cannabis. In a laboratory setting, cannabis and THC were noted to "produce dose-related deficits in reaction time, attention, motor performance and coordination, and information processing that can last up to 28 days after abstinence from the drugs."⁷

There are over 60 pharmacologically active cannabinoids in marijuana. One such chemical, cannabidiol (CBD), is a compound that may have anti-anxiety, anti-inflammatory and antispasmodic actions. It has been reported that CBD does not cause cognitive deficits or the perception of feeling "stoned." The level of THC in medically dispensed marijuana is extremely high while CBD is low. THC is the

chemical responsible for euphoria, or the "high" in marijuana. Indications for legally available marijuana for medicinal use vary from state to state and include cancer, glaucoma, AIDS, hepatitis, ALS, seizure disorders, Crohn's disease, Parkinson's disease and multiple sclerosis. Data collected in states where marijuana is legal for medicinal purposes suggests that the majority of those who possess medical marijuana user cards do not have one of these conditions.

Conclusion

There is a significant amount of evidence to support that the long-term use of marijuana is harmful to individuals and society, especially to adolescents. Research has shown that marijuana use can lead to an increased risk of chronic mental illnesses such as schizophrenia, depression, and anxiety by causing structural changes in a young, maturing brain. Adolescent use of marijuana can also lead to decreased intelligence levels and poor working memory which can interfere with educational attainment and create psychosocial and financial problems that no amount of increased tax revenue can offset. Although there are many in society who will lobby for legalization of this drug due to its "safety" profile, the evidence on this topic refutes this claim and we in South Dakota would be wise to continue to defeat any attempt at legalization of this harmful substance.

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About the Authors:

Shawn Van Gerpen, MD, Assistant Professor and Residency Director, Department of Psychiatry, University of South Dakota Sanford School of Medicine.

Tamara Vik, MD, Assistant Professor and Child and Adolescent Residency Director, Department of Psychiatry, University of South Dakota Sanford School of Medicine.

Timothy Soundy, MD, Professor and Chair, Department of Psychiatry, University of South Dakota Sanford School of Medicine.

20 Flaws in Study Finding No Health Problems in Adult Males Who Were Chronic Marijuana Users as Teens, Young Adults

Dr. Bertha K. Madras

A new study has caused quite a stir among would-be marijuana cognoscenti because it contradicts major research about the impact of marijuana on physical and mental health. The neuroscientist, Bertha K. Madras of Harvard Medical School looked briefly at the study. Dr. Madras served as Deputy Director for Demand Reduction in the White House Office of National Drug Control Policy from 2006 to 2008 . . . She writes:

A recent manuscript by Bechtold et al¹, describes a longitudinal assessment of a population of marijuana users which, after data collection, were divided into four user groups: (1) non-users to low use (48%, n=186); (2) limited to adolescent use (10%, n=38); (3) late initiators and increasing (20%, n=76); (4) early onset with chronic use (22%, n=86). Marijuana use was monitored from adolescence (age 15) into young adulthood (age 26). Ten years later, *and ten years after the last determination of marijuana use*, study authors asked the subjects, now at an average age of 35.8 years, to report their health status. Each of the four groups self-reported no differences in physical or mental health problems in their mid-thirties. The authors concluded that regardless of how much and how long marijuana was used, and regardless of race, the physical and mental health problems of these four groups were similar. That is, high marijuana use for prolonged periods was not associated with any physical or mental health problems. They

also claimed that this is a definitive study because it was longitudinal and superior to other published reports on long term health consequences of marijuana.

A critical evaluation of the validity of the findings and sweeping conclusions is essential, lest they are interpreted inappropriately. A perusal of the study and the authors' stated caveats in the manuscript reveal significant weaknesses, with the use of an unrepresentative, possibly archaic population, inadequate sample size, inadequate methodologies to assess mental health and physical problems, (self-reports, evaluation of psychiatric status without considering the "spectrum" nature of psychiatric conditions, and absence of addiction evaluation). The findings conflict with other well designed longitudinal studies that assess long term consequences of marijuana use with early age of initiation of marijuana.

