Medical Use and Health Effects of Cannabis

Joint Commission on Health Care
October 17, 2017 Meeting

Andrew Mitchell

Senior Health Policy Analyst

Study Mandate*

- Medical use of cannabis: House Courts of Justice requested by letter that the JCHC study therapeutic and detrimental side effects of THC-A and CBD oils
- Health effects of cannabis: Delegate Marshall requested via HJR 578 that the JCHC examine existing data on the health effects of cannabis
- Both studies were agreed to by JCHC members at the May 23, 2017 work plan meeting

* see slides 47-50 of the Appendix for further detail

Background – Terms and Definitions*

- Cannabis: generic term for products of the *Cannabis sativa* L plant
- Cannabinoids: pharmacologically active constituents of cannabis (e.g., Cannabidiol [CBD]; Δ^9-tetrahydrocannabinol [THC]†)
  - THC-A: precursor to THC that, when exposed to heat, changes (decarboxylates) into THC
- Marijuana: dried mixture of cannabis leaves and flowers
- Cannabis-related legislation
  - Decriminalization: policies that do not define possession for personal use or casual/nonmonetary distribution as a criminal offense
  - Medical Marijuana Law (MML): law removing state penalties for the use of marijuana for medicinal purposes under specified conditions
  - Cannabidiol Oil Law (COL): law permitting the use only of cannabis-derived CBD oil for medical purposes under specified conditions
    - Virginia's COL (Virginia Code §54.1-3408.3; 2015) provides an affirmative defense for use of CBD oil for intractable epilepsy; §54.1-3408.3 also provides an affirmative defense for use of "THC-A oil"
  - Recreational Marijuana Law (RML)/legalization: policies that remove criminal and civil penalties for the possession, use, and supply of marijuana for recreational purposes
- CBD oil (§54.1-3408.3): Cannabis plant extract containing: ≥15% CBD; ≤ 5% THC
- THC-A oil (§54.1-3408.3): Cannabis plant extract containing: ≥15% THC-A; ≤ 5% THC
- Excipient: inactive substance serving as a vehicle or medium for an active substance

† CBD and THC are also referred to as phytocannabinoids

Background – State Laws on Medical and non-Medical Use of Cannabis

Source: Adapted from NORML

Medicalized Cannabis Law Status:

MML: Fully Operational

MML: Not Yet Fully Operational

COL: Fully Operational

COL: Not Operational

★ Recreational Marijuana Law * see slides 51-53 of the Appendix for further detail

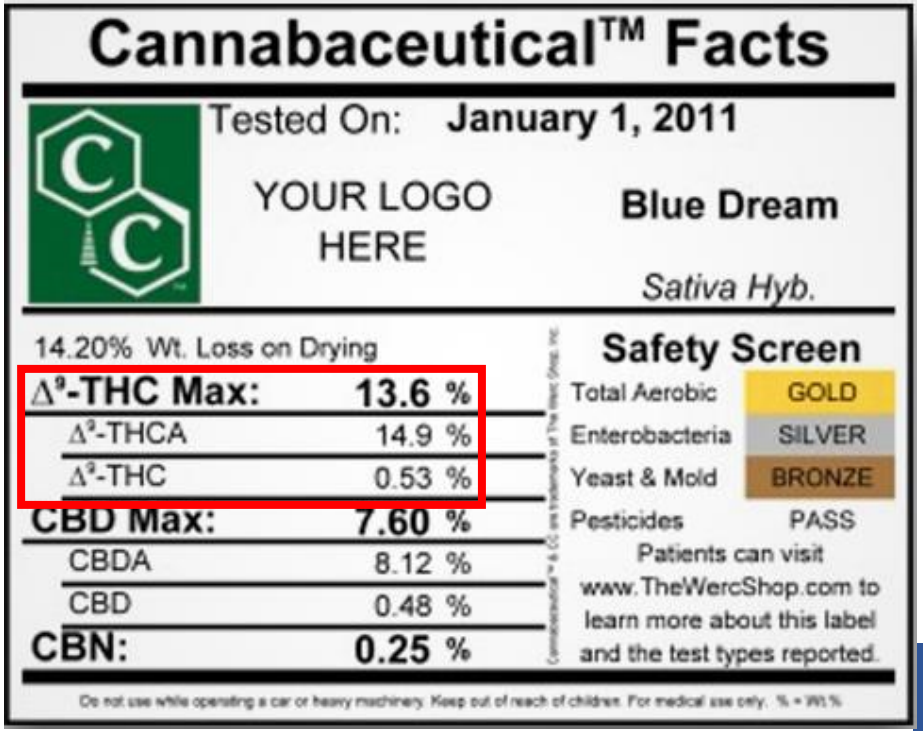
Medical Use of Cannabis

THC-A and CBD – Are They Psychoactive?

- Because neither THC-A nor CBD are “intoxicating”, they are traditionally considered non-psychoactive
- CBD interacts directly with the CB1 cannabinoid receptor in therapeutically relevant ways and there is evidence that it attenuates THC's psychoactive effects

- Decarboxylation of THC-A results in THC – a psychoactive cannabinoid that is intoxicating
  - Commonly used formula to calculate maximum potential THC is:

    0.877*%(THC-A) + %THC



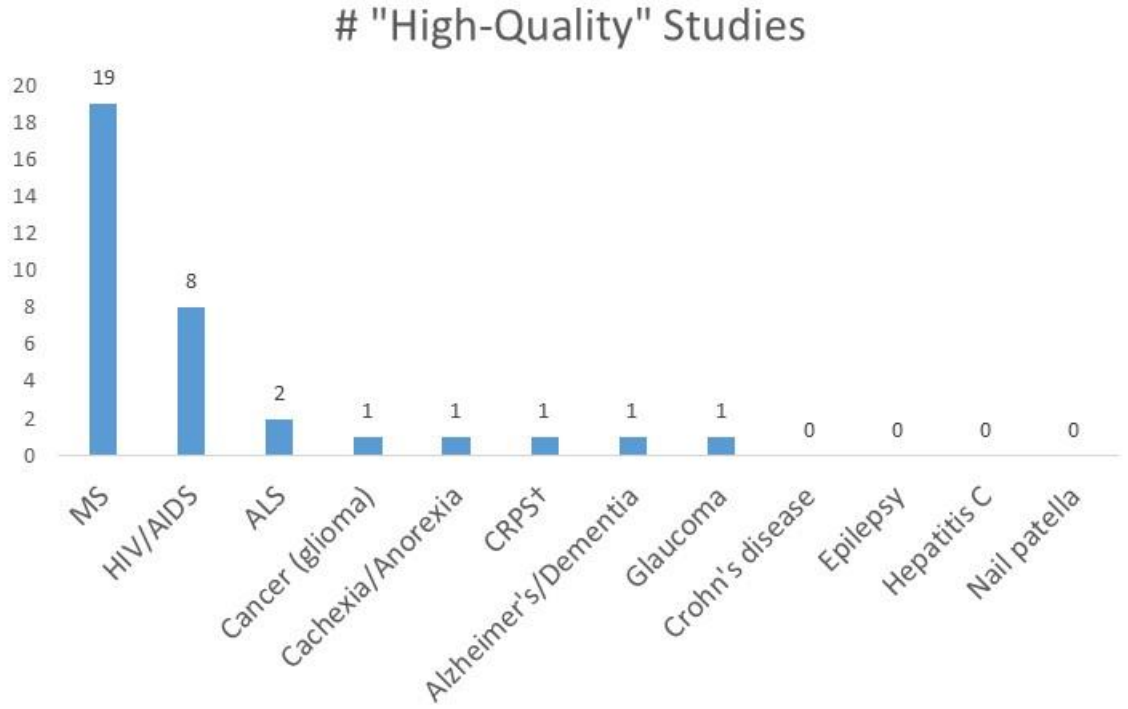
THC-A and CBD Oils – Psychoactive Effects*

- Psychoactive effects of CBD oil will be limited to psychoactive effects from 5% THC if THC is defined as maximum potential THC (if not, processors could add additional THC-A)
  - For CBD oil, DHP has indicated that it will interpret 5% THC as 5% *maximum potential* THC
- Psychoactive effects of THC-A oil may exceed psychoactive effects from 5% THC because:
  - Significant decarboxylation can occur if THC not stored at cold temperatures/away from sunlight
    - DHP administrative regulations (18 VAC 110-60) do not specify conditions under which processed oils awaiting sale must be stored
  - Consumers of THC-A oil products can easily promote decarboxylation of THC-A into THC, such as incorporating into baked goods or smoking
    - If THC-A is fully decarboxylated, THC-A could contain up to 18% maximum potential THC
    - Some MML States (e.g., LA, OH, PA) prohibit smoking of medical cannabis

* see slides 53-54 of the Appendix for further detail

Cannabis for Medical Use – Therapeutic Effects

- Of “high-quality” studies examining therapeutic effects of cannabinoids and reviewed recently by the National Academies, the vast majority relates to four conditions: chronic pain, nausea/vomiting (associated with chemotherapy), Multiple Sclerosis (MS) and HIV/AIDS
- Of the conditions/symptoms under consideration in 2016 by the House Courts of Justice for medical use of THC-A and CBD oils:
  - Significantly less research has been done on most
  - 60% of reviewed studies have assessed THC and /or CBD cannabinoids
  - 23% have assessed synthetic THC
  - 17% have assessed cannabis flower
  - None have assessed THC-A



Conditions Under Consideration by House Courts of Justice

† CRPS: Complex Regional Pain Syndrome

Source: National Academies of Medicine, Science & Engineering (2017)

Cannabis for Medical Use – Therapeutic Effects (2)

- Strong evidence of cannabis effectiveness:

Effect/Condition	Cannabis Flower	Cannabinoids		
		Unspecified	THC	CBD
Anti-emetics for chemotherapy-induced nausea/vomiting		x		
MS spasticity symptoms (patient-reported)		x		
Treatment of chronic pain in adults	x			

- Moderate evidence of cannabis effectiveness:

Effect/Condition	Cannabis Flower	Cannabinoids		
		Unspecified	THC	CBD
Short-term sleep outcomes associated with: MS, sleep apnea, fibromyalgia, chronic pain			x	x

- Limited evidence of cannabis effectiveness:

Effect/Condition	Cannabis Flower	Cannabinoids		
		Unspecified	THC	CBD
Appetite/weight loss associated with HIV/AIDS	x	x		
MS spasticity symptoms (clinician-measured)		x		
PTSD symptoms			x	x
Anxiety symptoms				x
Tourette syndrome			x	

Effect/Condition in purple: related to conditions under consideration by House Courts of Justice

Source: National Academies (2017)

Cannabis for Medical Use – Therapeutic Effects (3)

- Insufficient evidence† of cannabis effectiveness:

Effect/Condition	Cannabis Flower	Cannabinoids		
		Unspecified	THC	CBD
ALS symptoms		x		
Cancer-associated anorexia cachexia; anorexia nervosa		x		
Cancers, including glioma		x		
Dystonia			x	x
Epilepsy (Currently sole condition approved for cannabis oil use in VA)		x		
Huntington's disease symptoms		x		
Irritable bowel syndrome			x	
Parkinson's disease symptoms		x		
Spasticity in patients with spinal cord paralysis		x		
Abstinence from addictive substances		x		
Schizophrenia		x		

- Limited evidence of cannabis *ineffectiveness*:

Effect/Condition	Cannabis Flower	Cannabinoids		
		Unspecified	THC	CBD
Glaucoma intraocular pressure		x		
Depressive symptoms associated with chronic pain, MS			x	x
Symptoms associated with dementia		x		

† Insufficient evidence to support or refute existence of associations. Effect/Condition in purple: related to conditions under consideration by House Courts of Justice. Source: National Academies (2017)

Detrimental Side Effects of THC and CBD*

- Two reviews have found CBD to be generally well-tolerated and safe at high doses and with chronic use, although research on THC-A is minimal
- The majority of evidence on adverse effects of cannabinoids relates to therapeutic products containing THC or THC combined with CBD
- Cannabinoids have been found to be significantly associated with a higher risk of Adverse Events (AEs) – including serious AEs – compared to placebo

Disorder	2008 review	2015 meta-analysis
Eye	X	X
Gastrointestinal	X	X
General	X	X
Metabolism/Nutrition		X
Nervous System	X	X
Psychiatric	X	X
Renal/Urinary		X

Sources: Wang (2008); Whiting (2015)

- Among the 31 MML States, some have established standardized procedures for documenting and reporting of AEs by dispensers, practitioners and/or patients (e.g., MD, MN, NY, OH, PA)
- 18 VAC 110-60 does not include reporting requirements or procedures for reporting of AEs

* see slide 55 in the Appendix for further detail

THC – Interactions with Drugs

- Cannabis does not appear to be contra-indicated for other drugs
- There is evidence of interactions between cannabis (marijuana, cannabinoids) and other drugs, resulting in amplified or attenuated effects for either cannabis or the other drugs

Interaction	# Drugs:	
	Yes	Possible
Increased THC effect	0	3
Increased Central Nervous System depressant effect	4	1
Increased concomitant drug effect	0	7
Decreased concomitant drug effect	0	5

Source: Colorado Department of Public Health and Environment (CDPHE) (2016)

- 18 VAC 110-60 requires that dispensers of cannabis oils query the Prescription Monitoring Program (PMP) to ensure that the patient registration is valid and verify date/quantity of the last cannabis oil dispensing, but there is no legislative requirement that a pharmacist enter cannabis oil information (e.g., dose, quantity) into the PMP at the time of dispensing

