

CME Driving Under the Influence of Cannabis: A Framework for Future Policy

Robert M. Chow, MD,* Bryan Marascalchi, MD,† Winfred B. Abrams, MD,‡
Nathalie A. Peiris, MD,§ Charles A. Odonkor, MD,¶ and Steven P. Cohen, MD||¶

Marijuana is the most widely consumed illicit substance in the United States, and an increasing number of states have legalized it for both medicinal and recreational purposes. As it becomes more readily available, there will be a concurrent rise in the number of users and, consequently, the number of motor vehicle operators driving under the influence. This article examines the cognitive and psychomotor effects of cannabis, as well as current policy concerning driving under the influence of drugs. The authors performed a MEDLINE search on the epidemiology of cannabis use, its cognitive and psychomotor effects, and policies regarding driving under the influence of drugs. Twenty-eight epidemiological studies, 16 acute cognitive and psychomotor studies, 8 chronic cognitive and psychomotor studies, and pertinent state and federal laws and policies were reviewed. These search results revealed that marijuana use is associated with significant cognitive and psychomotor effects. In addition, the legalization of marijuana varies from state to state, as do the laws pertaining to driving under the influence of drugs. Marijuana is a commonly found illicit substance in motor vehicle operators driving under the influence of drugs. Current evidence shows that blood levels of tetrahydrocannabinol do not correlate well with the level of impairment. In addition, although acute infrequent use of cannabis typically leads to cognitive and psychomotor impairment, this is not consistently the case for chronic heavy use. To establish the framework for driving under the influence of cannabis policy, we must review the current published evidence and examine existing policy at state and federal levels. (*Anesth Analg* 2019;128:1300–8)

Driving under the influence of drugs (DUID) is a term used to describe the use of drugs or medications that can alter one's ability to properly and safely operate a motor vehicle. Historically this included the use of illicit substances but has since been expanded to include prescription medications. Due to increasing state legislation legalizing marijuana for both medicinal and recreational use, the focus of DUID should specifically examine the effects of driving under the influence of cannabis (DUIC). At this point in time, there has been no similar push at the federal level for the legalization of marijuana, which would originate from the US Congress.

At a federal level, the Controlled Substances Act classifies marijuana, its cannabinoid components and derivatives, as Schedule I substances. Schedule I classification is defined as drugs with no currently accepted medical use

and a high potential for abuse. Under federal law, physicians may only recommend medical marijuana and certify patients with qualifying medical illnesses, as opposed to writing a prescription with a route of administration, dosing regimen, and quantity. However, physicians can still prescribe synthetic cannabinoids that are US Food and Drug Administration approved in the traditional manner. Accordingly, even if doctors legally recommend some form of cannabis at the state level, they may be exposed to potential negative consequences under federal law.¹ Prosecution for marijuana-related offenses is at the discretion of the Executive Branch, especially the Department of Justice.

During the Obama administration, Deputy Attorney General James Cole distributed a memo asserting that as long as states that have legalized recreational marijuana use appropriately strict regulatory measures, they would not be subject to federal prosecution. However, should the regulations be insufficient, derelict states would potentially be subject to the enforcement of federal law.²

This memorandum by Deputy Attorney General Cole has since been rescinded by Attorney General Jeff Sessions. Thus, the policy of nonintervention has been replaced by one that allows US attorneys to prosecute offenders based on federal laws concerning marijuana-related activities.³

Marijuana is already the most commonly used illicit substance, and with the push for state legalization, its use will continue to grow. Policies for DUIC are in their nascent stages, and much work needs to be done to determine any relationships that may exist between marijuana use and driving ability.

METHODS

The literature search was conducted on the following topics: the use and abuse of marijuana, the psychomotor effects

From the *Department of Anesthesiology, Yale School of Medicine, New Haven, Connecticut; Departments of †Anesthesiology and Critical Care Medicine and ‡Physical Medicine & Rehabilitation, Johns Hopkins School of Medicine, Baltimore, Maryland; §Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, Maryland; ||Department of Anesthesiology, Neurology and Physical Medicine and Rehabilitation, Johns Hopkins School of Medicine, Baltimore, Maryland; and ¶Department of Anesthesiology and Physical Medicine & Rehabilitation, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Bethesda, Maryland.

Accepted for publication May 10, 2018.

Funding: This study was partially funded by the Centers for Rehabilitation Sciences Research, US Department of Defense.

The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.anesthesia-analgesia.org).

Reprints will not be available from the authors.

Address correspondence to Robert M. Chow, MD, Department of Anesthesiology, Yale School of Medicine, 330 Cedar St, TMP-3, New Haven, CT 06520. Address e-mail to Robert.chow@yale.edu.

Copyright © 2018 International Anesthesia Research Society
DOI: 10.1213/ANE.00000000000003575

of both acute and chronic marijuana use, as well as current recommendations, laws, and policies. Three authors (B.M., N.P., and R.C.) performed the literature search and reviewed the results to determine which studies were included in the review. The search was limited to English-language articles and articles translated into English. Studies concerning marijuana use and abuse, DUI, and the physiological effects of the drug were included from selected federal government databases and reports. Relevant studies concerning marijuana-related DUI were identified from a MEDLINE search of the terms “driving,” “psychomotor,” “cognitive,” and “marijuana or tetrahydrocannabinol (THC) or cannabis.” MeSH terms were determined by first conducting a preliminary search of the topic using short keyword terms, as well as browsing through the MeSH trees deemed to be essential to the subject. These terms initially produced 1257 results, of which 52 documents were selected for relevance based on our predefined selection criteria. A review and discussion of current federal and state policy and law were sourced from a review of state statutes, case law, the American Law Review, and federally funded documents from international DUI conferences.

The creation of the conceptual framework involved identifying factors related to DUI, the outcome of motor vehicle accidents (MVAs), and the relationships between these factors and the clinical outcome of interest. The aim was to provide a working schema for future hypothesis generation. No standardized approach exists for the creation of a conceptual framework. However, corroborative evidence and expert opinion were reviewed to determine specific influences impacting DUI. After identifying these elements, we created a diagram to depict the relationship among these various influences on DUI (Supplemental Digital Content 1, Figure 1, <http://links.lww.com/AA/C461>).