This type of study would not approach or fulfill rigorous criteria for longitudinal research, as exemplified by the 2014 NIDA funding opportunity with similar goals (*see Appendix*). The conclusions conceivably are compromised by the following perceived shortcomings of the study.

Population Concerns

1. **The sample size, 386 people, was too small to detect a marijuana effect on psychotic disorders or on other health conditions.** NIDA recommends a sample size of 10,000 to detect differences (*see Appendix*). About 50% of the subjects – age 14 - were selected on the basis of their high scores on anti-social behaviors (conduct problems) and the remainder from adolescents without high anti-social behavior scores, but it is not clear whether the drop-out rate from the study was equally represented by both categories. Did more people

with early onset anti-social behaviors drop out and does this skew the conclusions? Was there under-sampling of a population at highest risk? There is strong and accumulating evidence that marijuana use is associated with psychosis, with earlier age of onset of schizophrenia, and with worsening of psychotic/schizophrenic symptoms. These association studies were gleaned from thousands of people, not from fewer than 400 subjects, especially when only 86 people are in the high risk group. The small sample size would also make it difficult to detect other serious marijuana-associated medical problems. Reporting of cardiovascular complications related to marijuana and the extreme seriousness of these events (death rate of 25.6%) is increasing, but this occurs in a small number of users (one estimate is 1.8%). Marijuana is a possible risk factor for cardiovascular disease in young adults⁶, with a temporal association between marijuana use and heart attacks, sudden cardiac death, and for stroke, transient ischemic attack, and marijuana-induced arteritis.⁷ Pulmonary symptoms attributable to marijuana use, even with less intense use, include chronic bronchitis, daily cough, phlegm production (four quality studies document these findings). No power analysis indicates adequacy of sample size.

Think about this: The prevalence of schizophrenia is 1 in 100. If you sample only 86 subjects of the riskiest group, “early onset chronic users” category, it is unlikely that you can detect a significant increase in prevalence of psychosis or schizophrenia. Another example: a recent study found the incidence of serious cardiac effects of marijuana in 1.8% of heavy users. Was the sample of early onset chronic users (86 people) large enough to detect serious cardiac effects, especially from self-reports?

2. **The study does not have a drug-naïve population for comparative measures of outcomes.** They report that the amount of marijuana used during adolescence and early adulthood had no effect on the occurrence of a range of health problems.

Think about this: The study has no group that controls for a general, representative population, a non-drug using population. Some other studies have shown different outcomes among youth or young adults who choose not to use, those who use occasionally, or among heavy users. What populations are these groups compared to? Are the group sizes large enough to detect differences?

3. **The populations and use patterns investigated in this study are anachronistic and conceivably irrelevant for 2015.** Subjects were initially screened in 1987-1988, with a majority of users recruited that did not fall into the heavy use range (daily or near daily use), a use pattern increasingly observed at the present time. The majority of subjects used marijuana during the 1990's when the psychoactive THC content of marijuana was relatively low compared with current concentrations.

Think about this: The most serious health outcomes associated with marijuana use, including addiction, occur in heavy users (daily or near daily use) using for long periods of time. Currently, marijuana access has risen rapidly as its legal status changes; its perception of harm has plummeted among youth, along with a rising perception that as a medicine it is safe and can be used daily. Daily use of high potency marijuana among adolescents and young adults is near or at its highest level in nearly three decades. The populations of this

study may be irrelevant to current trends, especially since 2009, as marijuana potency is at its highest level ever; availability is greater because of reduced federal and state oversight, as daily use increases, and perception of harm declines. These factors conceivably influence self-reporting of effects and their magnitude. Are the outcomes of this study relevant to current use patterns and marijuana potency?