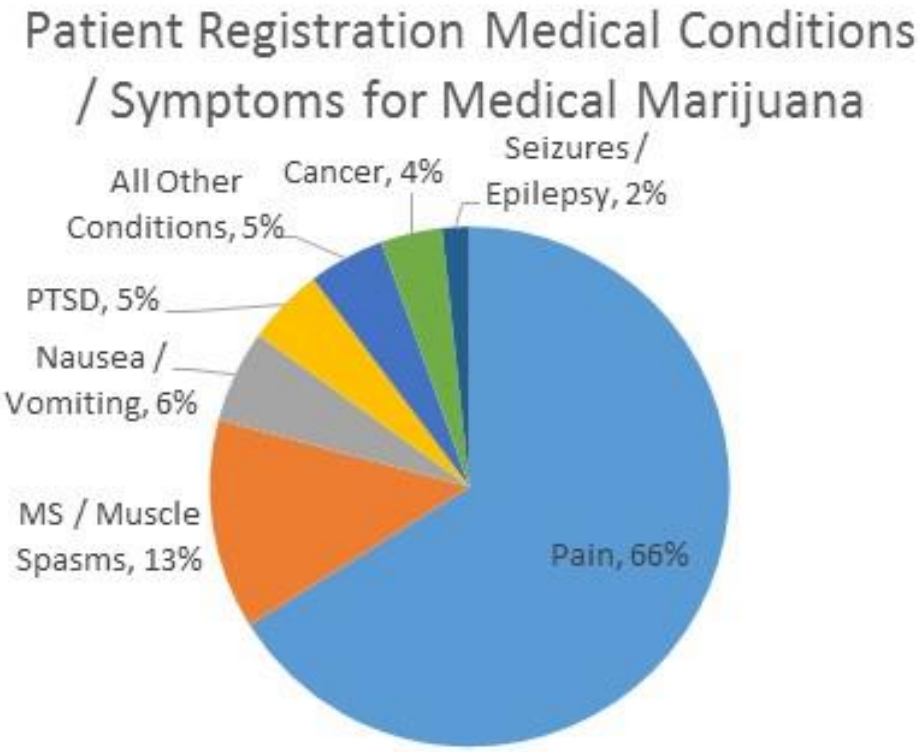
Detrimental Side Effects of THC-A and CBD Oil Excipients*

- As products not regulated by the FDA, THC-A and CBD oils could have detrimental effects if their inactive ingredients have detrimental side effects (e.g., use of peanut oil as carrier oil, for those with peanut allergies)
- Most other States permitting sale of medical cannabis products require labeling of inactive ingredients, such as type of excipient oil(s), or presence of additives:
  - Around 60% of MML States programs require labeling of all ingredients
  - Of three other COL States allowing in-State production, two (IA and MO) require labeling of all ingredients; one (TX) does not
- In Virginia, 18 VAC 110–60 only requires active ingredients to be listed

* see slide 56 in the Appendix for further detail

Cannabis for Medical Use – Prevalence in the United States*

- Across the US, around 850,000 patients are registered to use medical marijuana, ranging from around 1,000 (in AK) to over 100,000 (in AZ and MI)
- Patients registered to use medical marijuana represent, on average, 0.6% of Medical Marijuana Law (MML) States' populations, ranging from 0.1% (AK) to 3.9% (ME)
- Across MML States with available data, around two-thirds of medical marijuana patients are registered for its use to treat pain (chronic, severe, etc.)
- In Virginia, THC-A and CBD oils are not yet available, so no patients are currently registered to use them



* see slides 58-59 of the Appendix for further detail

Cannabis for Medical Use – Qualifying Conditions Across States*

- 30 of 31 MML States and 15 of 16 COL States list over 60 specific medical conditions or symptoms for which medical cannabis may be recommended by physicians
  - The majority of the most common qualifying conditions have a highly limited base of evidence upon which to draw conclusions (e.g., cancer, epilepsy, glaucoma)
- §18.2-250.1 of the Code of Virginia provides an affirmative defense for individuals with intractable epilepsy to use THC-A and CBD oils

* see slide 60 in the Appendix for further detail

Cannabis for Medical Use – Qualifying Conditions Across States (2)

- Among the 31 MML States, four permit physicians to make recommendations for conditions that are not explicitly listed in Code
  - CA: “Any other chronic or persistent medical symptom that is debilitating and may cause serious mental or physical harm”
  - DC: “Any condition for which treatment with medical marijuana would be beneficial”
  - FL: “Medical conditions of the same kind or class [as the enumerated list]”
  - MA: “other conditions as determined in writing by a qualifying patient’s physician”

Cannabis for Medical Use – Adding New Qualifying Conditions*

- Around 70% of MML States delegate authority to agencies overseeing medical marijuana programs to consider the addition of new conditions to those approved in Code (the remaining 30% require a strictly legislative process)
- Among 20 States with a model of delegated authority to approve new conditions:
  - All use a petition-based process to consider new conditions
  - Most make use of an advisory body to review petitions and make recommendations to the overseeing authority
  - Wide variations exist related to advisory body membership composition, size, appointment authority, etc.
  - One (MN) requires that determinations to add new conditions by the program's executive agency be submitted to the State legislature and adopted unless the legislature provides otherwise
- One of the 16 CBD oil States (IA) uses a delegated authority model, with recommendations for adding conditions made by an advisory council

* see slide 61 in the Appendix for further detail

Health Effects of Cannabis Use

Non-Medical Cannabis Use – Evidence of Adverse Associations*

- The strength of evidence on non-medical cannabis use and adverse health/social outcomes was recently reviewed by:
  - The National Academies: systematic review (2017)
  - The Colorado Department of Public Health and Environment: systematic review (2016)
  - The World Health Organization: expert review (2016)
- Of almost 50 health/social outcomes reviewed and most relevant to this study, the evidence base was determined to be limited or too insufficient to draw conclusions for the majority (56% - 66%, depending on the review)
- More broadly:
  - Literature suggests that certain populations may be at highest risk for adverse associations (e.g., adolescent users; users with a history of or genetic pre-disposition to psychotic disorders)
  - Magnitudes of adverse associations may be underestimated given rapid evolutions in the nature of marijuana exposure – including increased potency (from 4% in 1995 to 12% in 2014) and routes of administration with differential intoxicating effects
  - Health/social "impacts" of cannabis use relates to associations between cannabis use and outcomes – evidence on causal links remains highly limited

* see slide 62 in the Appendix for further detail

Non-Medical Cannabis Use – Evidence of Adverse Associations*

- Strong/moderate evidence in at least 2 reviews

Category	Outcome	Evidence Level†:	
		Strong	Moderate
Mental Health	Development of schizophrenia, other psychoses (dose-response relationship; highest risk in frequent users)	CO; NA; WHO;	CO
	Development of problem use/cannabis use disorder (among certain users)	CO; NA; WHO	
	Development of Substance Use Disorders	CO	CO; NA
	Cognitive function (acute effects of cannabis use)	CO;	WHO; NA
Physical Health	Motor vehicle crashes	CO; NA; WHO	
	Worsened: respiratory symptoms; chronic bronchitis	CO; NA; WHO	
	Overdose pediatric injuries (where cannabis is legalized)	CO	NA
	Lung cancer (*no association*)		CO; NA

CO = CDPHE review; NA = National Academies review; WHO = World Health Organization review

† For the CO review, strength of evidence depended on particular conditions or substances; for the WHO review, there were methodological differences in assessment of strength of evidence

* see slides 63-64 in the Appendix for further detail

Non-Medical Cannabis Use – Evidence of Adverse Associations

- Limited/insufficient evidence† in at least 2 reviews

Category	Outcome	Evidence Level:	
		Limited	Insufficient††
Mental Health	Maternal cannabis use and child's: academic achievement (decreased); delinquency	CO	NA
	Maternal cannabis use and child's psychosis		CO; NA
	Bipolar disorder: development	NA	CO
Physical Health	AMI (short-term triggering of)	CO; NA; WHO	
	Cancers (various)	CO; WHO; NA	
	Testicular tumors	CO; NA; WHO	
	Chronic Obstructive Pulmonary Disease	NA; WHO; CO	
	Maternal pregnancy complications	CO; NA	
	Maternal cannabis use and SIDS	CO	NA
	Mortality		CO; NA
	Asthma		CO; NA
	Occupational accidents/injuries	CO	NA

CO = CDPHE review; NA = National Academies review; WHO = World Health Organization review

† Insufficient evidence to support or refute existence of associations

†† For the CO review, strength of evidence depended on particular conditions or substances; for the WHO review, there were methodological differences in assessment of strength of evidence

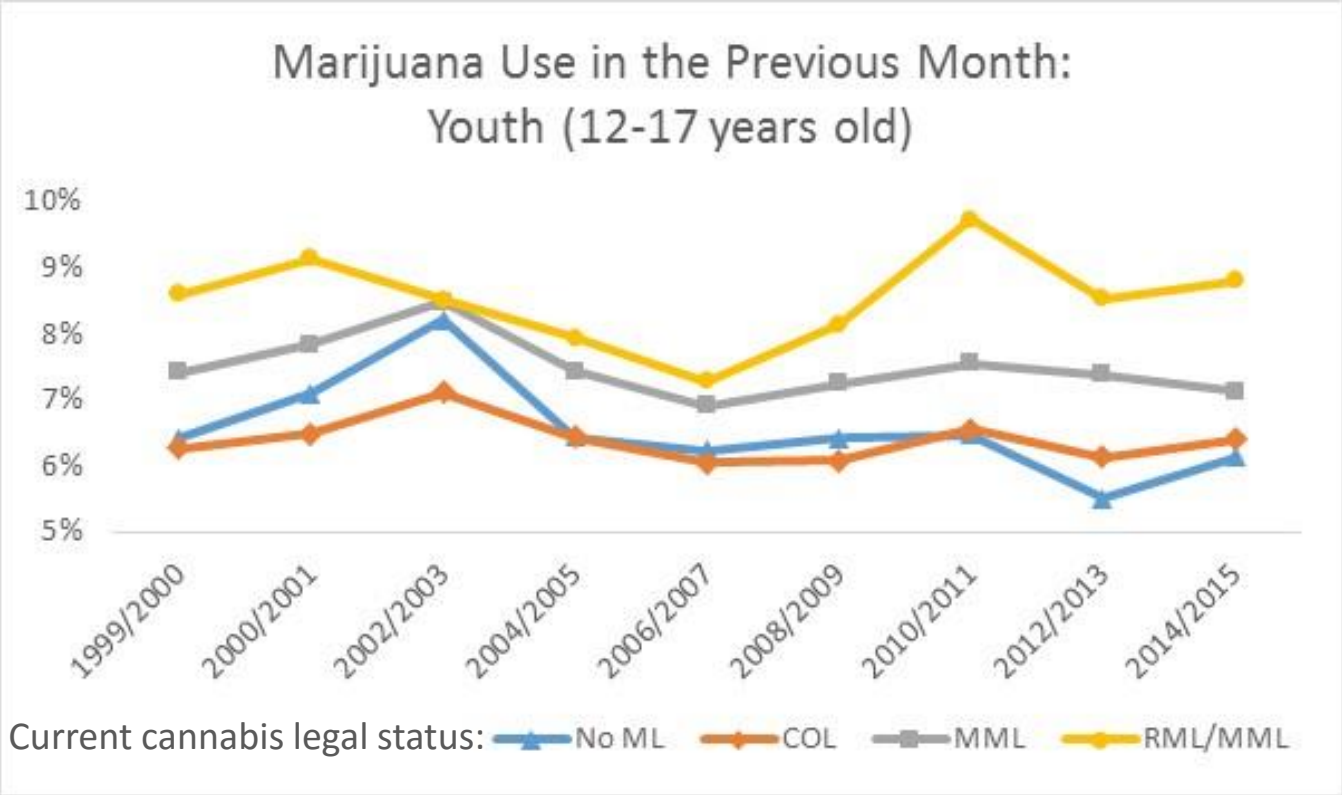
Non-Medical Cannabis Use – Associations with Selected Health Outcomes*

- Cognitive function (long-term effects): unclear evidence
  - While there are indications that greater cannabis exposure is associated with decreased long-term cognitive function, causal inference and generalizability are limited
- Brain development: unclear evidence
  - While brain imaging studies have found structural differences between early-onset cannabis users and non-users, causal relationships with cannabis and permanency of differences have not been established, and there is limited or insufficient evidence that cannabis use is associated with long-term outcomes (e.g., academic degree-earning; income)
- As “gateway” to other substances: unclear evidence
  - While cannabis use is associated with later illicit drug use, the order of drug initiation may not be a major factor in developing a substance use disorder, and associations between cannabis use and illicit drug use may reflect underlying, shared liabilities (e.g., predisposition towards addiction)

* see slides 65-67 in the Appendix for further detail on content of this slide and maternal cannabis use

Cannabis Legalization and Decriminalization – Trends in Youth Use*

- Between 1999 and 2015, youth use of marijuana appears to have remained relatively similar across time, with levels in current RML and/or MML States generally higher – in most cases even prior to passage of those States' laws – than in States that currently have CBD oil laws or do not permit any cannabis use