RESULTS

Epidemiology of Cannabis Use and Abuse

A National Survey on Drug Use and Health in 2015 found that approximately 117.8 million people used marijuana in their lifetime, which breaks down to about 3.9 million people between 12 and 17 years of age and 113.9 million >18 years of age. Considering solely the month before when the survey was conducted, a staggering 22.2 million people used marijuana during that time.⁴ A survey conducted in 2016 emphasized that marijuana is not only a problem affecting adults, showing that 23.9% of tenth graders and 35.6% of 12th graders used marijuana in the preceding year.⁵

Due to its euphoric effects mediated by binding to the cannabinoid receptor type 1 in the central nervous system, marijuana possesses significant potential for abuse. Such abuse may have potential negative societal ramifications, including during the operation of motor vehicles. In a study investigating MVA and the presence of marijuana, Brady and Li⁶ found that the prevalence of cannabinoid in fatal car crashes in 6 states (California, Hawaii, Illinois, New Hampshire, Rhode Island, and West Virginia) increased from 4.2% in 1999 to 12.2% in 2010.⁶ However, this study did not clarify whether marijuana was the sole agent involved. Examining the findings more closely, California and Hawaii had medical marijuana legalization during the entire course

of the study, Rhode Island had legalized marijuana from 2006 to 2010, while Illinois, New Hampshire, and West Virginia did not have laws legalizing medical marijuana. Therefore, this study was not able to ascertain whether state medical marijuana legalization correlated with marijuana DUI.

A survey conducted in France revealed that cannabis was the most common illicit drug detected in fatal MVA, being present in 6.8% of crashes.⁷ To gain a broader understanding of the changing prevalence of marijuana use in the United States, Shi⁸ conducted a database search of hospital discharges from 1997 to 2014, which revealed a 3.5-fold increase in average hospitalization rates per 1000 discharges for marijuana dependence and abuse. Given the retrospective study design, the methodology was not sufficient to determine the effect of dosing (eg, quantity of use) and chronicity on hospitalization rates, or the relationship between marijuana use and MVA. It also remains unclear whether the rise in hospitalization rates reflected a rise in usage. However, the authors did suggest that state policy relating to legalized medical marijuana or decriminalization laws did not contribute to their findings (Supplemental Digital Content 2, Table 1, <http://links.lww.com/AA/C462>).

Cannabis Use and Driving Impairment

Several studies have found acute marijuana use to be associated with a ≥ 2 -fold higher risk of crashing while driving a motor vehicle when compared to driving unimpaired.³⁷⁻⁴² In some cases, drivers under the influence of cannabis were more aware of their deficits and attempted to compensate by driving slower and taking less risks.⁴³⁻⁴⁷ However, these behaviors do not equate to a reduced risk of accidents. The deleterious cognitive and psychomotor effects of marijuana that increase with multitasking or task complexity cannot be ignored. Studies evaluating the effects of cannabinoids on driving ability have found that participants perform worse on divided-attention tasks, during situations with decision-making dilemmas, and during long monotonous drives followed by sudden changes requiring a quick reaction.^{44,45,47} The apparent detriment to driving ability as well as the correlation between acute marijuana use and MVA have been accounted for in our proposed framework (Supplemental Digital Content 1, Figure 1, <http://links.lww.com/AA/C461>).

Psychomotor effects related to acute cannabis use include increased lane weaving, steering wheel variability, and increased headway.⁴⁵⁻⁴⁸ These negative effects seem to be dose-dependent, worsening with higher doses.⁴⁹⁻⁵² The majority of psychomotor effects occur in the first 2 hours and dissipate within 3–6 hours.⁵³ Interestingly, few or none of these acute motor effects are found to be present in chronic users.⁵⁴ Light users acutely experience decreased attention and concentration for ≤ 6 hours, whereas persistent users do not experience this decline.⁵⁵ Persistent users are also less affected in performance accuracy during electroencephalogram testing.^{55,56} Policymakers must account for this evidence when drafting DUI legislation to maintain an adequate level of safety on public roadways without persecuting the unimpaired. This could potentially be accomplished by standardizing the screening protocols used to detect drivers operating motor vehicles under the influence of cannabis, and emphasizing psychomotor testing, because

it is possible that similar to the argument made for chronic opioid users, minor traffic violations can occur in marijuana users that are unrelated to impairment.

The effects of chronic marijuana use on safe driving also center on cognition. These effects include impaired decision making, concept formation, and planning.⁵⁷ Cognitive side effects can persist for long periods, with both regular cannabis users and chronic nonusers exhibiting decreased inhibition, working memory, and increased impulsivity for ≤ 20 hours after use.⁵⁸ There are conflicting data regarding the return to one's cognitive baseline after a period of abstinence.⁵⁸⁻⁶⁰ The study by Pope et al⁵⁹ suggests that cannabis-induced cognitive impairment is a temporary and reversible deficit, rather than an irreversible deficit that increases with duration of exposure. The study by Bolla et al⁶⁰ presented conflicting findings that instead suggest marijuana users may have persistent decision-making deficits and alterations in brain activity, with unclear evidence of a return to baseline after abstinence.

When alcohol is combined with marijuana, there is an increased risk of collision due to synergy affecting road tracking and lane weaving compared to when either alcohol or marijuana are used separately.^{49,61,62}

Marijuana use impairs driving ability by disrupting normal proprioception, coordination, and reaction time in addition to reducing sustained, divided, and selective attention.⁵⁶ Notably, the degree of impairment does not necessarily correlate with one's level of intoxication because occasional users are more affected at lower plasma levels of THC and for longer durations of time.^{55,56,63-65}

The psychomotor effects of combined opioid and cannabis use are not as clear. The current literature indicates that cannabis and opioid medications may act synergistically due to similarities in their intracellular signaling mechanisms.⁶⁶⁻⁶⁸ However, no studies were found that specifically investigated the psychomotor effects of these agents when used together. Driving under the influence of opioids alone is an issue that has been addressed by individual states. Current state law concerning driving under the influence of opioids is variable and often relies on prosecutorial discretion to provide protection of the driving public and prosecution of the truly impaired. Fourteen states define "under the influence" as "incapable of driving safely," 8 states define "under the influence" using the word "impaired," and 17 states have 0 tolerance policies, whereby body fluid levels of any amount of drug capable of impairing driving performance may be grounds for sanction. However, blood levels of opioids that cause impairment in all individuals have not been determined, and implied consent for toxicology testing of motorists differs from state to state.⁶⁹ Given the parallels between the 2, it seems likely that DUI policy will mirror several aspects of current driving under the influence of opioids policy.

There are a paucity of studies exploring the synergistic effects between benzodiazepines and cannabis, which has been emphasized in the opioid literature. Lile et al⁷⁰ conducted a small study which revealed that, although the effects of diazepam on the psychomotor changes caused by THC were limited, heart rate increased and mild sedative effects were observed (Supplemental Digital Content 3-4, Tables 2-3, <http://links.lww.com/AA/C463>, <http://links.lww.com/AA/C464>).

Current State of Marijuana Law

Traditionally, the US Food and Drug Administration is responsible for approving medications for public use; however, the widespread legalization of marijuana has come from the passing of legislation at the state as opposed to federal level. It began in 1996, when California allowed for the medical use of marijuana with the passing of Proposition 215. Since then, the legal use of medicinal marijuana has expanded to 28 other states, with 9 states legalizing marijuana for adult recreational use and 12 states decriminalizing nonmedical marijuana.¹ However, in the remaining states, marijuana possession is a misdemeanor or even a felony offense and, regardless of state law, remains illegal at a federal level. For this reason, many states that permit the use of medical marijuana prohibit patients from transporting marijuana across state lines. This lack of consistency between state and federal laws and among individual state laws is a source of confusion and possibly legal perilment for both patients and physicians.