4. **The population is not representative of the general population: (a) the prevalence of concussions (27.7%) is inordinately high. (b) death by gunfire is inordinately high.** No explanations are offered for the abnormally high prevalence of concussions or death by gunfire, and whether this population has a higher than average prevalence of cognitive impairment. Was there a relationship between concussions and marijuana use or self-reporting of adverse health problems?

Think about this: The overall rate of traumatic brain injury (concussions) presenting in emergency departments in the United States (recent CDC statistics) is 19 per 100,000 persons; for males in this age group, it is about 470 per 100,000 persons (or 4.7 for each 1,000 persons). A concussion rate of 27% of this population (270 per 1000 persons) is about 60 times higher than the general population within this age range. Some research studies with rigorous criteria exclude subjects with traumatic brain injury because of the potential for cognitive impairment. The high numbers of concussions and deaths due to gunfire are anomalous if compared to statistics within the general population. Is this sample representative?

5. **Self-reported medical health problems by these subjects differ from population statistics, on the basis of occurrence by race.** According to CDC statistics in 2010, the prevalence of diseases in the general population among African American (AA) adults compared to white (W) adults is different than reported in this study. The CDC ratios (AA:W) for the general population are: Diabetes, CDC = 1.6:1; this study = 4:0. Chronic kidney disease, CDC = 1.14:1, this study = 0:0.6. Sexually transmitted diseases, CDC = 4:1; this study = 0.5:1.1.

Think about this: The health problems self-reported by the African-Americans and white subjects may or may not be accurate, but they differ from the CDC prevalence data for the general population. Differences highlight the need for recruiting sufficiently large numbers of subjects to be representative of the population as a whole. Do differences reflect the unusual populations of this study, which may not generalize to the entire population?

Methodological Concerns: Outcome Measures

6. **The purpose of the study was to determine whether different patterns of marijuana use among youth affected mental and physical health differently. All findings are based on self-reports, an inadequate method for measuring outcomes – self reports, because of potential bias, recall errors, and reliance on self-knowledge of medical conditions.** The authors did not investigate medical records, did not confirm marijuana and other drug use with biometric tests, did not interrogate contacts, and did not inquire about sequence of use of other drugs.

Think about this: More than 75% of people harboring a substance use disorder (SUD), based on objective DSM-IV criteria (Diagnostic and Statistical Manual-IV), do not think they have a SUD and do not seek treatment². To rely solely on self-reporting of mental or physical health problems with a questionnaire, raises doubts about the overall study design and conclusions. Other examples: Fifty percent of men who die of heart disease had no obvious symptoms. A diagnosis of diabetes or high blood pressure is made by biometric testing, not by self-reports. Without confirmation from medical records or physician-initiated tests, is it possible to be self-aware of high blood pressure or diabetes with certainty?

7. **Following from #6 above, there is no evidence that subjects reported health outcomes based on their medical records. Authors did not report whether study participants had visited a physician during the past year, past five years or ten years since the last contact. Confirmation of medical conditions by a medical record would strengthen the conclusions.** The core outcomes of this study are mental and physical health. Knowing whether the mental and physical health of subjects in this study had been objectively diagnosed by a physician or specialist (psychiatrist, addiction medicine) is critical. The unknown medical record, combined with an assumption that subjects' self-reports were accurate, diminish the convictions of the authors' conclusions.

Think about this: Many health problems are not apparent to individuals until they are measured by a healthcare professional; addiction, high blood pressure, diabetes, cancer, cognitive impairment. Were all subjects reporting results from a recent annual checkup?

Unless this information and results are provided, can one assume that self-reports are accurate?