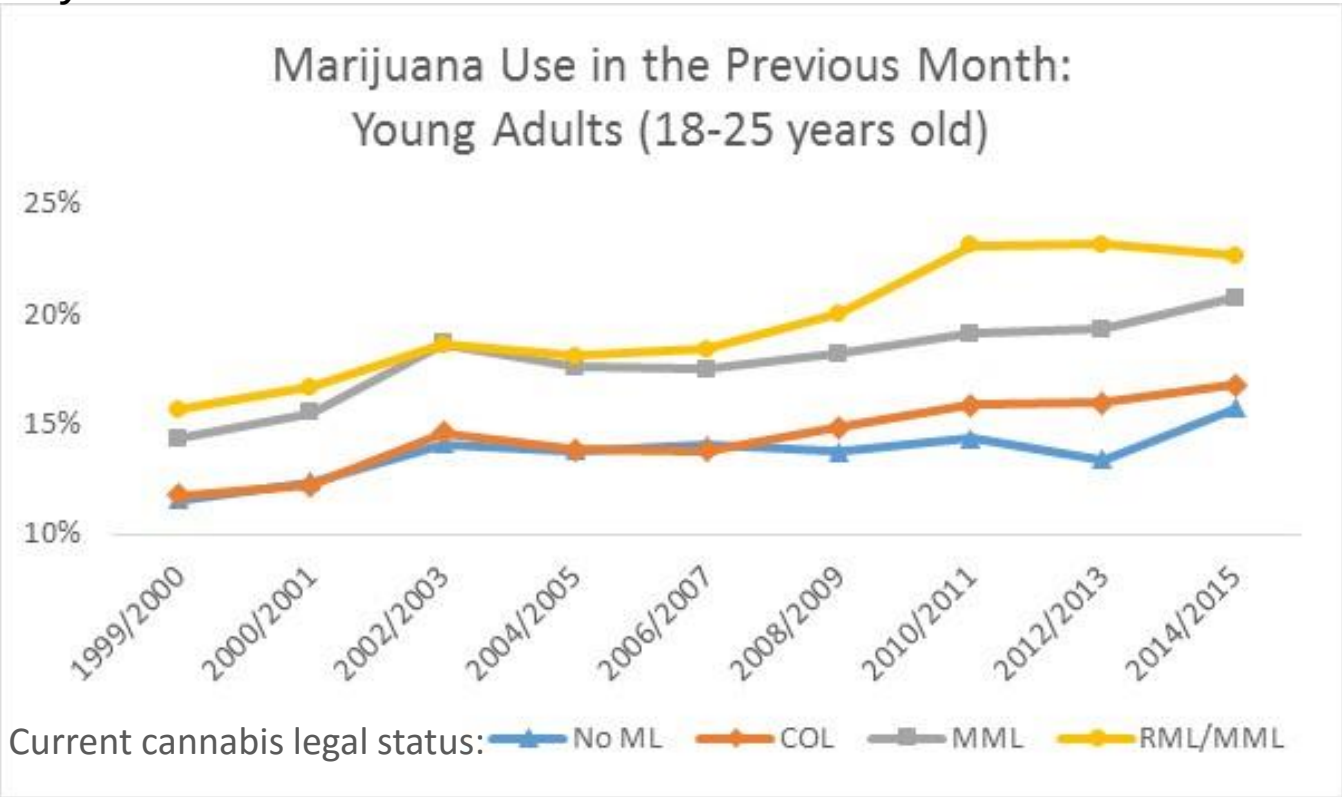


No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

* see Slide 68 in the Appendix for further detail

Cannabis Legalization and Decriminalization – Trends in Young Adult Use*

- Since 1999, young adult use of marijuana has increased overall, and has been consistently higher in current RML and/or MML States – in most cases even prior to passage of those States' laws – than in States that currently have CBD oil laws or do not permit any cannabis use



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

* see Slide 69 in the Appendix for further detail

Cannabis Legalization and Decriminalization – Evidence on Associations with Cannabis Use

- There may be several reasons underlying higher marijuana use in States with medical marijuana laws (MMLs) and recreational marijuana laws (RMLs)
  - Community norms that are more supportive of cannabis use, contributing to MML/RML enactment and higher use; and/or
  - Changes in community attitudes due to MML/RML enactment (e.g., lowered perceived riskiness), leading to higher use; and/or
  - Increased availability of cannabis for non-medical purposes due to MML/RML enactment, leading to higher use
- Specific models of MML regulation may differentially impact use
  - For example, there is evidence that regulations restricting access (e.g., patient registry requirements) have a negative association with recreational use, while regulated dispensaries have a positive association

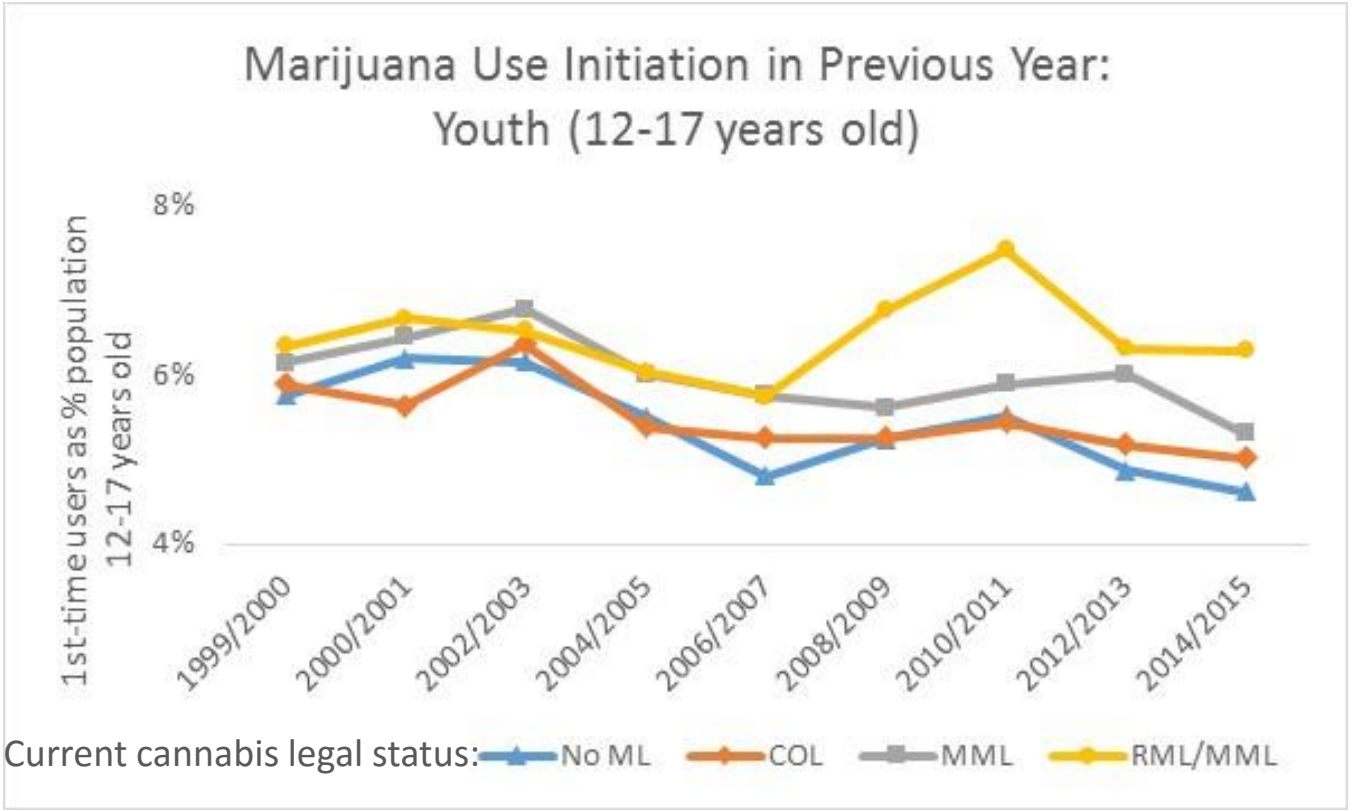
Cannabis Legalization and Decriminalization – Evidence on Associations with Cannabis Use (2)*

- MMLs
  - While there is evidence that passage of MMLs is associated with decreased perceived risk of harm of marijuana, most research – with some exceptions – finds that MML enactment has non-significant or negative associations with changes in youth use
  - Fewer studies analyze changes in adult consumption, but these provide consistent evidence of increased adult use
- RMLs
  - A recent study found divergent results in WA and CO, with marijuana use increasing among some middle and high school students in WA, but remaining unchanged in CO; in both States, perceived harmfulness of marijuana either decreased or remained unchanged
- In both the MML and RML contexts, the few studies focusing on high-risk users tend to find increased use after passage of marijuana laws

* See slides 70-72 in the Appendix for further detail on associations of legalization/decriminalization with: methods of cannabis use; opioid use; hospitalizations

Cannabis Legalization and Decriminalization – Trends in Youth Age of Initiation

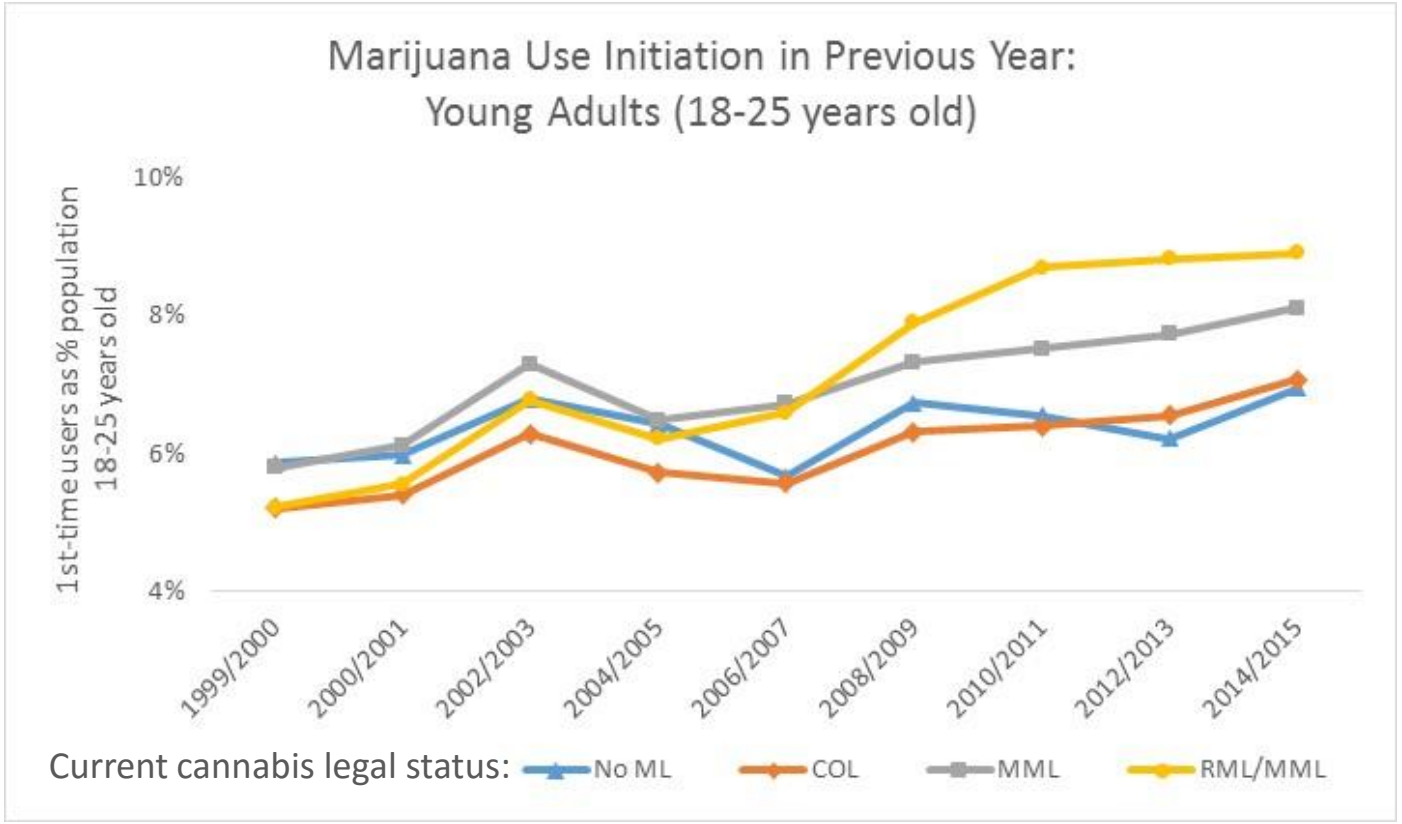
- Since 1999, the percentage of youth initiating marijuana use at this age has decreased overall – with the exception of RML States – and has been generally higher in current RML and/or MML States – in most cases even prior to passage of those States' laws – than in States that currently have CBD oil laws or do not permit any cannabis use



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

Cannabis Legalization and Decriminalization – Trends in Young Adult Age of Initiation

- Since 1999, the percentage of young adults initiating marijuana use at this age has increased overall, particularly in RML States, and has been generally higher in current MML States – in most cases even prior to passage of those States' laws – than in States that currently have CBD oil laws or do not permit any cannabis use



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

Cannabis Legalization and Decriminalization – Evidence on Associations with Age of Initiation*

- Emerging evidence suggests that passage of MML and/or RML laws may be associated with earlier initiation of marijuana use, although:
  - Magnitude of associations may be modest
  - Earlier initiation may be indicative of time-limited experimentation and not ongoing use
  - Research is limited

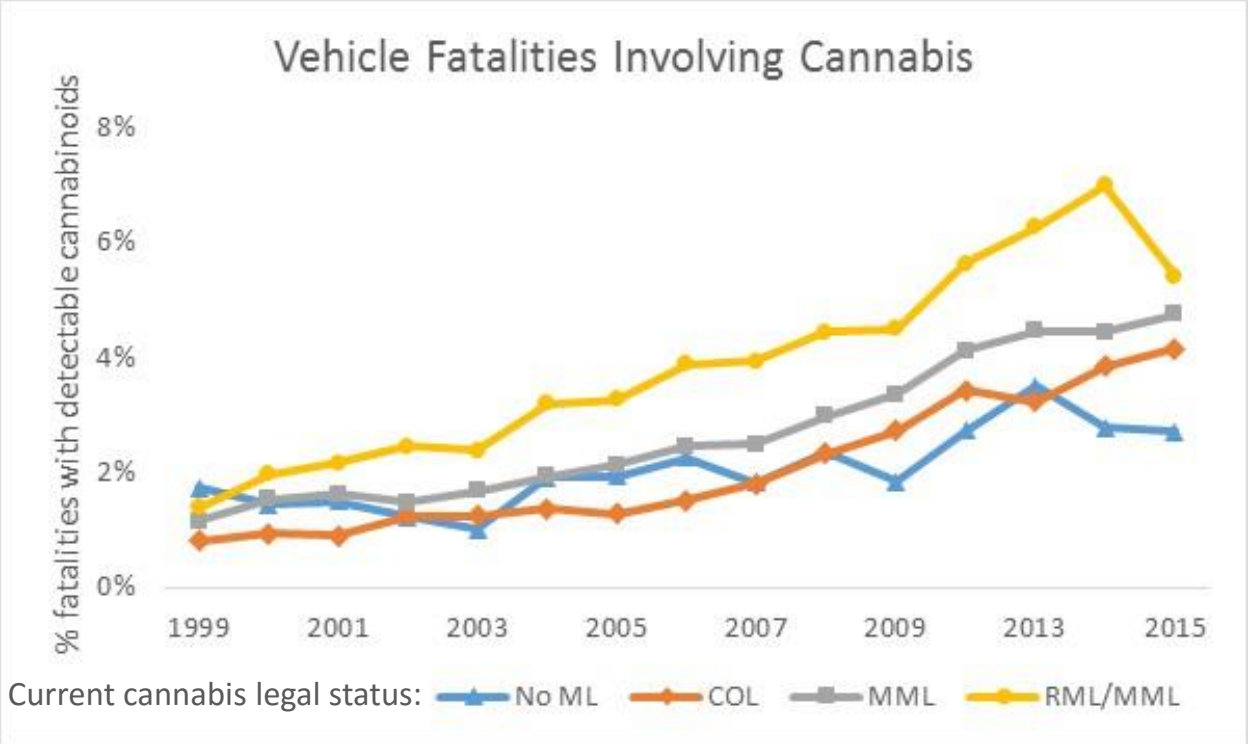
* see slide 73 in the Appendix for further detail