It is worth mentioning that the legal issues surrounding the recommending and prescribing of marijuana are not insignificant. Recommending or prescribing medical marijuana may make the prescribers liable for the driving actions of their patients under the traditional physician-patient duty of care contract. This liability may even extend to the person and property of the patient as well as third parties, as outlined in a recent review on opioids and driving.⁶⁹ During our literature search, we could find no specific example whereby a physician was held liable for a patient DUI and having a subsequent accident. However, a review on the subject written by an attorney-physician found that case law supported the argument that physicians can be held liable by third parties when their prescribing practices fall short of standard of care and result in an injury or death to that party, including from MVA.⁸⁹

At the federal level, the Controlled Substances Act classifies marijuana, along with its cannabinoid components and derivatives, as Schedule I substances. The Schedule I classification is reserved for drugs with no currently accepted medical use and a high potential for abuse. Under federal law, Schedule I substances may only be dispensed and possessed by a federally approved research program requiring a federal and, in many states, a state research registration. Therefore, much about marijuana's medicinal effects remains unknown due to the considerable efforts that researchers must go through to comply with state and federal regulations to perform randomized clinical trials. Under federal law, physicians may only recommend medical marijuana to patients with qualifying medical illnesses and in some states certify them with such illnesses (which may or may not be supported by strong evidence), as opposed to writing a prescription for marijuana use.

The impact of marijuana being widely available has societal implications on the general population's ability to operate motor vehicles while DUIs.^{90,91} Yet a poorly delineated boundary exists between the legal use of marijuana and the possibility of motor impairment that may result (Table 1).

Current Policy and Process for DUI

Given the increasing number of states that have passed laws for medicinal and recreational use of marijuana, health care providers should be aware of marijuana's effects on public

Table 1. State Laws Concerning Recreation and Medicinal Marijuana Usage

Law	Applicable States
No Laws Legalizing Marijuana	AL, GA, ID, IN, IA, KS, KY, MS, MO, NE, NC, OK, SC, SD, TN, TX, UT, VA, WV, WI, WY
Medical Marijuana Legalized	AZ, AR, CT, DE, FL, HI, IL, LA, MD, MI, MN, MT, NH, NJ, NM, NY, ND, OH, PA, RI
Marijuana Legalized for Recreational and Medicinal Use	AK, CA, CO, DC, ME, MA, NV, OR, VT, ^a WA

^aSigned into law by Governor Phil Scott, effective July 1, 2018.

safety. Although it is too early to determine the long-term implications of legalizing marijuana, studies have shown an increasing trend toward DUIC in states that have marijuana laws.^{13,92,93} Johnson et al⁹² found that DUIC increased after legalization in California from 2007 to 2010 to 8.5% of the weekend, nighttime drivers, and in some jurisdictions, the rate was nearly 1 in 5. In Washington State, an analysis of blood toxicology results in those suspected to be driving impaired has shown an increase in the prevalence of THC and its main metabolite when comparing pre- versus postmarijuana legalization periods.⁴¹ In these studies, marijuana detection did not appear to be an incidental finding. Johnson et al⁹² found no increase in other illegal drugs, and there were few cases (n = 13) where drivers tested positive for both THC and alcohol, decreasing the probability of alcohol as a confounding factor. This increase in the number of motor vehicle operators DUIC warrants a closer look at the evaluation and screening processes used to determine the level of impairment in these drivers.

The process begins once an officer detects erratic driving or a traffic violation indicative of intoxication.⁹⁴ The officer then signals the vehicle to stop, and both parties pull over to the side of the road.⁹⁴ If the driver is suspected of DUI, then an alcohol breathalyzer test is administered to determine the blood alcohol concentration (BAC). In some instances, the BAC will not correlate with the level of impairment, increasing the suspicion of other intoxicating agents, including marijuana.⁹⁴ Currently, there is no noninvasive test to measure the level of marijuana intoxication, meaning that a blood sample needs to be tested. However, the ability of law enforcement officers to obtain a blood sample varies by location.

Depending on the state where the infraction occurs, there are different policies governing the ability of an officer to obtain a tissue or body fluid sample for testing.⁹¹ In some states, operating a motor vehicle on public roads implies informed consent for testing, while others require a warrant to obtain samples for testing.⁹¹

Testing for marijuana use is based on the detection of metabolites that appear after the peak and decline of blood THC levels after marijuana is smoked. About 10% of plasma THC is metabolized via cytochrome P450 into 11-hydroxy-THC (THC-OH) and carboxy-THC (TH-COOH), a psychoactive and nonpsychoactive compound, respectively.⁹⁵ The psychoactive component peaks first and then declines rapidly, but the nonpsychoactive component can persist for several hours.

Carboxy-THC is the compound commonly screened for in urine assays.⁹⁵ The results of the urine immunoassay are

Table 2. State Laws Concerning DUID

Law	Applicable States
Implied Consent to Toxicology Testing for All Motorists	
No implied consent ^a	MA, NJ, WV
Implied consent for toxicological testing in all circumstances	All states except AL, AK, MA, NJ, WV
Permit the forced taking of a specimen over the objection of a driver ^b	AK, CA, DE, FL, HI, IL, IA, LA, ME, MD, MI, MS, NE, NV, NH, NM, NY, NC, ND, OK, PA, SC, TX, VT, VA, WA, WI, WY, DC, PR
Criminal or enhanced penalties for refusal to submit a test	AR, IN, LA, MD, MN, NE, NM, OH, RI
Arrest for refusal to submit a test	NV
Standard of Impairment Used for DUID Conviction ^c	
Zero tolerance	AZ, DE, GA, IL, IN, IA, MI, MN, NV, NC, OH, PA, RI, SD, UT, VA, WI
Under the influence	All states except NY and TX
Incapacity	AL, AR, IL, KS, MD, NV, NM, ND, OK, PA, SD, VT, WI, WY
Impairment	AZ, FL, HI, IN, KY, MT, SC, VA

Abbreviation: DUID, driving under the influence of drugs.
^aAL and AK have no implied consent laws unless the accident involves serious injury or death.
^bMajority limited to a crash involving serious injury or death.
^cTX sets a standard of intoxication, which it defines as “not having the normal use of mental or physical faculties by reason of ingestion of a drug.”

confirmed by positive gas chromatography-mass spectrometry testing. The difficulty in screening for carboxy-THC is in the interpretation of the test results to determine whether a driver is impaired. The concentration of carboxy-THC in the urine does not necessarily correlate with acute impairment, especially in persistent users. This issue is further complicated by carboxy-THC being detectable in the urine for weeks despite abstinence from marijuana use and without acute impairment (Table 2).⁹⁵