8. **Following from #6, #7 above, mental health diagnoses were based on questionnaires, not on biometric testing or long term assessment (mental health diagnosis requires more than a single session and evaluation over the span of months).** The diagnosis of psychosis, mood disorders, anxiety disorders, may rely solely on a person's response to a single oral or written questionnaire or impressions of their own health, but a definitive diagnosis for a serious mental health problem, such as schizophrenia, requires systematic questioning and over a significant period of time to determine whether symptoms persist and are not temporary aberrations. Moreover, mental health problems including substance use disorders (addiction) occur along a continuum of mild to severe. It is possible that the focus on a diagnosis of a psychotic disorder in the current study limited their ability to detect subtle effects of marijuana use on brain function, thought processes or early psychotic symptoms. Scores were not generated that reflect this continuum. Authors arbitrarily selected a cut-off point to rate the presence or absence of a diagnosis.

Think about this: It is simple to detect one's own asthma or headache but, for many mental health problems, self-diagnosis may be inaccurate. Can one know if they are developing subtle signs of a mental problem or cognitive impairment unless measured objectively? Can one know if an early stage of cancer is present unless discovered by imaging, by biopsy, or gene expression profiling? Can one know if asymptomatic heart disease is present without ECG testing? Is self-diagnosis of an early stage of mental illness reliable?

Were subjects reporting their personal self-assessment or were they reporting results from a physician's medical and psychiatric examination?

Methodological Concerns: Marijuana Use

9. **The investigators divided marijuana users over time into four groups, using model fit statistics. The chart showing marijuana use over time for these four groups provides no error bars indicating whether these groups are significantly different or overlap at each age during the study.**

Think about this: One would assume the groups were different, based on the four-group solution that was selected on the basis of model fit statistics, substantive interpretation, face validity of classes, parsimony, and consistency of findings with prior research. But, it would be helpful if error bars representing range of use at each age were included to assure the reader that the group divisions based on subjective criteria (interpretation, face validity of classes, parsimony, and consistency of findings with prior research) are transparently clear at each age.

10. **Some data of the marijuana use component are missing: 46% of the subjects had voids in data.** Almost half of the subjects did not report marijuana use at various times during the 10 years of survey. This partial set of data is problematic, even though authors claim missing data was similar to those who yielded full data sets and it is possible to interpolate missing data. Reasons for these data gaps should be provided.

Think about this: If a segment of data are not available, does it invalidate or skew the chart showing trends of the four groups?

11. Marijuana use was not questioned at the end of the study (age 36 years). Strong longitudinal studies have shown that early onset and continued heavy use of marijuana is associated with or may be a causative agent in long term adverse effects on educational achievement, employment, welfare dependency, use of other illicit drugs, psychotic symptoms, I.Q. reduction, others³⁻⁵. This study provides marijuana use rates until age 26, measures life outcomes at age 36 but doesn't ask subjects whether they used marijuana from age 26-36 until age 36, and if so, frequency and amount. Most users apparently were not consuming daily or nearly daily until age 26, and three of the four groups had largely stopped using by the age of 26. Why was marijuana use not measured at the end of the study?

Think about this: It is critical to know whether the people using marijuana from age 15-26 years, were still using at age 36, at which age health outcomes were questioned. If you are studying whether marijuana has interfered with the mental and physical health of subjects at the present time, it is not logical to interrogate whether they are currently using, or if they stopped and when they stopped? If they stopped 10 years before the study, then long term consequences may be less likely.

12. Marijuana potency was far lower (1980's to 1990's) during the period of marijuana consumption of this population. This conceivably affects outcomes and consequences.

13. Quantity, frequency, potency of marijuana use is a critical measure. Frequency and potency were not questioned. The main outcome measure was the number of times

marijuana was used during the year. The patterns of use, number of times used each day, potency, were not interrogated during each annual survey. This void makes it difficult to compare with other studies.

Methodological Concerns: Outcomes Not Measured

14. **Marijuana addiction (cannabis use disorder or CUD), among the most significant of the adverse effects of marijuana was not interrogated.** The prevalence of CUD is related to age of onset, quantity and frequency of use and closely linked to other life outcomes.

Think about this: Addiction is among the most prominent effects of chronic marijuana use, and yet the study did not ask about addiction.