Cannabis Legalization and Decriminalization – Impaired Driving

- According to toxicological analyses, cannabis is one of the most commonly detected drugs in fatally injured drivers
- Multiple meta-analyses have concluded that collision risk is significantly increased by cannabis use
- However:
  - Methods used to measure alcohol-related Driving Under the Influence are limited in applicability to marijuana-related drugged driving (e.g., THC concentrations can remain in the system for weeks)
  - Bias in findings may result from systematic State variation in the percentage of fatalities tested for drugs, and evolving data collection processes over time

Cannabis Legalization and Decriminalization – Impaired Driving (2)*

- Vehicle fatality statistics collected nationally are limited in indicating whether drugs detected from lab tests contributed to impairment and accidents
- Increased vehicle fatalities involving cannabinoids over time – both overall and with differences by marijuana legal status – may reflect:
- Increased cannabis use overall/in certain States; and/or
- Increased testing for cannabis overall/in certain States; and/or
- Variations in testing procedures and data quality, overall/in certain States



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law

Source: Fatality Analysis Reporting System (FARS)

* see slide 74 in the Appendix for further detail

Cannabis Legalization and Decriminalization – Evidence on Associations with Impaired Driving

- MMLs: mixed evidence
  - Increased prevalence of cannabinoids among drivers involved in fatal crashes in some MML states, such as Colorado, compared to non-MML States; however:
  - Both MMLs and dispensaries have also been associated with reduced traffic fatalities, especially among adults 25 to 44 years of age
- RMLs: mixed evidence
  - Legalizing recreational marijuana use in Colorado, Oregon and Washington was associated with higher collision claim frequencies in CO, OR and WA (by about 3%) than would have been expected without legalization; however:
  - Changes in motor vehicle crash fatality rates for WA and CO were not statistically different from those in similar states without recreational marijuana legalization three years after legalization

Methods Used by States to Limit Illicit Cannabis Use

- Legal penalties for unlawful possession of marijuana:

Level of Past Year Marijuana Use	Lowest Offense			Highest Offense	
	Avg. Allow-able limit†	Avg. Min. Incarceration	Avg. Min. Fine	Avg. Max. Incarceration	Avg. Max. Fine
10 Lowest-Use States	1.35 oz	168 days	$1,505	25 years	$115,325
10 Highest-Use States	1.67 oz	0.2 days	$1,035	4.25 years	$69,010

† Allowable limit refers to maximum quantity allowable to remain at lowest level of offense; Source: NORML

- Legal penalties for marijuana use (“Internal possession” laws)
  - WY: It is a misdemeanor – punishable by incarceration up to 6 months or fine up to $750 – for any person to be under the influence of a controlled substance, except when administered or prescribed by a licensed practitioner
  - SD: It is a misdemeanor to intentionally consume any substance (except alcohol) with the intent of intoxication regardless of jurisdiction in which the substance was ingested, except when the substance is prescribed by a licensed practitioner
- MML tax revenues
  - 9 MML States tax cannabis products through retail and/or excise taxes
  - 2 of those States earmark a percentage of revenue for drug abuse prevention, counseling and treatment services

Methods Used by Other Countries and States to Limit Illicit Cannabis Use

- Internationally, methods to limit illicit drug use have varying applicability to cannabis use

Approach to Drug Misuse/Addiction	Description	Country examples	Applicability to Cannabis*
Zero Tolerance	Prohibitionist in all aspects (possession, use, distribution); no distinction between "hard" and "soft" drugs	Japan, Sweden	++
Dissuasion Commissions	Legal commission that can recommend treatment and education	Portugal	++
Hygienic Drug Consumption Rooms	Facilities into which drug users can bring their own drugs (e.g., opioids) for consumption under supervision in a hygienic setting (e.g., clean needles)	Canada, Denmark, Germany, Netherlands, Norway, Spain, Switzerland	–
Drug Courts	Judge-led oversight of drug treatment in lieu of traditional justice system routes	USA, Australia, Canada and the UK	++
Prison-Based Treatment / Therapeutic Communities	Low- to high-intensity drug and/or drug-free treatment focused on secondary and tertiary prevention	Widespread	+

* –: Minimal applicability; +: Some applicability; ++: High degree of applicability

Source: Home Office (2014)

Methods Used by Other Countries and States to Limit Illicit Marijuana Use (2)*

- The impact of specific methods to limit illicit drug use is often not clear. For example:
  - Sweden's zero tolerance policy reflects strong cultural disapproval of drug consumption, making it difficult to attribute low levels of drug use to the policy itself vs. underlying cultural attitudes
  - Portugal's Dissuasion Commissions are part of a national system of decriminalization and nationwide access to treatment, making unknown the relative contribution of dissuasion commissions to below European-average drug use and harm in Portugal
  - Observed relationships between increased or decreased legal penalties and marijuana use are not straightforward

* See slides 75 – 80 of the Appendix for further detail

Summary – THC-A and CBD oils

- While THC-A and CBD are considered non-psychoactive (i.e., “non-intoxicating”), THC-A can decarboxylate into THC – a substance that is intoxicating/psychoactive. Because there are several ways that THC-A can decarboxylate into THC (e.g., by heating), psychoactive effects of THC-A oil may exceed the oil’s 5% maximum THC content (e.g., up to 18% THC potential)
- Evidence of therapeutic effects of THC and CBD is highly limited – even more so for THC-A – with only one condition under consideration by the House Courts of Justice (patient-reported MS symptoms) having strong evidence of therapeutic effects.
- While there is evidence that CBD is well-tolerated, data on detrimental side effects of THC-A are highly limited, and CBD and/or THC have been associated with both Adverse Events and drug interactions. Further, detrimental effects of CBD and THC-A *oils* could result from inactive ingredients in the oils.
- Almost all MML and COL States restrict access to cannabis for medical use to patients with certain qualifying conditions (e.g., chronic pain), although a handful of MML States permit relatively wide discretion to physicians to recommend cannabis for conditions not explicitly listed. 70% of MML States empower the authority overseeing its medical marijuana program to consider the addition of new conditions to those approved in Code.

Summary – Adverse Health Effects of Cannabis Use

- Recent reviews of adverse associations between cannabis use and health have determined the evidence base to be limited or too insufficient to draw conclusions for the majority of health and social outcomes evaluated. Nonetheless, broader research suggests that certain populations may be at highest risk for adverse associations, and magnitudes of adverse associations may be underestimated given rapid evolutions in the nature of marijuana exposure.
- Self-reported survey data suggest that levels of cannabis use/age at initiation among current RML and MML States are generally higher at the present time compared to COL States and those without cannabis laws, and have generally been higher than those States since 1999. Data also suggest that trends in youth use/age at initiation may differ from young adult use (e.g., flat/declining vs. rising levels).
- Most research does not find MML enactment to be associated with increased use of cannabis among youth, although there is a smaller body of evidence suggesting increased use among adults. Evidence on RML enactment and changes in use is more limited. There is a limited body of evidence indicating that MML and/or RML enactment may be modestly associated with earlier initiation of cannabis use.
- While there is strong evidence of increased collision risk due to cannabis use, there is mixed evidence on associations between MML or RML enactment and changes in levels of impaired driving, and methodological challenges in measuring cannabis-caused impairment abound.
- In the US, methods used to limit illicit cannabis use include legal penalties, “internal possession laws”, and taxes on cannabis products with a percentage of revenue earmarked for drug abuse prevention, counseling and treatment services.
- Internationally, methods used to limit illicit cannabis use include zero tolerance policies, “dissuasion commissions”, and drug courts (drug courts are also common in the US). However, the impact that these methods have on limiting illicit drug use is often not clear.

Policy Options

Policy Options

Option 1: Take No Action

Policy options to address decarboxylation of THC-A into THC in THC-A oil

Option 2: Introduce legislation to amend §54.1-3408.3(A) of the Code of Virginia, redefining THC-A oil as a processed Cannabis plant extract that contains not more than 5% maximum potential THC by weight

OR one or both of the following:

Option 3: Introduce legislation to amend §18.2-250.1(C) of the Code of Virginia, making smoking or heating of THC-A oil above naturally occurring temperatures a disqualification for an affirmative defense for possession of THC-A oil

Option 4: By letter of the JCHC Chair, request that DHP amend 18 VAC 110-60 by: requiring THC-A oil processors to ensure that the percentage of THC remains within 10% of the level measured for labeling under 18 VAC 110-60-290, and; establishing a stability testing schedule for THC-A oil processors

Policy Options (2)

Policy option related to THC-A and CBD oil dispensing requirements

Option 5: Introduce legislation to amend the Code of Virginia:

- Requiring THC-A and CBD oil processors to register their formulations with DHP for a fee – with each registration application including a list of all active and inactive ingredients and any other items deemed necessary by DHP – for the purposes of including THC-A and CBD oils in the list of substances tracked by the Prescription Monitoring Program (PMP)
- Requiring pharmacists who dispense THC-A and/or CBD oil to enter dispensing information (e.g., dose, quantity) into the PMP at the time of dispensing

Policy Options (3)

Policy option related to monitoring of Adverse Events

Option 6: By letter of the JCHC Chair, request that DHP and VDH review models in other States for the monitoring and reporting of Adverse Events related to use of cannabis for medical purposes, providing a report to the JCHC with a recommended model for Virginia by October 1, 2018

Policy Options (4)

Policy options related to the process for adding new qualifying conditions as an affirmative defense for use of THC-A or CBD oils

Option 7: Introduce legislation to amend the Code of Virginia authorizing DHP to add new conditions, through administrative rulemaking, for which practitioners may provide written certifications for THC-A and CBD oils, requiring DHP to:

- Constitute a regulatory advisory panel, composed of at least a majority of Board-certified physicians, whose purpose will be to evaluate petitions for the addition of new conditions and make recommendations for their approval or denial to the Director of DHP;
- Establish processes that ensure opportunity for public comment related to regulatory advisory panel evaluations;
- For new conditions approved by the Director of DHP: draft regulations to add the condition through the Administrative Procedures Act Process
  - With ***or*** without sending determinations to the Chairs and ranking minority members of the HWI and Senate and Education and Health Committees by January 1 of each year before adding the condition for GA opportunity to legislatively provide otherwise

Policy Options (5)

Policy options related to the process for adding new qualifying conditions as an affirmative defense for use of THC-A or CBD oils (continued)

OR

Option 8: By letter of the JCHC Chairman, request DHP to form a stakeholder work group to review models in other States of delegated approval to executive agencies to approve new conditions, providing a report to the JCHC with a recommended model for Virginia by October 1, 2018

OR

Option 9: Introduce legislation to amend §54.1-3408.3(B) of the Code of Virginia to allow physician recommendation for any condition determined by the physician to benefit from THC-A or CBD oil

Policy Options (6)

Policy option related to non-medical use of cannabis

Option 10: Introduce legislation to amend the Code of Virginia to authorize the Virginia Department of Taxation to administer, on THC-A and CBD oils, a consumer retail sales tax of 5.6% ***or*** a processor excise tax at 5.6%, with tax revenues deposited into a fund for the purposes of funding programs to prevent illicit cannabis use

Public Comment

Written public comments on the proposed options may be submitted to JCHC by close of business on November 7, 2017.

Comments may be submitted via:

- E-mail: jchcpubliccomments@jchc.virginia.gov
- Fax: 804-786-5538
- Mail: Joint Commission on Health Care
  P.O. Box 1322
  Richmond, Virginia 23218

Comments will be provided to Commission members and summarized during the JCHC's November 21st decision matrix meeting.