DISCUSSION

This conceptual framework takes into account the influence of the proposed principal domains on DUIC (Supplemental Digital Content 1, Figure 1, <http://links.lww.com/AA/C461>). The framework proposes 4 domains: legalization, DUIC, impaired drivers, and MVA. With regard to legalization, the number of people involved in DUIC is expected to rise with the expanding utilization of cannabis for both medicinal and recreational purposes.¹ The currently available literature reveals 3 potential groups under which marijuana users DUIC fall. The first is comprised of infrequent users, who tend to demonstrate increased blood levels of THC along with significant psychomotor impairment. The second involves chronic users who demonstrate increased blood levels of THC with slight or no impairment. Finally, chronic users demonstrate increased levels of THC with persistent psychomotor deficits. The domain of impaired drivers is a potential point of regulatory action that can be influenced by state and federal policies and laws. Finally, MVA are the preventable outcomes that can be avoided by properly imposing limitations on impaired motor vehicle operators.

At this point in time, there is no widely accepted approach to regulating drivers under the influence of

Table 3. State Laws Concerning DUI/C

Applicable State(s)	Legal THC Limit
CO	Blood: 5.0 µg/L
IA	Urine THC-COOH: 50.0 µg/L
MT	Blood: 5.0 µg/L
NV	Urine THC: 10.0 µg/L Blood THC: 2.0 µg/L Urine THC-COOH: 15.0 µg/L Blood THC-COOH: 5.0 µg/L
OH	Urine THC: 10.0 µg/L Blood THC: 2.0 µg/L Urine THC-COOH: 35.0 µg/L Blood THC-COOH: 50.0 µg/L Urine THC-COOH with alcohol or drugs: 15.0 µg/L Blood THC-COOH with alcohol or drugs: 5.0 µg/L
PA	THC or THC-COOH: 1.0 µg/L in blood or urine
WA	5.0 µg/L in blood
AZ, DE, GA, IL, IN, MI, MN, NC, RI, SD, UT, VA, WI	Zero tolerance
All other states	No policy: no legally defined limit or zero tolerance policy

Abbreviations: DUI/C, driving under the influence of cannabis; THC, tetrahydrocannabinol; THC-COOH, carboxy-THC.

cannabis. Part of the problem stems from the inability of law enforcement officers to obtain tissue samples for testing because laws vary from state to state. In addition, there is no federal statutory limit for blood levels of THC while operating a motor vehicle, and individual states have been able to define their own limits within their own borders without consistency from state to state. Unless there are federal laws that establish implied consent, allow law enforcement officers to obtain specimens despite a motorist’s objections, and standardize the approach to testing, this issue will likely remain a barrier to a coherent policy (Table 3).

Although this problem may be new to the United States, European countries have been faced with these challenges for years. Sixteen countries in Europe have set legal nonzero THC concentrations at or above which drivers are prosecuted for driving under the influence of marijuana, ranging from 0.5 to 50.0 µg/L depending on whether blood or blood serum, or THC or THC-COOH, is tested for.⁹⁶ However, 1 issue that yet again raises problems with these policies is that there is a lack of scientific consensus to support the standardization of a set of screening protocols and the establishment of a set marker for level of impairment.

This may be due in part to the lack of linear correlation between THC levels in the blood and THC levels in the brain.⁹⁷ This is further complicated by the fact that marijuana’s metabolites are detectable in the blood many days after use, long after signs of impairment have disappeared.^{98,99} Finally, there is considerable individual variation concerning central nervous system effects based on the chronicity of use and other factors.¹⁰⁰ As mentioned earlier, persistent users can have high levels of THC in the blood while displaying subtle or no impairment.^{55,56} Given the equivocal evidence correlating specific blood levels of THC with psychomotor impairment, there may not be a place for a standardized federal limit of THC to indicate impairment. As noted previously, emphasis should be placed on

Table 4. Conceptual Framework Utilizing the Proposed Hypotheses to Investigate DUI/C

Hypothesis Source	Hypothesis
Wolff et al ⁹⁹	THC blood level of 5 µg/L if marijuana only is present and 3 µg/L threshold when detected in combination with alcohol
DRUID Project ¹⁰¹	The DRUID project has suggested that a THC blood level of 3.8 µg/L is equivalent to a blood alcohol concentration of 0.05%, which is the established legal limit in several European countries
Proposed conceptual framework	
Given this variation, alcohol and THC blood tests should be used in conjunction with a psychomotor evaluation conducted by a trained specialist who is able to identify different degrees of impairment in motor vehicle operators.	

Abbreviations: DUI/C, driving under the influence of cannabis; DRUID, driving under the influence of drugs; THC, tetrahydrocannabinol.

psychomotor tests to detect impairment, using blood or saliva testing only as a supplementary component to establish presence.

The DRUID project and an expert panel on drug-impaired driving reviewed the available evidence to develop recommendations on thresholds for blood THC levels. The DRUID project, based on roadside surveys, has suggested that a THC blood level of 3.8 µg/L is equivalent to a BAC of 0.05%, which is the established legal limit in several European countries (in the United States. Utah has passed legislation lowering the legal BAC limit from 0.08% to 0.05% as of the end of 2018).¹⁰¹ Wolff et al⁹⁹ have taken a different approach and recommended 2 different thresholds: a THC blood level of 5 µg/L if marijuana is the sole agent present and a lower 3 µg/L threshold when marijuana is detected in combination with alcohol.

Given this variation and the proposed conceptual framework, our hypothesis is that alcohol and THC blood tests can be used in conjunction with a psychomotor evaluation conducted by a trained specialist who is able to identify varying degrees of impairment in motor vehicle operators. With combinations of substances, it is more important to verify any impairment as opposed to impairment due to a specific causative agent, which may not be possible. Testing general psychomotor performance in a standardized method would be ideal, leveraging techniques from current existing sobriety tests (Table 4).

Rather than establishing a legal limit for THC in the blood, the standardization of psychomotor screening protocols can help to set the framework for DUI/C policy (Table 5).

The Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain, and Current Opioid Misuse Measurement are among several assessment tools created for the purpose of assessing risk for individuals who are prescribed opioids for the treatment of chronic pain.¹⁰²⁻¹⁰⁴ These screening assessments are often used in the office by primary care and pain physicians before prescribing opioids. This process helps to identify patients who may be at risk for aberrant medication-related behavior. Using these assessment tools, providers can make a determination as to the appropriateness of long-term opioid treatment. If opioids are deemed a potential treatment option for a patient, additional resources can be allotted for the monitoring and

Table 5. Recommendations for Screening for DUIC

DUIC Screening Method	Implementation
Prescription verification	Utilize local prescription drug monitoring program
Legal	Verify federal versus state law and jurisdiction
Surveillance	Obtain witness accounts, video recording of the event in question
Laboratory assessment	Measure blood levels of THC: THC blood level of <5 µg/L if marijuana is the sole agent, <3 µg/L if alcohol is present
Physical assessment	Administer a field sobriety test, preferably by a Drug Recognition Expert
Cognitive assessment	Test working memory, power of attention, and continuity of attention

These screening tools should be used together to determine sobriety. Abbreviations: DUIC, driving under the influence of cannabis; THC, tetrahydrocannabinol.