15. **Life outcomes were not measured (employment, educational achievement) at the end of the study.** Other strong longitudinal studies have interrogated life outcomes and concluded that marijuana has adverse long term effects on employment and educational achievements, other social consequences, as a function of age of onset and quantity used³⁻⁵.

Think about this: Longitudinal studies indicate that heavy continuous marijuana use is associated with lower socioeconomic status and achievements (e.g. college education, employment) than infrequent or no use. When an individual is using marijuana very frequently for a number of years, are they more or less likely to maintain a job, complete high school or college education, be on welfare?

16. Cognitive testing was not measured. Cognitive impairment is one of the hallmarks of acute and possibly long term marijuana use. It is also associated with other adverse life outcomes.

Think about this: If you were designing a study to learn whether an intoxicant, known to interfere with learning, memory, executive function, affects your mental and physical health, would you omit evaluating learning and memory and other types of brain function, from the study?

17. A number of health problems questioned (e.g. cancer, high blood pressure, heart attacks, strokes) arise later than the average age of the subjects (mid-30's). The health questionnaire was filled out by marijuana users in their mid-30's, an age at which most significant health problems are not yet manifest.

18. Acute effects of marijuana were not asked: intoxication, accidents, emergency department mentions, unplanned pregnancies, HIV-AIDS. For example, a recent European study collected Emergency Department data from 14 European centers for six months to determine acute toxicity of marijuana. Of the sample, 356 (16.2 %) involved marijuana alone or together with other drugs/alcohol and 1.6 % with marijuana alone. Of the 35 non-fatal lone marijuana presentations, the most commonly reported features were agitation/aggression (22.9 %), psychosis (20.0 %), anxiety (20.0 %) and vomiting (17.1 %). There was one fatality due to prolonged cardiac arrest, with no other drugs detected.⁶

Think about this: Acute marijuana toxicity can lead to emergencies requiring medical attention. Does omission of this from the questionnaire achieve a comprehensive view of medical consequences of marijuana?

Citations and Comparison with Other Studies

19. **Authors omit mention of important recent longitudinal studies that show different outcomes than their own study.** Other carefully controlled and longitudinal studies have shown that early age of onset of marijuana use is associated with a number of mental and physical consequences, including addiction, cognitive deficits, mental health problems, educational, employment outcomes and others. Citations 3 and 4 are not mentioned, others are dismissed with a list of weaknesses, even though the current study is fraught with significant weaknesses.
20. **The authors attempt to support their conclusions by dismissing well designed reports by others.** In the introduction, they do not discuss severe limitations of their own study: (e.g. daily use of high potency marijuana is currently at its highest level in 30 years of surveys, in contrast with their subjects' marijuana use over 10-20 years ago; weaknesses of self-reported medical and psychiatric conditions, and others as stated above). Instead, the introduction curiously offers a critique, entitled *Limitations in Prior Research*. In it they conclude that “prior research has produced mixed findings regarding the associations between chronic marijuana use and indicators of physical and mental health, ...and that individuals who begin using marijuana frequently during early adolescence and those who use at high frequencies throughout adolescence and young adulthood tend to develop more

health problems (i.e., psychotic symptoms, respiratory problems) than infrequent/nonusers, *in contradistinction to their own findings.*

Think about this: In their own critique of reports by others, they state that early onset, frequent marijuana users tend to develop more health problems than infrequent users, but there is no effort to reconcile their negative findings with positive findings of others.

(1) They claim this study is among a “handful of studies that have been able to prospectively delineate subgroups of individuals with varying developmental patterns of marijuana use from adolescence into young adulthood”. The strength of the present study was to document marijuana use, but not in depth and not confirmed by biometric testing, annually for the decade of life encompassing adolescence and early adulthood. Yet, other research has interrogated key variables, age of onset, frequency and quantity of marijuana use (confirmed with biometric testing), some in prospective, longitudinal studies, others in cross-sectional studies. The medical record at the study’s inception is of limited value because it is neither comprehensive nor independently verified. The initial assessment of 15 year old boys was inadequate and was not followed by a longitudinal assessment, except for marijuana use. The 10 year hiatus in collection of marijuana use data is a weakness. Self-reports of mental and physical health are inappropriate.