(All public comments are subject to FOIA release of records)

Appendix

Study Mandate

House Courts of Justice letter request:

- Can CBD and THC-A oil have psychoactive or detrimental side effects?
- Is CBD oil beneficial in the treatment of illnesses listed in HB 1637 and SB 1298:
  - Alzheimer's Disease
  - Amyotrophic Lateral Sclerosis (ALS)
  - Cachexia / Wasting Syndrome
  - Cancer
  - Complex Regional Pain Syndrome
  - Crohn's Disease
  - Glaucoma
  - Hepatitis C
  - HIV/AIDS
  - Multiple Sclerosis
  - Nail Patella

Study Mandate

HJR 578: Access and evaluate existing data concerning:

- The mental health side effects of marijuana use
- The physical side effects of marijuana use
- Neurodevelopmental and physiological effects of maternal marijuana use on a fetus
- Rates of marijuana use in the Commonwealth and other states, particularly states that have legalized use of marijuana for medical and recreational purposes, states that have legalized use of marijuana for medical purposes only, and states that have decriminalized marijuana, with a focus on rates of use among adults and teenagers, and develop a comparison of rates of use in states that have and have not legalized or decriminalized the use of marijuana
- Average age of first use of marijuana among marijuana users in states that have and have not legalized or decriminalized the use of marijuana and determine whether age of first use has changed over time in those states

Study Mandate

HJR 578: Access and evaluate existing data concerning:

- Most common methods of use of marijuana in states that have and have not legalized or decriminalized the use of marijuana and determine whether methods of use change over time in those states
- Effects of marijuana use on brain development, particularly among teenagers, and whether the use of marijuana as a teenager effects school dropout rates and educational success in secondary and postsecondary education and adult rates of employment, earnings, and welfare dependency
- Whether, in states that have legalized or decriminalized the use of marijuana, changes have occurred in rates of driving under the influence
- Whether evidence from other states or countries that have legalized or decriminalized the use of marijuana indicates that relaxing laws concerning marijuana use by adults has an impact on use of marijuana by teenagers
- The conditions by which products containing marijuana or delta-9-tetrahydrocannabinol (THC) have been approved for medical use by the U.S. Food and Drug Administration

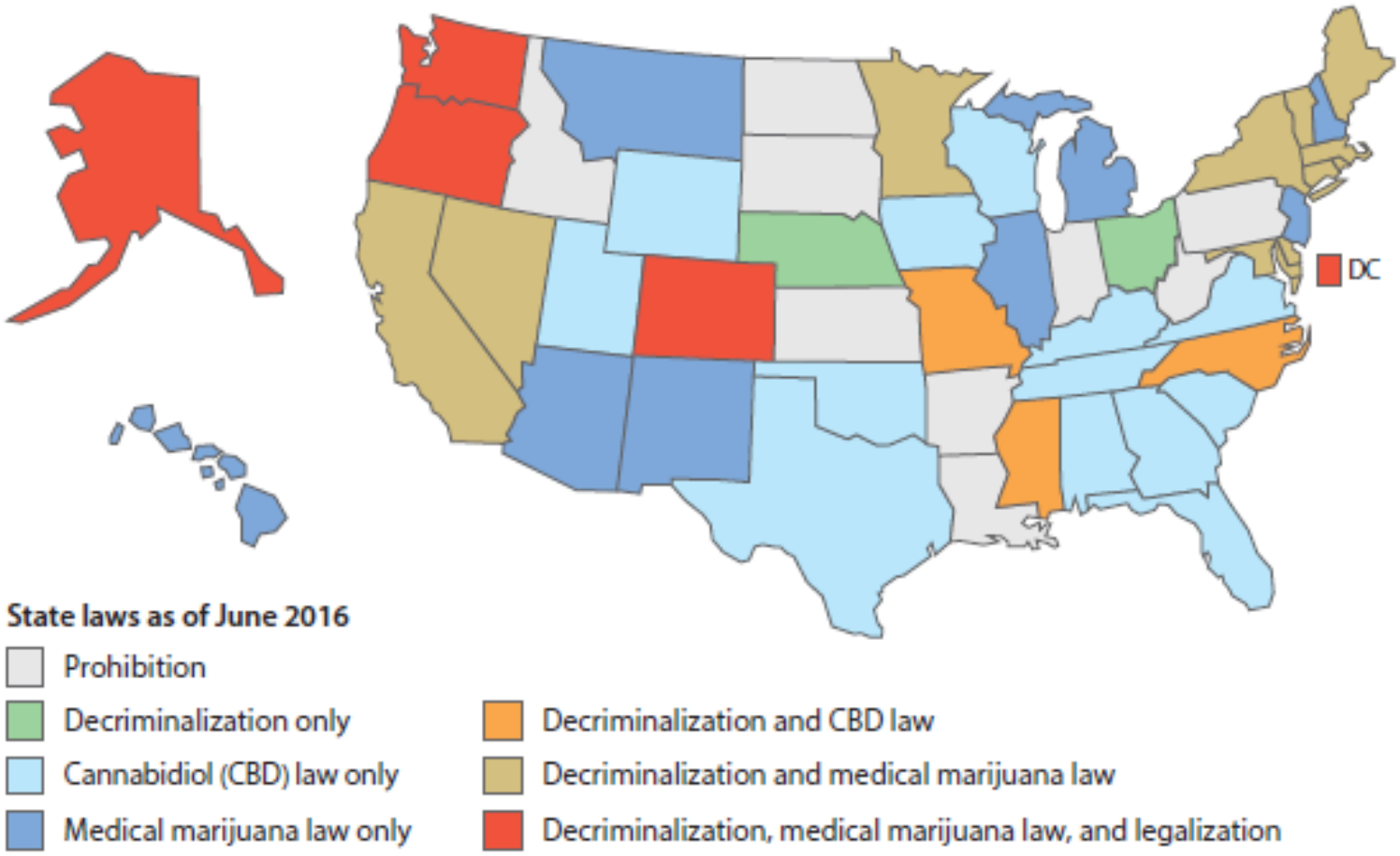
Study Mandate

HJR 578: Access and evaluate existing data concerning:

- The status of laws governing the use of marijuana for medical purposes in the Commonwealth including the rates of use of marijuana for medical purposes, the number of prescriptions and certifications for use of cannabidiol oil or THC-A oil issued by practitioners of medicine or osteopathy, and the purposes for which such prescriptions or certifications have been issued
- Laws of other states and countries legalizing the use of marijuana for medical purposes and the number of individuals authorized to use marijuana for medical purposes in states that have legalized the use of marijuana for medical purposes
- States and countries with the lowest rates of adult marijuana use and teen marijuana use, evaluating those states' and countries' laws regarding possession of marijuana, and determining whether those states and countries use legal processes to punish individuals who possess marijuana or direct individuals who possess marijuana to treatment and recovery, or do not enforce the laws in any significant way, essentially decriminalizing the use of marijuana
- The methods, tactics and interventions, including a focus on treatment, recovery, and legal penalties, that have been used in other states and countries to limit marijuana use and develop recommendations for implementing such methods, tactics, and interventions in the Commonwealth.

Background – State Laws on Medical and non-Medical Use of Cannabis

- Distinctions between legalization, decriminalization, COL, MML and RML



Source: Pacula (2017)

Background – Year of Passage of COLs, MMLs, and RMLs

State	Year of Passage:		
	COL	MML	RML
Alabama	2014		
Alaska		1998	2015
Arizona		2011	
Arkansas		2016	
California		1996	2016
Colorado		2001	2012
Connecticut		2012	
Delaware		2011	
District of Columbia		2010	2017
Florida		2016	
Georgia	2015		
Hawaii		2000	
Illinois		2013	
Indiana	2017		
Iowa	2014		
Kentucky	2014		

State	Year of Passage:		
	COL	MML	RML
Louisiana		2016	
Maine		1999	2017
Maryland		2014	
Massachusetts		2013	2016
Michigan		2008	
Minnesota		2014	
Mississippi	2014		
Missouri	2014		
Montana		2004	
Nevada		2001	2017
New Hampshire		2013	
New Jersey		2010	
New Mexico		2007	
New York		2014	
North Carolina	2014		
North Dakota		2016	

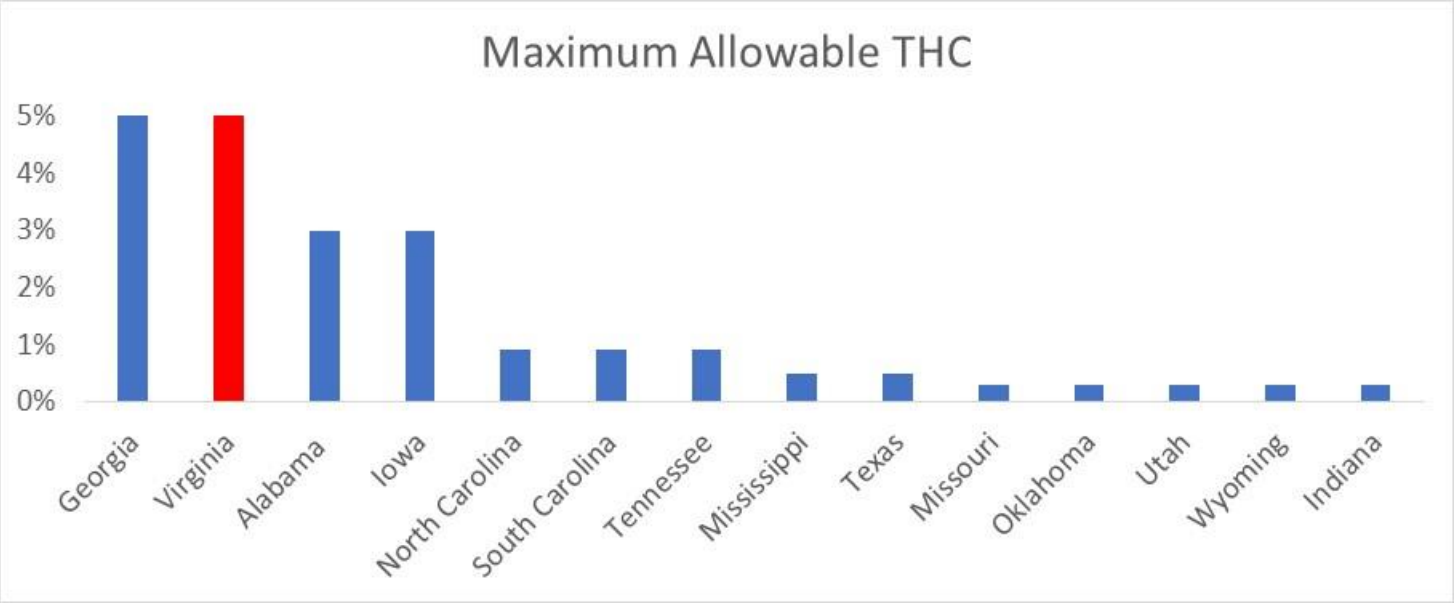
State	Year of Passage:		
	COL	MML	RML
Ohio		2016	
Oklahoma	2015		
Oregon		1998	2015
Pennsylvania		2016	
Rhode Island		2006	
South Carolina	2014		
Tennessee	2014		
Texas	2015		
Utah	2015		
Vermont		2004	
Virginia	2015		
Washington		1998	2012
West Virginia		2016	
Wisconsin	2014		
Wyoming	2015		

THC-A and CBD Oils – Psychoactive Effects

- Research indicates that THC-A is prone to decarboxylation under varying storage conditions (e.g., a half-life of 35 days at room temperature in sunlight)
- According to the Head of Analytical Research & Development at GW Pharmaceuticals:
  - Stability data on milled plants indicate that, after one year of storage in airtight containers:
    - 20% to 30% decarboxylation can occur at room temperature (e.g., 77° F)
    - No meaningful decarboxylation of THC-A into THC occurs when the storage temperature remains at ≤ 41° F
  - It would not be difficult for consumers of THC-A oil products to promote decarboxylation of THC-A into THC, such as through cooking or baking

THC-A and CBD Oils – Psychoactive Effects

- The percentage of allowable THC is highest in Virginia and Georgia



Source: NCSL (2017)

Detrimental Side Effects of THC and CBD

- Cannabinoids have been found to be significantly associated with a higher risk of Adverse Events (AEs) – including serious AEs – compared to placebo (threefold higher odds according to most recent meta-analysis)
- Specific serious and non-serious individual AEs found to be significantly associated with THC and/or CBD (2015 meta-analysis) include:

- Asthenia
- Balance
- Confusion
- Diarrhea
- Disorientation
- Dizziness
- Drowsiness
- Dry mouth
- Euphoria
- Fatigue
- Hallucination
- Nausea
- Somnolence
- Vomiting

THC-A and CBD oils – Detrimental Side Effects of Excipients

- While the FDA does not require identification of inactive ingredients for prescription drugs on labels themselves, they are required on package inserts accessible to consumers
- Current DHP regulations on processors (18 VAC 110-60) require:
  - No use of pesticides or petroleum-based solvents during the cultivation, extraction, production, or manufacturing process
  - Processing, packaging, and labeling according to the FDA's Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements
  - Labeling of results of an: active ingredient analysis, contaminants and toxins analysis, heavy metal analysis, and pesticide chemical residue analysis

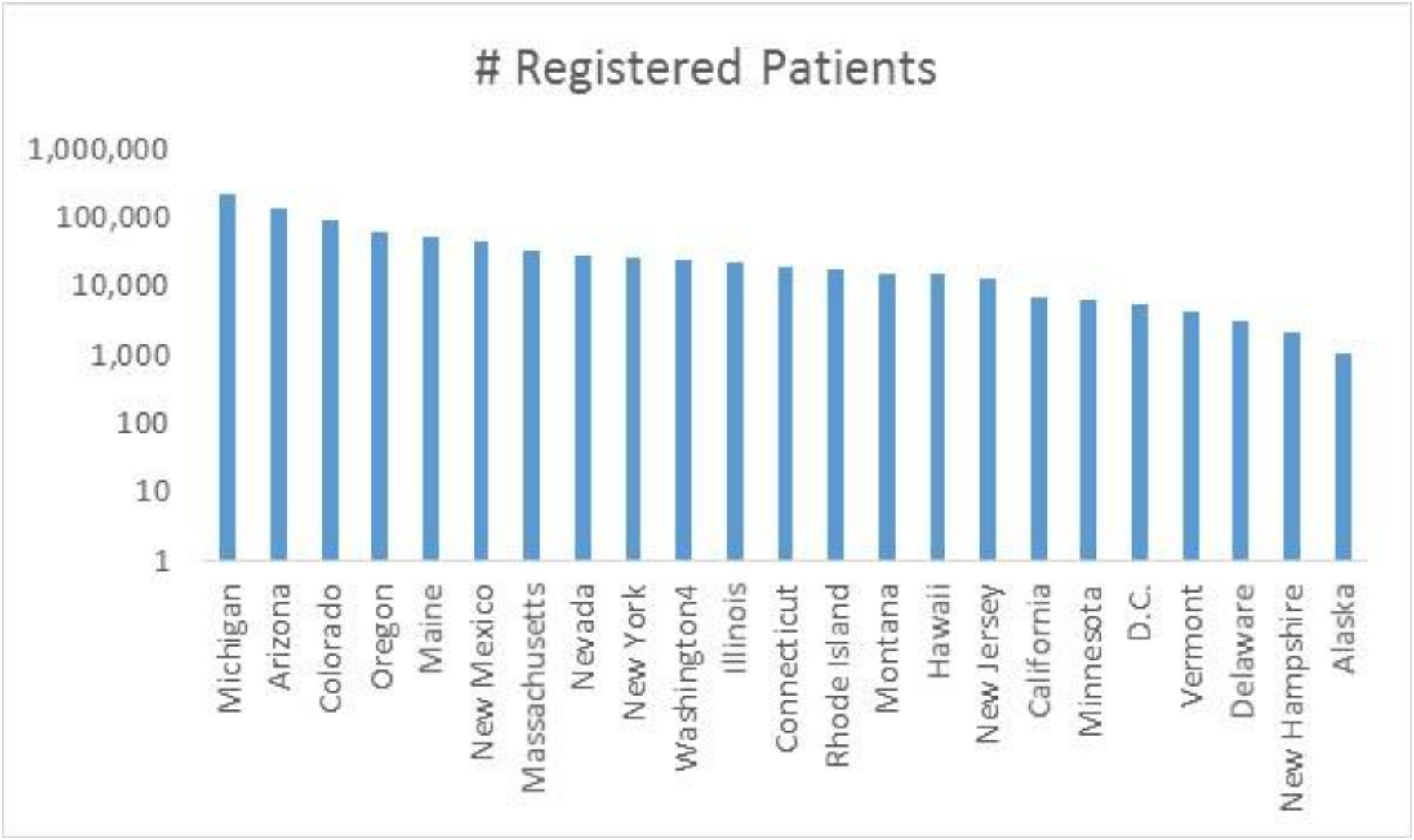
FDA-approved Cannabinoid Medications

- Three synthetic cannabinoid (THC) medications are currently approved by the FDA for treatment of two conditions