Table 6. Recommendations for Screening for Prescribing Cannabis

Cannabis Screening Tool	Practical Application
Prescription verification	Utilize local prescription drug monitoring program
Determine level of risk	Administer Opioid Risk Tool ¹⁰² or similar validated instrument to extrapolate for nonopioid substance abuse
Laboratory assessment	Administer oral swab or urine drug screen

If the urine drug screen is consistent with the local prescription drug monitoring program and the patient is deemed to be low risk, one can consider prescribing medical marijuana. If the patient is on opioids, a reduction in opioid dose should be considered, especially if the marijuana will be prescribed for pain.

management of that patient. This includes frequent random urine drug screens, short-term prescriptions, close follow-up, and designation of a proxy.

Although these tools stratify risk for abuse in general and may be adaptable for cannabis use, they have not been validated in this context. There are several important differences between medicinal marijuana and opioids, including legality, consequences of abuse, and the fact that physicians do not actually prescribe medical marijuana and follow patients to assess the risk:benefit ratio but instead write a letter of recommendation certifying that a patient has a medical condition that qualifies for medicinal marijuana use. Given the inherent risks of cannabis, the lack of medical oversight is inconsistent with the regulations governing the dispensation of analgesic medications with greater safety profiles such as adjuvants, muscle relaxants, and nonsteroidal anti-inflammatory drugs. The lack of consistent follow-up after initiation of treatment will also limit the generation of data regarding effectiveness in large-scale populations and inevitably result in some patients continuing and escalating use despite ineffectiveness and an unfavorable risk:benefit ratio.

The domain of DUIC within the proposed conceptual framework includes the acute effects of marijuana as well as potentially other substances. This is due to the fact that marijuana will likely be prescribed for patients with several different concurrent diseases, who will continue to experience pain even with treatment.¹⁰⁵ When one considers that even first-line medications only modestly alleviate pain in a small percentage of patients, it is likely that most medicinal marijuana users will utilize other medications that can depress the nervous

system, with 1 study finding that more than two-thirds of chronic patients were taking multiple prescriptions that carry additive effects, often from several drug categories.¹⁰⁶

For those receiving opioids, these cumulative risks are substantial. Between 6.2% and 39% of medicinal marijuana users also consume prescription opioids, which could lead to adverse additive or synergistic effects, although the required close supervision of chronic opioid users would hopefully mitigate some of the risks.^{107,108} Health care providers who prescribe medicinal marijuana often decrease the amount of opioids prescribed concurrently. A time-series analysis of medical marijuana laws in the United States from 1999 to 2010 showed that states with medical cannabis laws had a lower mean opioid overdose mortality rate compared to states without medical cannabis laws.¹⁰⁹ Therefore, the authors of this article advise similar precautions for prospective marijuana prescribers (Table 6).

As marijuana use continues to grow and establish a firm foothold in modern society, it is imperative that an infrastructure be created to help guide future laws and policies. Utilizing the principle domains of the legalization of marijuana, DUIC, driver impairment, and MVA, we hope to assist in establishing such a conceptual framework. ■

DISCLOSURES

Name: Robert M. Chow, MD.

Contribution: This author helped develop the outline and researched the use and abuse of marijuana, as well as the effects of chronic opioid usage. This author also helped synthesize and edit the information into its current form.

Name: Bryan Marascalchi, MD.

Contribution: This author helped research the epidemiology and legal aspects of marijuana usage. This author also helped write the methods section.

Name: Winfred B. Abrams, MD.

Contribution: This author helped research the increased access to marijuana, implications and acute psychomotor and cognitive effects of marijuana usage.

Name: Nathalie A. Peiris, MD.

Contribution: This author helped review societal implications, psychomotor effects, and driving under the influence of drugs policy.

Name: Charles A. Odonkor, MD.

Contribution: This author helped research the increased access to marijuana, implications, and acute psychomotor and cognitive effects of marijuana usage.

Name: Steven P. Cohen, MD.

Contribution: This author helped edit the manuscript and advised in various aspects to help improve the content.

This manuscript was handled by: Honorio T. Benzon, MD.

REFERENCES

1. National Conference of States Legislatures. State medical marijuana laws. Available at: <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>. Accessed June 4, 2017.
2. The US Department of Justice. Justice Department Issues Memo on Marijuana Enforcement. Available at: <https://www.justice.gov/opa/pr/justice-department-announces-update-marijuana-enforcement-policy>. Accessed April 11, 2018.
3. The US Department of Justice. Justice Department Announces Update to Marijuana Enforcement Policy. Available at: <https://www.justice.gov/opa/pr/justice-department-issues-memo-marijuana-enforcement>. Accessed April 11, 2018.
4. Substance Abuse and Mental Health Services Administration. Results from the 2015 National Survey on Drug Use and Health: Detailed Tables. 2015. Available at: [https://www.samhsa.gov/data/sites/default/files/NSDUH-DeTabs-2015/NSDUH-DeTabs-2015.htm#tab1-16a](https://www.samhsa.gov/data/sites/default/files/NSDUH-DeTabs-2015/NSDUH-DeTabs-2015/NSDUH-DeTabs-2015.htm#tab1-16a). Accessed June 15, 2017.