(2) They claim that “few longitudinal studies have examined whether young men who exhibit early and chronic developmental patterns of marijuana use are more likely to exhibit both physical and mental health problems in their mid-30s”. Unfortunately, this

study does not answer this question because of the quality of the outcome measures, no marijuana use patterns recorded for 10 years, and the only medical and mental health outcomes are reported by mothers of the subjects around age 15, and by the subjects themselves at ~ age 36.

(3) They claim that “Many studies have failed to control for important confounding factors, such as health problems that predated the onset of regular marijuana use and co-occurring use of tobacco, alcohol, and hard drugs”. Yet, they did not interrogate documented and age-appropriate deficits associated with marijuana use, at the onset of the study-in-depth psychiatric status, cognitive impairment, declining academic performance, school drop-out rates, accidents, and others, were not interrogated in this survey.

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Appendix

An Example of a Well-Designed Longitudinal Study

NIDA Funding Opportunity: <http://grants.nih.gov/grants/guide/rfa-files/RFA-DA-15-015.html>

Research Design and sample should describe the following:

- **A longitudinal single-cohort design to prospectively examine the neurodevelopmental and behavioral effects of substance use from early adolescence through the period of risk for substance use and substance use disorders.**
- **Participants, approximately ages 9-10 at baseline**, who are largely naïve to substance use at the time of study enrollment; the focus on a largely asymptomatic population at baseline provides the opportunity to define brain and behavioral risk factors and trajectories before the onset of substance use;
- **A design with a sample size that is sufficiently large to achieve the study goals;** preliminary estimates indicate **a sample size of approximately 10,000 participants**

(combined across sites) at the end of the 5-year funding cycle would be needed, **though a smaller sample can be proposed if justified by feasibility and statistical-power analyses;**

- **A sampling strategy designed to establish a community-based sample that is broadly representative of and generalizable to the U.S. general population as a whole, including males and females, as well as major racial, ethnic, and sociodemographic subgroups of the population; it is recognized that the level of precision achieved for various subgroups may vary, and that probability-based sampling and oversampling of certain demographic subgroups or geographical regions may be required;**
- **A sampling design that considers *oversampling* of population subgroups at greater risk for uptake of substance use during adolescence (e.g., positive family history of substance use disorders, externalizing psychopathology, disinhibitory traits, prenatal exposure to substances);**
- **A research approach that considers incorporating genetically informative designs (e.g., family based) or subjects (e.g., twins, siblings);**
- **A sampling design to produce geographical variation of macro-level factors associated with substance use (e.g., state-level policies concerning the permissiveness of marijuana, alcohol, and tobacco use; regional variation in prevalence of marijuana, alcohol, and tobacco use; rural, urban and suburban populations);**
- **State-of-the-art data-collection procedures (e.g., computer-administered/assisted interviews), practices (e.g., cultural matching) and quality-control processes (e.g., random verification, logic-checking);**

- **Standardized measures that, where possible, are compatible with data-harmonization efforts** (e.g., PhenX Toolkit) and ongoing studies of substance use and neurodevelopment;
- **Comprehensive multi-informant** (e.g., respondent, parent/guardian, sibling, etc. as appropriate) assessment of substance use to permit estimates of prevalence, incidence, and change in use patterns (e.g., quantity, frequency) by specific substances (e.g., nicotine, alcohol, marijuana), products and product types (cigarettes, e-cigarettes, snuff, beer, liquor, joints, blunts), and modes of administration (e.g., inhalation, oral, drinking, nasal); measures of change should be sensitive enough to detect dynamic patterns among adolescents as they enter and pass through the period of risk for substance use;