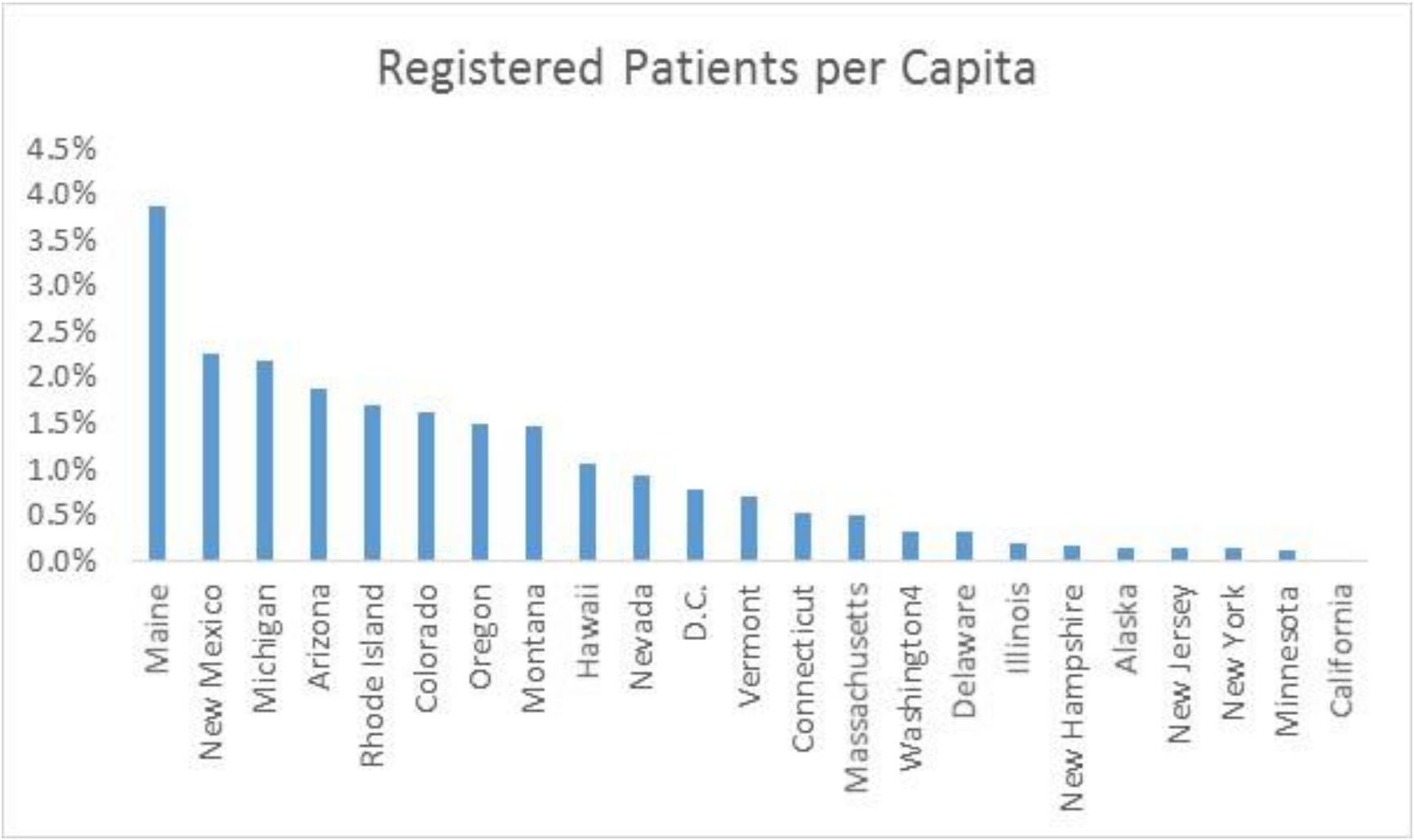
Active Ingredient	Brand Name	AIDS-related anorexia	Chemotherapy-induced Nausea/Vomiting
• Dronabinol	• Syndros • Marinol	X	X
• Nabilone	• Cesamet		X

- A third CBD-based medication – Epidiolex – is currently under FDA fast-track approval

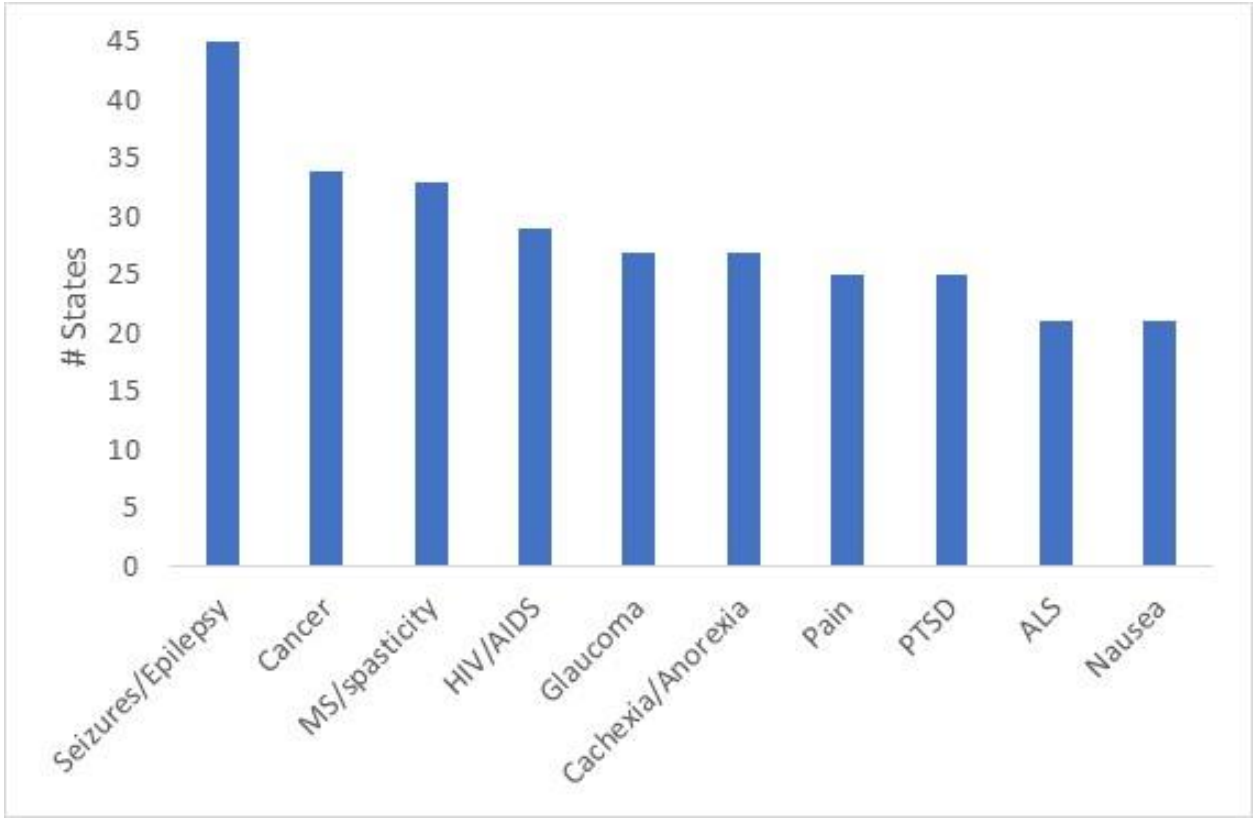
Cannabis for Medical Use – Prevalence in the United States



Cannabis for Medical Use – Prevalence in the United States



Cannabis for Medical Use – 10 Most Common Qualifying Conditions Across States



- WI allows physicians to provide certification for CBD oil for any medical condition
- Six MML States (CT, FL, MN, NJ, PA, WV) allow physicians to provide certifications for any terminal illness

Cannabis for Medical Use – Consideration of Additional Conditions

- Among 20 States with delegated authority to approve new conditions:
  - All use a petition-based process to consider new conditions
  - Most (65%) make use of an advisory body to review petitions and make recommendations to the overseeing authority
    - 24% define advisory board membership in Code
    - 38% require gubernatorial appointment for some or all members
    - Membership size ranges from 4 – 16 (average of 12) and the percentage of board membership required to be physicians ranges from 0% - 100% (average of 50%)

Non-Medical Cannabis Use – Impacts vs. Associations on Health Outcomes

- Evidence on the health/social "impacts" of cannabis use relates to associations between cannabis use and health/social outcomes, not causation
  - Federal placement of marijuana as a Schedule I drug severely limits ability to conduct gold standard studies from which causal inference can be most strongly inferred (e.g., Randomized Control Trials (RTCs))
    - Even if RTCs were possible, difficulty in blinding participants to cannabis vs. placebo could bias results
  - Existing observational studies generally cannot rule out alternatives to causation, such as reverse causation or unobserved influences affecting both cannabis use and health
  - Self-reported marijuana use could bias findings in any direction

Non-Medical Cannabis Use – Evidence of Adverse Associations

- Non-concurrence among reviews

Category	Outcome	Strong	Moderate	Limited	Insuf-ficient	Mixed
Behavioral Health	Cognitive function (chronic effects of cannabis use)			NA		CO
	Anxiety disorder/symptoms			NA		CO
	Depressive disorders (development of)		NA			CO
	Depressive disorders (changes in course/symptoms)				NA	CO
	Suicidal ideation/attempts		NA			CO
	Maternal cannabis use and child's cognitive function		CO		NA	
	Maternal cannabis use and child's growth		CO		NA	
Physical Health	Maternal cannabis use and low birth weight	NA				CO
	Stroke		CO	NA		

CO: CDPHE review; NA: National Academies review

Non-Medical Cannabis Use – Evidence of Adverse Associations

- Outcomes reviewed by a single review

Category	Outcome	Strong	Mod-erate	Limited	Insuf-ficient	Mixed
Behavioral Health	Mania/hypomania in individuals with bipolar disorders		NA			
	PTSD (development of; severity)				NA	
	Social anxiety disorder		NA			
	Maternal cannabis use and:					
	Depression			CO		
	Attention problems		CO			
	Young child's IQ		CO			
	Tobacco initiation				NA	
Physical Health	Metabolic syndrome and diabetes			NA		
	Infant NICU admission			NA		
	AMI (long-term use)				NA	
	HIV immune status				NA	
	HPV				NA	
	Cyclic vomiting (cannabinoid hyperemesis syndrome)		CO			
Social Outcomes	Lower high school graduation	CO				
	Less likely to earn college degree			CO		
	Unemployment/low income				NA	

CO: CDPHE review; NA: National Academies review

Non-Medical Cannabis Use – Adverse Associations with Maternal Marijuana Use

- Cannabis is the most-used illicit drug among women of childbearing age (3.4% of pregnant women 15-44 years old)
- THC crosses the placenta, raising concerns of possible adverse physical and developmental effects to the fetus
- The National Academies (2017) concluded:
  - Fetal growth and development: smoked cannabis use during pregnancy is linked to newborn lower birth weight
  - Neonatal conditions: no adverse outcomes associated with cannabis exposure, but studies are limited
  - Later outcomes:
    - Studies do not support an effect of cannabis exposure on overall cognitive function, although there is more consistent evidence of adverse outcomes for adolescents, including increased delinquency, greater cigarette and cannabis use, and increased mental health symptoms
    - It is difficult to attribute the outcomes to prenatal exposure
- CO DPHE (2016) found moderate evidence of associations between maternal use and decreased IQ, and limited evidence for other outcomes (e.g., academic ability)