5. National Institute on Drug Abuse. Monitoring the Future Study: Trends in Prevalence of Various Drugs. Available at: <https://www.drugabuse.gov/trends-statistics/monitoring-future/monitoring-future-study-trends-in-prevalence-various-drugs>. Accessed June 15, 2017.
6. Brady JE, Li G. Trends in alcohol and other drugs detected in fatally injured drivers in the United States, 1999-2010. *Am J Epidemiol*. 2014;179:692-699.
7. Biecheler MB, Peytavin JF, Facy F, Martineau H; SAM Group. SAM survey on "drugs and fatal accidents": search of substances consumed and comparison between drivers involved under the influence of alcohol or cannabis. *Traffic Inj Prev*. 2008;9:11-21.
8. Shi Y. Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever. *Drug Alcohol Depend*. 2017;173:144-150.
9. Valen A, Bogstrand ST, Vindenes V, Gjerde H. Increasing use of cannabis among arrested drivers in Norway. *Traffic Inj Prev*. 2017;18:801-806.
10. Institóris L, Hidvégi E, Dobos A, et al. The role of illicit, licit, and designer drugs in the traffic in Hungary. *Forensic Sci Int*. 2017;275:234-241.
11. Rooney B, Gouveia GJ, Isles N, et al. Drugged drivers blood concentrations in England and Wales prior to the introduction of per se limits. *J Anal Toxicol*. 2017;41:140-145.
12. Lemos NP, San Nicolas AC, Volk JA, Ingle EA, Williams CM. Driving under the influence of marijuana versus driving and dying under the influence of marijuana: a comparison of blood concentrations of δ 9-tetrahydrocannabinol, 11-hydroxy- δ 9-tetrahydrocannabinol, 11-nor-9-carboxy- δ 9-tetrahydrocannabinol and other cannabinoids in arrested drivers versus deceased drivers. *J Anal Toxicol*. 2015;39:588-601.
13. Couper FJ, Peterson BL. The prevalence of marijuana in suspected impaired driving cases in Washington State. *J Anal Toxicol*. 2014;38:569-574.
14. Bezemer KD, Smink BE, van Maanen R, Verschraagen M, de Gier JJ. Prevalence of medicinal drugs in suspected impaired drivers and a comparison with the use in the general Dutch population. *Forensic Sci Int*. 2014;241:203-211.
15. Bogstrand ST, Gjerde H. Which drugs are associated with highest risk for being arrested for driving under the influence? A case-control study. *Forensic Sci Int*. 2014;240:21-28.
16. Gjerde H, Sousa TR, De Boni R, et al. A comparison of alcohol and drug use by random motor vehicle drivers in Brazil and Norway. *Int J Drug Policy*. 2014;25:393-400.
17. Li G, Brady JE, Chen Q. Drug use and fatal motor vehicle crashes: a case-control study. *Accid Anal Prev*. 2013;60:205-210.
18. Gjerde H, Christophersen AS, Normann PT, Assum T, Oiestad EL, Mørland J. Norwegian roadside survey of alcohol and drug use by drivers (2008-2009). *Traffic Inj Prev*. 2013;14:443-452.
19. Vindenes V, Strand DH, Kristoffersen L, Boix F, Mørland J. Has the intake of THC by cannabis users changed over the last decade? Evidence of increased exposure by analysis of blood THC concentrations in impaired drivers. *Forensic Sci Int*. 2013;226:197-201.
20. Institóris L, Tóth AR, Molnár A, Arok Z, Kereszty E, Varga T. The frequency of alcohol, illicit and licit drug consumption in the general driving population in South-East Hungary. *Forensic Sci Int*. 2013;224:37-43.
21. Gómez-Talegón T, Fierro I, González-Luque JC, Colás M, López-Rivadulla M, Javier Álvarez F. Prevalence of psychoactive substances, alcohol, illicit drugs, and medicines, in Spanish drivers: a roadside study. *Forensic Sci Int*. 2012;223:106-113.
22. Vindenes V, Jordbru D, Knapskog AB, et al. Impairment based legislative limits for driving under the influence of non-alcohol drugs in Norway. *Forensic Sci Int*. 2012;219:1-11.
23. Steentoft A, Simonsen KW, Linnert K. The frequency of drugs among Danish drivers before and after the introduction of fixed concentration limits. *Traffic Inj Prev*. 2010;11:329-333.
24. Senna MC, Augsburger M, Aebi B, et al. First nationwide study on driving under the influence of drugs in Switzerland. *Forensic Sci Int*. 2010;198:11-16.
25. Holmgren A, Holmgren P, Kugelberg FC, Jones AW, Ahlner J. Predominance of illicit drugs and poly-drug use among drug-impaired drivers in Sweden. *Traffic Inj Prev*. 2007;8:361-367.
26. Khiabani HZ, Bramness JG, Børneboe A, Mørland J. Relationship between THC concentration in blood and impairment in apprehended drivers. *Traffic Inj Prev*. 2006;7:111-116.
27. Laumon B, Gadegbeku B, Martin JL, Biecheler MB; SAM Group. Cannabis intoxication and fatal road crashes in France: population based case-control study. *BMJ*. 2005;331:1371.
28. Augsburger M, Donzé N, Ménétrey A, et al. Concentration of drugs in blood of suspected impaired drivers. *Forensic Sci Int*. 2005;153:11-15.
29. Brookoff D, Cook CS, Williams C, Mann CS. Testing reckless drivers for cocaine and marijuana. *N Engl J Med*. 1994;331:518-522.
30. Robertson RD, Mainegra Hing M, Pashley CR, Brown SW, Vanlaar WGM. Prevalence and trends of drugged driving in Canada. *Accid Anal Prev*. 2017;99:236-241.
31. Christophersen AS, Gjerde H. Prevalence of alcohol and drugs among car and van drivers killed in road accidents in Norway: an overview from 2001 to 2010. *Traffic Inj Prev*. 2014;15:523-531.
32. Asbridge M, Mann R, Cusimano MD, et al. Cannabis and traffic collision risk: findings from a case-crossover study of injured drivers presenting to emergency departments. *Int J Public Health*. 2014;59:395-404.
33. Legrand SA, Silverans P, de Paeppe P, Buylaert W, Verstraete AG. Presence of psychoactive substances in injured Belgian drivers. *Traffic Inj Prev*. 2013;14:461-468.
34. Wiese Simonsen K, Steentoft A, Bernhoft IM, Hels T, Rasmussen BS, Linnert K. Psychoactive substances in seriously injured drivers in Denmark. *Forensic Sci Int*. 2013;224:44-50.
35. Giovanardi D, Castellana CN, Pisa S, et al. Prevalence of abuse of alcohol and other drugs among injured drivers presenting to the emergency department of the University Hospital of Modena, Italy. *Drug Alcohol Depend*. 2005;80:135-138.
36. Bédard M, Dubois S, Weaver B. The impact of cannabis on driving. *Can J Public Health*. 2007;98:6-11.
37. Asbridge M, Hayden JA, Cartwright JL. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ*. 2012;344:e536.
38. Li MC, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. Marijuana use and motor vehicle crashes. *Epidemiol Rev*. 2012;34:65-72.
39. Baldock M. Cannabis and the risk of crash involvement. *Flinders J Law Reform*. 2008;10:795-814.
40. Bates MN, Blakely TA. Role of cannabis in motor vehicle crashes. *Epidemiol Rev*. 1999;21:222-232.
41. Beirness DK, Simpson HM, Williams AF. Role of cannabis and benzodiazepines in motor vehicle crashes. *Transport Res Circ*. 2006;E-C096:12-21.
42. Ramaekers JG, Berghaus G, van Laar M, Drummer OH. Dose related risk of motor vehicle crashes after cannabis use. *Drug Alcohol Depend*. 2004;73:109-119.
43. Lamers CT, Ramaekers JG. Visual search and urban driving under the influence of marijuana and alcohol. *Hum Psychopharmacol*. 2001;16:393-401.
44. Smiley A. Marijuana: on-road and driving simulator studies. In: Kalant H, Corrigal W, Hall W, Smart, RG, eds. *The Health Effects of Cannabis*. Toronto: Centre for Addiction and Mental Health; 1999:173-191.
45. Lenné MG, Dietze PM, Triggs TJ, Walmsley S, Murphy B, Redman JR. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. *Accid Anal Prev*. 2010;42:859-866.
46. Ramaekers JG, Robbe HW, O'Hanlon JF. Alcohol, and actual driving performance. *Hum Psychopharmacol*. 2000;15:551-558.
47. Ronen A, Gershon P, Drobiner H, et al. Effects of THC on driving performance, physiological state and subjective feelings relative to alcohol. *Accid Anal Prev*. 2008;40:926-934.
48. Ménétrey A, Augsburger M, Favrat B, et al. Assessment of driving capability through the use of clinical and psychomotor tests in relation to blood cannabinoid levels following oral administration of 20 mg dronabinol or of a cannabis decoction made with 20 or 60 mg Delta9-THC. *J Anal Toxicol*. 2005;29:327-338.