Behavioral Measures and Biospecimens should describe the following:

- **Comprehensive and multi-level assessment of predictors, mediators, moderators, and outcomes associated with substance use** (e.g., demographics, pubertal status, personality traits, parental monitoring, peer group deviance, family structure, parent-child relationships, prosocial behaviors, romantic relationships, stressful events, availability of substances, state and local policies related to marijuana, alcohol, and tobacco use, educational attainment, learning disability designation or receipt of services, crime, unemployment, experience and/or witnessing of trauma or violence);
- **Assessment of concurrent and historical participation in interventions that may prevent or mitigate substance use and its consequences** (e.g., pre- and post-natal prevention programs; Head Start; receipt of counseling, psychotherapy and other

behavioral health interventions or services; family or classroom-based prevention interventions);

- **Comprehensive measurement of confounders and other risk factors** (e.g., prenatal exposure, abuse or trauma, drug availability, exposure to environmental risk factors, sport injuries especially to the head, etc.);
- **Rigorous quantitative and categorical assessment of symptomatology and psychiatric disorders, including severity;**
- **Family history assessment of substance use disorders and other psychopathology;**
- **Age-appropriate assessment of HIV-risk knowledge and behaviors;**
- **Neuropsychological battery of tests that is developmentally sensitive and that allows for the assessment of major neurobehavioral dimensions associated with substance use** (e.g., attention, information processing, learning and memory, cognitive control, motivation, emotional regulation, disinhibition, risk taking);
- **Screening for drug intoxication prior to behavioral, cognitive, or functional imaging sessions and neuropsychological assessment, with delineated thresholds for inclusion/exclusion;**
- **Clear and justified inclusion/exclusion criteria to identify individuals unable to complete the assessment protocol for various reasons** (e.g., use of certain prescribed medications, language/reading impairments, **brain injury**, severe mental illness, etc.);
- **Detailed plans and procedures to collect, process, analyze, and store biospecimens** (e.g., urine, blood, saliva, hair) indicative of substance exposure;

- **Additional biospecimens should be collected for subsequent research on genetic/epigenetic factors influencing or affected by substance use, with accompanying plans for analyses.**

About the Author

Dr. Bertha K. Madras is Professor of Psychobiology, Department of Psychiatry at Harvard Medical School (HMS), and is cross-appointed at the Massachusetts General Hospital. She served as Deputy Director for Demand Reduction (prevention, intervention, treatment) in the White House Office of National Drug Control Policy (ONDCP), a Presidential appointment confirmed unanimously by the US Senate. At Harvard, her multidisciplinary research focuses on neuropsychiatric diseases and addiction biology, documented in over 150 manuscripts and as co-editor of books “The Cell Biology of Addiction”, “Effects of Drugs in the Human Nervous System”, “Imaging of the Human Brain in Health and Disease”. At ONDCP, she incorporated Screening, Brief Intervention, Referral to Treatment (SBIRT) into the national drug control strategy, spearheaded SBIRT CPT®, other billing code approvals, Medicaid reimbursement, SBIRT adoption by Health Resources and Services Administration, the Veterans Administration, recruitment of Federal healthcare insurers, a UN declaration of endorsement, and other initiatives. In service to the public, she directed creation of a Museum exhibit, a CD (licensed by Disney Corp), “Changing your mind: drugs in the brain” for the Boston Museum of Science. She has given hundreds of presentations worldwide, on how drugs affect the brain and consults to government, organizations and industry. She holds 19 patents, is a recipient of a NIDA Public Service award, a NIH MERIT award, American Academy Addiction Psychiatry Founders’ Award, and Marian Fischman Award. A brain imaging agent strategy she developed was cited

by The Better World Report, 2006, as one of “25 technology transfer innovations that changed the world”. Her experiences in translational neurobiology, government and public service afford her a unique perspective on science and public policy.