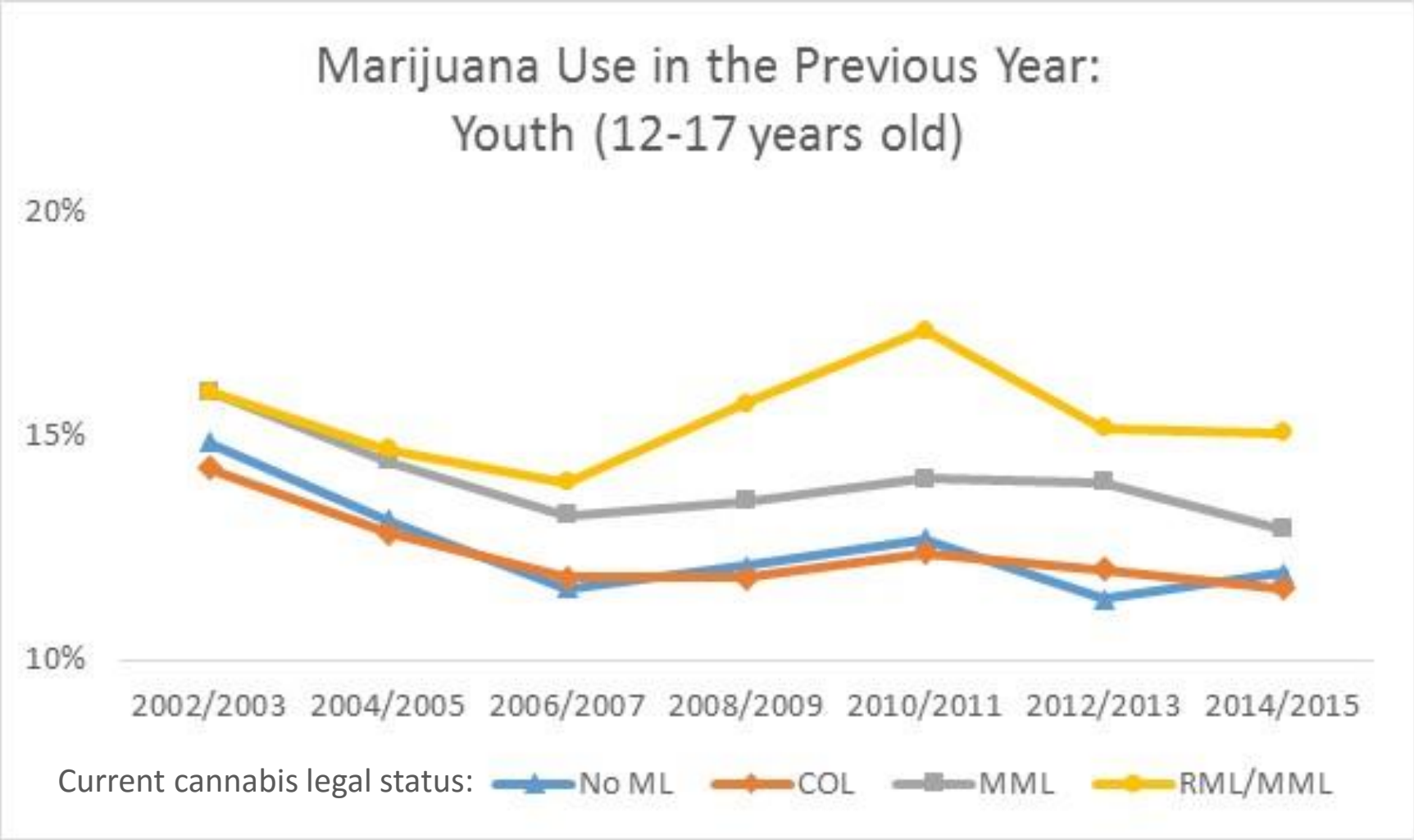
Non-Medical Cannabis Use – Associations with Cognitive Function, Other Substances

- Evidence on long-term effects of cannabis use on cognitive function is mixed
  - Studies with the longest follow-up periods and/or greater cannabis exposure tend to indicate stronger evidence of relationships compared to studies with shorter follow-up and/or weaker cannabis exposure
  - However, causal inference and generalizability are limited by the dearth of cohort studies, low cannabis exposure levels, and unaccounted for confounders
- Whether cannabis is a “gateway” to other illicit substances remains unknown:
  - Several studies have found cannabis use as a predictor for later illicit drug use (e.g., approximately 40% of cannabis users progress to use of other illicit drugs)
  - However, several studies also find existence of:
    - Alternative use sequencing
    - Cannabis use may prompt tobacco use which, in turn, increases likelihood of use of other substances
    - The order of drug initiation is not a major factor in developing a SUD
  - Associations between cannabis use and illicit drug use may reflect underlying, shared liabilities (e.g., predisposition towards addiction)

Non-Medical Cannabis Use – Adverse Associations with Brain Development

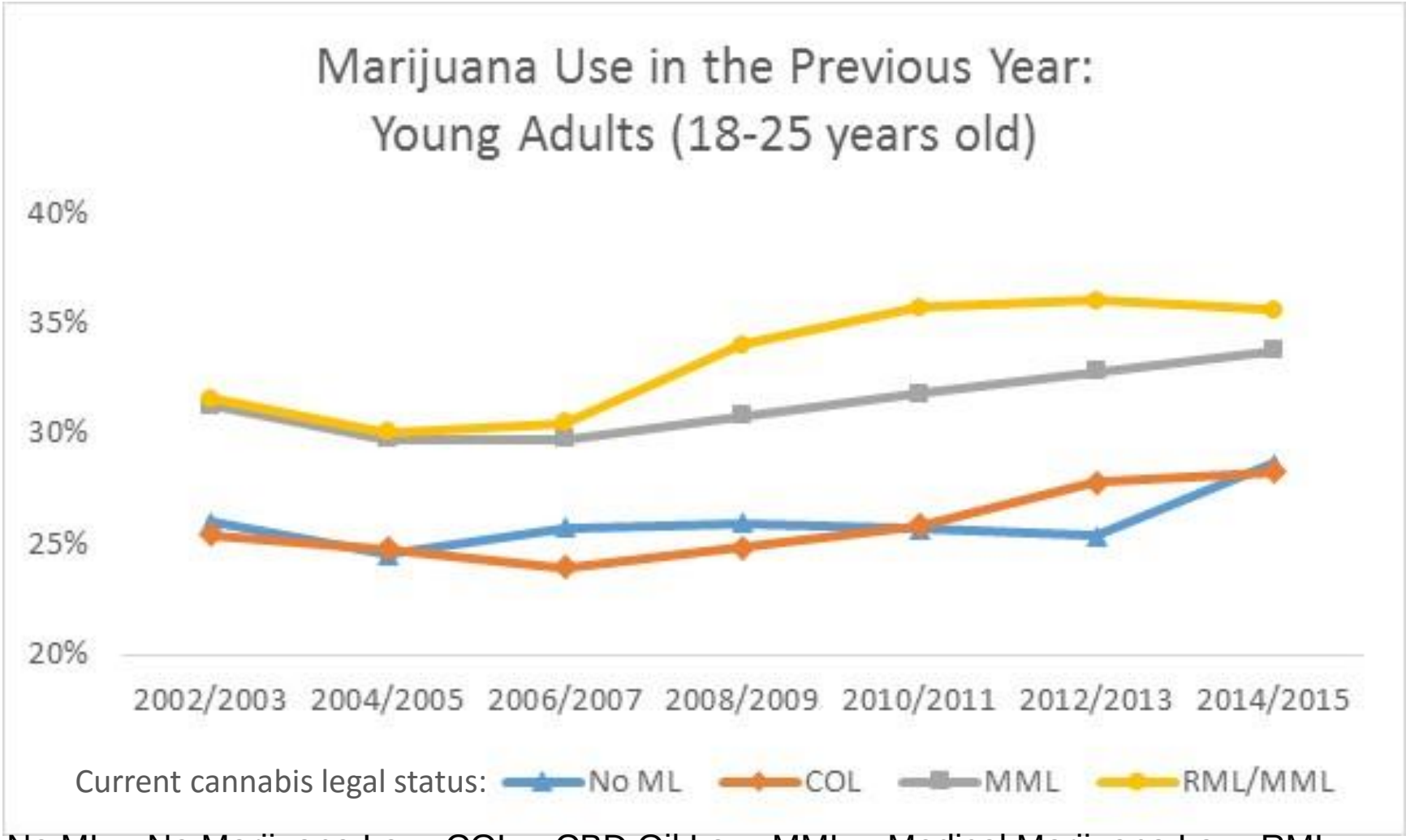
- Brain imaging studies have found structural differences between early-onset cannabis users and non-users (e.g., decreased white matter volume associated with greater impulsivity). However:
  - Evidence is mixed on permanency or consequences of differences
  - It isn't clear whether differences preceded or succeeded cannabis use
- There is limited or insufficient evidence that cannabis use is associated with:
  - Likelihood of earning a college degree (CO DPHE)
  - Unemployment/low income (National Academies)
- More broadly, there is a limited base of evidence on which to draw conclusions between cannabis use and effects on adolescent cognitive development

Cannabis Legalization and Decriminalization – Trends in Youth Use



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

Cannabis Legalization and Decriminalization – Trends in Young Adult Use



No ML = No Marijuana Law; COL = CBD Oil Law; MML = Medical Marijuana Law; RML = Recreational Marijuana Law; Source: National Survey on Drug Use and Health (NSDUH)

Cannabis Legalization and Decriminalization – Methods of Use

- Individuals in MML states were statistically significantly more likely to vape or eat marijuana compared to non-MML States

MML Status	Preferred Method of Use		
	Smoked	Vaped	Eaten
No	84.3%	19.1%	8.1%
Yes	78.9%	21.7%	9.25%

Source: Borodovsky (2016)

Cannabis Legalization and Decriminalization – Evidence on Methods of Use

- Data from WA and CO (both RML States) indicate that:
  - Among all ages, smoking marijuana continues to predominate as a usual method of use, followed by vaping and eating
  - Usual methods of use appear to be relatively stable over time

Age Group	Smoked	Vaped	Eaten	Year(s)
Middle School (WA)	65% - 74%	5% - 7%	12% - 15%	2014
High School (CO)	85% - 89%	5% - 6%	2% - 5%	2011 – 2015
Adults (CO)	79% - 89%	30% - 36%	34% - 39%	2011 – 2015

Sources: CDPHE (2016); NWHIDTA (2016)

- Recent research and surveys have found that individuals in MML states are significantly more likely to vape or eat marijuana compared to non-MML States (e.g., among high school students, 40% in MML States consumed as edible vs. 26% in non-MML States), although smoking remains predominate in both (79% - 84%)
- It is important to note that research on the influence of marijuana policies on methods of marijuana consumption is nascent

Cannabis Legalization and Decriminalization – Evidence on Associations with Other Health Outcomes

- Opioids – MML associated with:
  - Lower annual opioid overdose mortality rate and hospitalizations related to opioid dependence or abuse (~25%)
  - Significant reductions in Medicare/Medicaid prescriptions for conditions for which marijuana is a plausible alternative treatment
- Hospitalizations:
  - MML associated with 3x higher rates of pediatric exposure
  - RML (CO) associated with increased marijuana-related hospitalizations
  - MML dispensaries (CA) associated with increased marijuana-related hospitalizations

Cannabis Legalization and Decriminalization – Evidence on Associations with Age of Initiation

- Emerging evidence suggests that MML and/or RML may be associated with earlier initiation of marijuana use, although research is limited
  - One study found that MML implementation was associated with a 0.32 percentage point increase in first-time marijuana use among adolescents and young adults aged 12–20
    - However, there were no associations between MML and past-month marijuana use, suggesting that the lower age at initiation may not have reflected increases in ongoing use
  - A second study found no statistically significant differences in age of onset of smoking, vaping, or edibles between respondents from MML and non-MML states
  - Internationally, there is evidence from Australia that decriminalization was associated with earlier age at initiation in the short-term, but not 5 years after the decriminalization policy had been in place

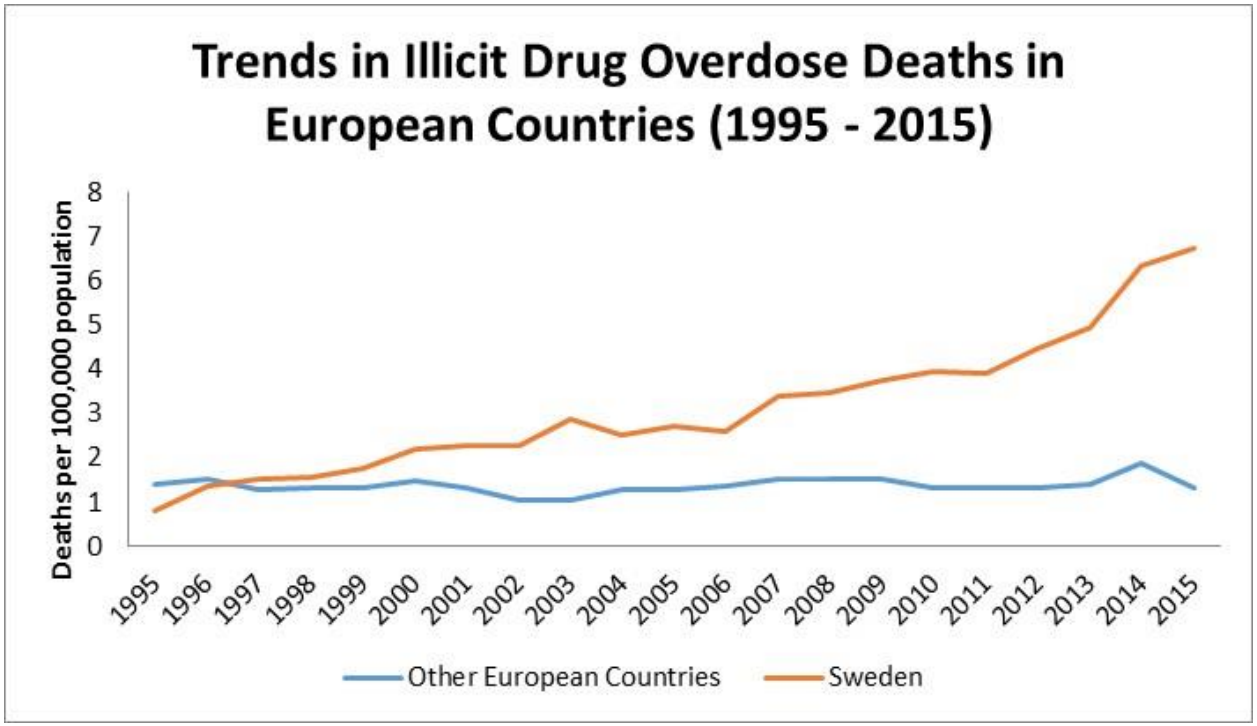
Cannabis Legalization and Decriminalization – Impaired Driving