49. Robbe H. Marijuana's impairing effects on driving are moderate when taken alone but severe when combined with alcohol. *Hum Psychopharmacol*. 1998;13:70–78.
50. Kurtzthaler I, Hummer M, Miller C, et al. Effect of cannabis use on cognitive functions and driving ability. *J Clin Psychiatry*. 1999;60:395–399.
51. Sexton BF, Tunbridge RJ, Brook-Carter PG, et al. The influence of cannabis on driving. *TRL Report*. 2000;477:106.
52. Ramaekers JG, Kautert G, van Ruitenbeek P, Theunissen EL, Schneider E, Moeller MR. High-potency marijuana impairs executive function and inhibitory motor control. *Neuropsychopharmacology*. 2006;31:2296–2303.
53. Neavyn MJ, Blohm E, Babu KM, Bird SB. Medical marijuana and driving: a review. *J Med Toxicol*. 2014;10:269–279.
54. Schwoppe DM, Bosker WM, Ramaekers JG, Gorelick DA, Huestis MA. Psychomotor performance, subjective and physiological effects and whole blood Δ^9 -tetrahydrocannabinol concentrations in heavy, chronic cannabis smokers following acute smoked cannabis. *J Anal Toxicol*. 2012;36:405–412.
55. Hart CL, van Gorp W, Haney M, Foltin RW, Fischman MW. Effects of acute smoked marijuana on complex cognitive performance. *Neuropsychopharmacology*. 2001;25:757–765.
56. Hart CL, Ilan AB, Gevins A, et al. Neurophysiological and cognitive effects of smoked marijuana in frequent users. *Pharmacol Biochem Behav*. 2010;96:333–341.
57. Bondallaz P, Favrat B, Chtioui H, Fornari E, Maeder P, Giroud C. Cannabis and its effects on driving skills. *Forensic Sci Int*. 2016;268:92–102.
58. Price JW. Marijuana and workplace safety: an examination of urine drug tests. *J Addict Dis*. 2014;33:24–27.
59. Pope HG Jr, Gruber AJ, Hudson JL, Huestis MA, Yurgelun-Todd D. Cognitive measures in long-term cannabis users. *J Clin Pharmacol*. 2002;42:415–475.
60. Bolla KI, Eldreth DA, Matochik JA, Cadet JL. Neural substrates of faulty decision-making in abstinent marijuana users. *Neuroimage*. 2005;26:480–492.
61. Dubois S, Mullen N, Weaver B, Bédard M. The combined effects of alcohol and cannabis on driving: impact on crash risk. *Forensic Sci Int*. 2015;248:94–100.
62. Sayer G, Ialomiteanu A, Stoduto G, et al. Increased collision risk among drivers who report driving after using alcohol and after using cannabis. *Can J Public Health*. 2014;105:e92–e93.
63. Hunault CC, Mensinga TT, Koen BE, et al. Cognitive and psychomotor effects in males after smoking a combination of tobacco and cannabis containing up to 69 mg delta-9-tetrahydrocannabinol. *Psychopharmacology*. 2009;204:85–94.
64. Battistella G, Fornari E, Thomas A, et al. Weed or wheel! FMRI, behavioural, and toxicological investigations of how cannabis smoking affects skills necessary for driving. *PLoS One*. 2013;8:e52545.
65. Bosker WM, Kuypers KP, Theunissen EL, et al. Medicinal $\Delta(9)$ -tetrahydrocannabinol (dronabinol) impairs on-the-road driving performance of occasional and heavy cannabis users but is not detected in Standard Field Sobriety Tests. *Addiction*. 2012;107:1837–1844.
66. Welch SP, Eads M. Synergistic interactions of endogenous opioids and cannabinoid systems. *Brain Res*. 1999;848:183–190.
67. Welch SP, Thomas C, Patrick GS. Modulation of cannabinoid-induced antinociception after intracerebroventricular versus intrathecal administration to mice: possible mechanisms for interaction with morphine. *J Pharmacol Exp Ther*. 1995;272:310–321.
68. Pugh G Jr, Welch SP, Bass PP. Modulation of free intracellular calcium and cAMP by morphine and cannabinoids, alone and in combination in mouse brain and spinal cord synaptosomes. *Pharmacol Biochem Behav*. 1994;49:1093–1100.
69. Wilhelmi BG, Cohen SP. A framework for “driving under the influence of drugs” policy for the opioid using driver. *Pain Physician*. 2012;15:ES215–ES230.
70. Lile JA, Kelly TH, Hays LR. Separate and combined effects of the GABAA positive allosteric modulator diazepam and Δ^9 -THC in humans discriminating Δ^9 -THC. *Drug Alcohol Depend*. 2014;143:141–148.
71. Ilan AB, Smith ME, Gevins A. Effects of marijuana on neurophysiological signals of working and episodic memory. *Psychopharmacology (Berl)*. 2004;176:214–222.
72. Grant JE, Chamberlain SR, Schreiber L, Odlaug BL. Neuropsychological deficits associated with cannabis use in young adults. *Drug Alcohol Depend*. 2012;121:159–162.
73. Auer R, Vittinghoff E, Yaffe K, et al. Association between lifetime marijuana use and cognitive function in middle age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. *JAMA Intern Med*. 2016;176:352–361.
74. Conroy DA, Kurth ME, Brower KJ, Strong DR, Stein MD. Impact of marijuana use on self-rated cognition in young adult men and women. *Am J Addict*. 2015;24:160–165.
75. Crane NA, Schuster RM, Fusar-Poli P, Gonzalez R. Effects of cannabis on neurocognitive functioning: recent advances, neurodevelopmental influences, and sex differences. *Neuropsychol Rev*. 2013;23:117–137.
76. Herrmann ES, Cone EJ, Mitchell JM, et al. Non-smoker exposure to secondhand cannabis smoke II: effect of room ventilation on the physiological, subjective, and behavioral/cognitive effects. *Drug Alcohol Depend*. 2015;151:194–202.
77. Metrik J, Aston ER, Kahler CW, Rohsenow DJ, McGeary JE, Knopik VS. Marijuana's acute effects on cognitive bias for affective and marijuana cues. *Exp Clin Psychopharmacol*. 2015;23:339–350.
78. Curran HV, Brignell C, Fletcher S, Middleton P, Henry J. Cognitive and subjective dose-response effects of acute oral delta 9-tetrahydrocannabinol (THC) in infrequent cannabis users. *Psychopharmacology (Berl)*. 2002;164:61–70.
79. Weinstein A, Brickner O, Lerman H, et al. A study investigating the acute dose-response effects of 13 mg and 17 mg delta 9-tetrahydrocannabinol on cognitive-motor skills, subjective and autonomic measures in regular users of marijuana. *J Psychopharmacol*. 2008;22:441–451.
80. Desrosiers NA, Ramaekers JG, Chauchard E, Gorelick DA, Huestis MA. Smoked cannabis' psychomotor and neurocognitive effects in occasional and frequent smokers. *J Anal Toxicol*. 2015;39:251–261.
81. Arterberry BJ, Treloar HR, Smith AE, Martens MP, Pedersen SL, McCarthy DM. Marijuana use, driving, and related cognitions. *Psychol Addict Behav*. 2013;27:854–860.
82. Solowij N, Stephens RS, Roffman RA, et al; Marijuana Treatment Project Research Group. Cognitive functioning of long-term heavy cannabis users seeking treatment. *JAMA*. 2002;287:1123–1131.
83. Pope HG Jr, Gruber AJ, Hudson JL, Huestis MA, Yurgelun-Todd D. Neuropsychological performance in long-term cannabis users. *Arch Gen Psychiatry*. 2001;58:909–915.
84. Yücel M, Solowij N, Respondek C, et al. Regional brain abnormalities associated with long-term heavy cannabis use. *Arch Gen Psychiatry*. 2008;65:694–701.
85. Battistella G, Fornari E, Annoni JM, et al. Long-term effects of cannabis on brain structure. *Neuropsychopharmacology*. 2014;39:2041–2048.
86. Thames AD, Kuhn TP, Williamson TJ, Jones JD, Mahmood Z, Hammond A. Marijuana effects on changes in brain structure and cognitive function among HIV+ and HIV- adults. *Drug Alcohol Depend*. 2017;170:120–127.
87. Eldreth DA, Matochik JA, Cadet JL, Bolla KI. Abnormal brain activity in prefrontal brain regions in abstinent marijuana users. *Neuroimage*. 2004;23:914–920.
88. Matochik JA, Eldreth DA, Cadet JL, Bolla KI. Altered brain tissue composition in heavy marijuana users. *Drug Alcohol Depend*. 2005;77:23–30.
89. Edersheim JG, Stern TA. Liability associated with prescribing medications. *Prim Care Companion J Clin Psychiatry*. 2009;11:115–119.
90. West T. Driving With Cannabis in a Vehicle. National Conference of State Legislatures. Available at: http://www.ncsl.org/Portals/1/Documents/transportation/Driving_With_Cannabis_in_Vehicle.pdf. Accessed June 4, 2017.
91. Walsh JM. A State-by-State Analysis of Laws Dealing With Driving Under the Influence of Drugs. Available at: <https://www.nhtsa.gov/staticfiles/nti/pdf/811236.pdf>. Accessed June 12, 2017.
92. Johnson MB, Kelley-Baker T, Voas RB, Lacey JH. The prevalence of cannabis-involved driving in California. *Drug Alcohol Depend*. 2012;123:105–109.