Conflict of Interest

I declare that I have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled: *“20 Flaws in Study Finding No Health Problems in Adult Males Who Were Chronic Marijuana Users as Teens, Young Adults.”*



A New Era of Reefer Madness

By Eric A. Voth, M.D., FACP

For many years, the pro-marijuana lobby has drawn on the seemingly absurd images from the 1938 movie, *"Reefer Madness."* It has been portrayed as the ultimate example of overreaction and flawed marijuana policy. When marijuana experts express concern about the vast impact that marijuana is increasingly exacting on the society, such concerns are dismissed as *"Reefer Madness"* hysteria.

Take note, this *"Reefer Madness"* tactic is a page from the "Big Tobacco" playbook identical to the strategies of the tobacco lobby. Such ploys seek to undermine and minimize the attitudes of the public toward marijuana. Sadly, that strategy is working.

With the recent legislative sessions, we now see medical excuse marijuana extending into 23 states. Frank legalization has happened in Colorado, Washington State, Alaska, and Oregon with other states giving consideration to legalization.

The lessons of the 1970s, during the time that we had the nation's highest use of marijuana have been forgotten. Thirteen states either had legalized or decriminalized marijuana. The associated marijuana problems prompted reversal of such policy. But

wait! 40 years later we are experiencing the same creeping, insidious social changes and acceptance of marijuana with one gigantic difference: the marijuana itself.

The typical pot of the 1970s was typically 2-3% THC content, but that has vastly changed. Analyses of Colorado marijuana strains are showing averages of 20% THC content, some leaf plants up to 30%, and hash-oil derivatives to 70-80 % THC concentrations. Some might suggest, "all the better to get stoned with."

This new surge in THC concentration is particularly concerning if we consider that most of the medical literature demonstrating associations with psychosis, violence, and brain changes has been conducted when the average ambient THC concentrations were half or less of the marijuana currently on the street ¹⁻⁹. Not surprisingly, chronic marijuana use is now associated with chronic structural and functional brain changes ^{9, 10}.

I would advance the position that we are facing a true period of new "reefer madness." Research is demonstrating a clear association between marijuana and violence, domestic abuse, psychosis, mania, and negative behaviors. The popular media is scattered with episodes of marijuana-related violent crime or suicide.

What particularly concerns me is that the social impact of marijuana on violent or psychotic behavior is being overlooked. The pot lobby has done such an effective job of minimizing the public view of marijuana, that even medicine and law enforcement do not consistently recognize the possible causal effect. I continually interface with physicians

who claim "it must have been laced with PCP or K-2" rather than acknowledging that 20-70% THC is the cause of such problems.

Taken to its logical extension, the criminal justice and healthcare delivery systems really need to systematically examine the multitude of young violent criminals that have a drug history to determine if marijuana is, in fact, central to their behavior. The fact that the age of these individuals are typically late teens or early twenties strongly suggests that they are in the middle of the marijuana risk spectrum. Such data would be helpful in driving public health policy changes to reduce marijuana use and its social consequences.

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About the Author

Dr. Voth is a specialist In Internal Medicine, Pain management, and Addiction Medicine as well as a medical director at Stormont-Vail Health Care in Topeka, Kansas. He is the chairman of the Institute On Global Drug Policy, is recognized as an international authority on drug use, and lectures on drug policy-related issues, pain management, and appropriate prescribing practices. Dr. Voth previously served as the former medical director of the St. Francis Chemical Dependence Services. He also serves as an advisor on alcohol and drug abuse issues to the Kansas State Board Of Healing Arts, is a member of the National Advisory Committee For the Center For Substance Abuse Treatment of HHS, and is A Clinical Associate Professor of Internal Medicine at The University of Kansas School Of Medicine.

Dr. Voth has advised Reagan, Clinton, both Bush administrations, and has advised or testified for numerous Congressional Offices on drug related issues. He has appeared on or consulted to, numerous other radio media, and has been quoted by numerous international print media.