93. Salomonsen-Sautel S, Min SJ, Sakai JT, Thurstone C, Hopfer C. Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado. *Drug Alcohol Depend.* 2014;140:137–144.
94. Page T. The Drug Recognition Expert (DRE) Response to the Drug Impaired Driver. Available at: <http://www.ndaa.org/pdf/The%20Drug%20Recognition%20Expert%20Page%20article.pdf>. Accessed June 4, 2017.
95. Phillips JA, Holland MG, Baldwin DD, et al. Marijuana in the workplace: guidance for occupational health professionals and employers: Joint Guidance Statement of the American Association of Occupational Health Nurses and the American College of Occupational and Environmental Medicine. *Workplace Health Saf.* 2015;63:139–164.
96. Wong K, Brady JE, Li G. Establishing legal limits for driving under the influence of marijuana. *Inj Epidemiol.* 2014;1:26.
97. Mura P, Kintz P, Dumestre V, Raul S, Hauet T. THC can be detected in brain while absent in blood. *J Anal Toxicol.* 2005;29:842–843.
98. Bergamaschi MM, Karschner EL, Goodwin RS, et al. Impact of prolonged cannabinoid excretion in chronic daily cannabis smokers' blood on per se drugged driving laws. *Clin Chem.* 2013;59:519–526.
99. Wolff K, Brimblecombe R, Forfar JC, et al. *Driving Under the Influence of Drugs: Report from the Expert Panel on Drug Driving.* London: Department for Transport; 2013.
100. Fabritius M, Favrat B, Chtioui H, et al. THCCOOH concentrations in whole blood: are they useful in discriminating occasional from heavy smokers? *Drug Test Anal.* 2014;6:155–163.
101. Schulze H, Schumacher M, Urmeew R, et al. Driving under the influence of drugs, alcohol and medicine in Europe: findings from the DRUID project. *European Monitoring Centre for Drugs and Drug Addiction.* Luxembourg: Publications office of the European Union; 2012.
102. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med.* 2005;6:432–442.
103. Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. *Pain.* 2004;112:65–75.
104. Butler SF, Budman SH, Fernandez KC, et al. Development and validation of the current opioid misuse measure. *Pain.* 2007;130:144–156.
105. Nunberg H, Kilmer B, Pacula RL, Burgdorf J. An analysis of applicants presenting to a medical marijuana specialty practice in California. *J Drug Policy Anal.* 2011;4:1.
106. Giummarra MJ, Gibson SJ, Allen AR, Pichler AS, Arnold CA. Polypharmacy and chronic pain: harm exposure is not all about the opioids. *Pain Med.* 2015;16:472–479.
107. Reisfield GM, Wasan AD, Jamison RN. The prevalence and significance of cannabis use in patients prescribed chronic opioid therapy: a review of the extant literature. *Pain Med.* 2009;10:1434–1441.
108. Rudisill TM, Zhu M, Kelley GA, Pilkerton C, Rudisill BR. Medication use and the risk of motor vehicle collisions among licensed drivers: a systematic review. *Accid Anal Prev.* 2016;96:255–270.
109. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. *JAMA Intern Med.* 2014;174:1668–1673.