- Analyses of the National Highway Traffic Safety Administration indicate:
  - Increased percentage of drivers tested over time (e.g., increase by 6 – 9 percentage points between 2005 and 2009)
  - Systematic variation between States in the percentage of fatally injured drivers tested for drugs
  - Varying temporal trends in the percentage of fatally injured drivers tested for drugs by State

Methods Used by Other Countries and States to Limit Cannabis Use

- Zero tolerance (Swedish model)
  - Model rests on 3 pillars: control (~75% drug budget), prevention (~1%) and treatment (~24%)
  - While Sweden has below-average cannabis use, it is comparable to others with less prohibitionist policies (e.g., Portugal)
  - Zero tolerance reflects strong cultural disapproval of drug consumption, making it difficult to attribute low levels of drug use to the policy itself vs. underlying cultural attitudes

- With zero tolerance applicable to all illicit drugs – not just marijuana – critics highlight elevated overdose rates as an adverse consequence of the across-the-board application of the model



Source: European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)

Methods Used by Other Countries and States to Limit Cannabis Use

- Dissuasion Commissions (Portugal):
  - The objective is to explore the need for treatment and promote recovery
    - The Commission – composed of a lawyer, a doctor and a social worker – links the offender to a network of support services
  - In 2012:
    - 78% of cases referred to dissuasion commissions involved cannabis only
    - 67% of rulings resulted in provisional suspension, where the individual was deemed not to be drug-dependent
  - With dissuasion commissions part of a national system of decriminalization and nationwide access to treatment, it is not known the relative contribution of dissuasion commissions to below European-average drug use and harm in Portugal

Methods Used by Other Countries and States to Limit Cannabis Use

- Drug Courts
  - Drug courts are commonly used in the US to provide treatment alternatives to incarceration
    - Judges work with treatment providers to impose sanctions and rewards; users are held to account by the judge for their progress
  - A limited evidence base upon which to draw conclusions generally has found positive associations between drug courts and reduced recidivism – and mixed evidence on their cost-effectiveness – but: methodologies are often weak; rigorous studies find modest reductions in recidivism; and studies on substance use outcomes are lacking; evidence on juvenile courts lags that of adult courts
- In Virginia:
  - In FY16, around one-half of individuals referred to Community Service Boards by courts, correctional facilities or law enforcement for Substance Use Disorder services reported marijuana drug use
  - The Supreme Court of Virginia oversees Virginia's Drug Treatment Court system for adults and juveniles

Methods Used by Other Countries to Limit Cannabis Use

- Lowest and highest prevalence of marijuana use among young adults (15-34) in European countries

Country	Marijuana Use Prevalence	Year of Data Collection
Turkey	0.4%	2011
Greece	3.2%	2004
Romania	3.3%	2013
Cyprus	4.2%	2012
Lithuania	5.1%	2012
Portugal	5.1%	2012
Hungary	5.7%	2007
Sweden	6.3%	2014
Austria	6.6%	2008
Latvia	7.3%	2011

Country	Marijuana Use Prevalence	Year of Data Collection
Germany	11.1%	2012
UK	11.7%	2014
Finland	13.5%	2014
Estonia	13.6%	2008
Netherlands	15.6%	2014
Spain	17.0%	2013
Denmark	17.6%	2013
Italy	19.0%	2014
France	22.1%	2014
Czech Republic	23.9%	2014

Source: EMCDDA (2017d)

Methods Used by Other Countries to Limit Cannabis Use

- Legal penalties in European countries:

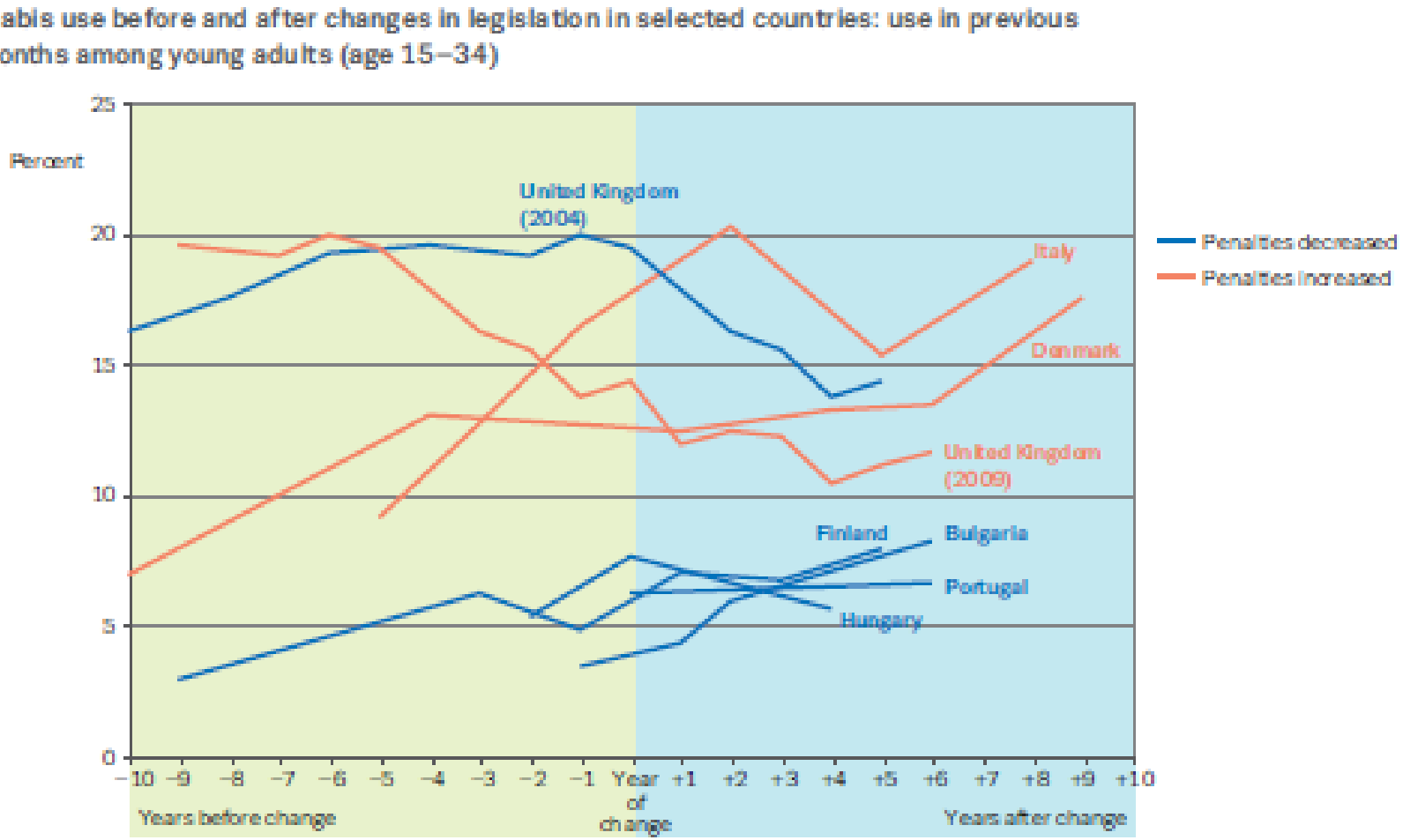
Cannabis Use among young adults (15-34)	Possibility of Incarceration for Drug Possession:	%	N
10 Lowest Use Countries	For any minor possession	70%	7
	Not for minor drug possession	30%	3
10 Highest Use Countries	For any minor possession	70%	7
	Not for minor drug possession	30%	3

Cannabis Use Among Young Adults (15-34)	Possibility of Treatment Alternatives to Punishment (i.e., incarceration and/or fine)	%	N
10 Lowest Use Countries	No possibility	40%	4
	Treatment in addition to punishment	20%	2
	Treatment → reduced/eliminated punishment	40%	4
10 Highest Use Countries	No possibility	60%	6
	Treatment → reduced/eliminated punishment	40%	4

Source: EMCDDA (2017b)

Methods Used by Other Countries to Limit Cannabis Use

- Relationships between legal penalties for marijuana possession and marijuana use are not straightforward:



Source: EMCDDA (2017a)

References

References

Slide 3:

- GW Pharmaceuticals, 2017. *2017 Glossary of Cannabinoid Terms*, UK: GW Pharmaceuticals.
- Pacula, R.L. & Smart, R., 2017. Medical Marijuana and Marijuana Legalization. *Annual Review of Clinical Psychology*, 13(1), pp.397–419.

Slide 4:

- National Organization for the Reform of Marijuana Laws (NORML), 2017. Medical Marijuana.

Slide 6:

- Russo, E.B. & Marcu, J., 2016. Chapter Three - Cannabis Pharmacology: The Usual Suspects and a Few Promising Leads. *Advances in Pharmacology*, 80 (Supplement C).

Slides 7, 51:

- Lindholst, C., 2010. Long term stability of cannabis resin and cannabis extracts. *Australian Journal of Forensic Sciences*, 42(3), pp.181–190.
- McPartland, J.M. et al., 2017. Affinity and Efficacy Studies of Tetrahydrocannabinolic Acid A at Cannabinoid Receptor Types One and Two. *Cannabis Cannabinoid Res*, 2(1), pp.87–95.

References

Slides 8-10:

- National Academies of Sciences, Engineering and Medicine, 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, Washington, DC: The National Academies Press.

Slides 11, 55:

- Bergamaschi, M. et al., 2011. Safety and Side Effects of Cannabidiol, a Cannabis sativa Constituent. *Current Drug Safety*, 6.
- Iffland, K. & Grotenhermen, F., 2017. An Update on Safety and Side Effects of Cannabidiol: A Review of Clinical Data and Relevant Animal Studies. *Cannabis Cannabinoid Res*, 2(1), pp.139–154.
- Wang, T. et al., 2008. Adverse effects of medical cannabinoids: a systematic review. *CMAJ*, 178(13), pp.1669–1678.
- Whiting, P. et al., 2015. Cannabinoids for medical use: A systematic review and meta-analysis. *JAMA*, 313(24), pp.2456–2473.

Slide 12:

- Colorado Department of Public Health and Environment (CDPHE), 2016. *Monitoring Health Concerns Related to Marijuana in Colorado: 2016*, Colorado, USA: CDPHE.

References

Slides 19-21, 63-64:

- Colorado Department of Public Health and Environment (CDPHE), 2016. *Monitoring Health Concerns Related to Marijuana in Colorado: 2016*, Colorado, USA: CDPHE.
- National Academies of Sciences, Engineering and Medicine, 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, Washington, DC: The National Academies Press.
- World Health Organization (WHO), 2016. *The health and social effects of nonmedical cannabis use*, Geneva, Switzerland: WHO.
- Semple, D.M., McIntosh, A.M. & Lawrie, S.M., 2005. Cannabis as a risk factor for psychosis: systematic review. *Journal of Psychopharmacology*, 19(2), pp.187–194.

Slides 22, 66-67:

- Levine, A. et al., 2016. Evidence for the Risks and Consequences of Adolescent Cannabis Exposure. *Journal of the American Academy of Child & Adolescent Psychiatry*, 56(3), pp.214–225.
- Mayet, A. et al., 2015. The Gateway Hypothesis, Common Liability to Addictions or the Route of Administration Model?: A Modelling Process Linking the Three Theories. *European Addiction Research*, 22(2), pp.107–117.
- Meier, M.H. et al., 2017. Associations between adolescent cannabis use and neuropsychological decline: a longitudinal co-twin control study. *Addiction.*
- Secades-Villa, R. et al., 2015. Probability and predictors of the cannabis gateway effect: A national study. *Int J Drug Policy*, 26(2), pp.135–142.

References

Slides 23-24:

- Substance Abuse and Mental Health Services Administration (SAMHSA), 2017. *National Survey on Drug Use and Health (NSDUH)*, USA: SAMHSA.

Slide 25:

- Cerdá, M. et al., 2017. Association of state recreational marijuana laws with adolescent marijuana use. *JAMA Pediatrics*, 171(2), pp.142–149.
- Pacula, R.L. et al., 2014. Assessing the Effects of Medical Marijuana Laws on Marijuana Use: The Devil is in the Details. *J Policy Anal Manage*, 34(1), pp.7–31.

References

Slide 26

- Anderson, M., 2015. Medical Marijuana Laws and Teen Marijuana Use. *American Law and Economics Review*, 17, pp.495–528.
- Choo, E.K. et al., 2013. The Impact of State Medical Marijuana Legislation on Adolescent Marijuana Use. *Journal of Adolescent Health*, 55(2), pp.160–166.
- Cerdá, M. et al., 2017. Association of state recreational marijuana laws with adolescent marijuana use. *JAMA Pediatrics*, 171(2), pp.142–149.
- Cerdá, M. et al., 2012. Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug Alcohol Depend*, 120(1–3), pp.22–27.
- Johnson, J., Hodgkin, D. & Harris, S.K., 2016. The design of medical marijuana laws and adolescent use and heavy use of marijuana: Analysis of 45 states from 1991 to 2011. *Drug and Alcohol Dependence*, 170(Supplement C), pp.1–8.
- Hasin, D.S. et al., 2015. State Medical Marijuana Laws and Adolescent Marijuana Use in The United States: 1991 – 2014. *Lancet Psychiatry*, *2*(7), pp.601–608.
- Hasin, D. et al., 2017. Us adult illicit cannabis use, cannabis use disorder, and medical marijuana laws: 1991-1992 to 2012-2013. *JAMA Psychiatry*, 74(6), pp.579–588.
- Lynne-Landsman, S.D., Livingston, M.D. & Wagenaar, A.C., 2013. Effects of State Medical Marijuana Laws on Adolescent Marijuana Use. *Am J Public Health*, 103(8), pp.1500–1506.

References

Slide 26 (continued)

- Martins, S.S. et al., 2015. State-level medical marijuana laws, marijuana use and perceived availability of marijuana among the general U.S. population. *Drug and Alcohol Dependence*, 169(Supplement C), pp.26–32.
- Pacula, R.L. et al., 2014. Assessing the Effects of Medical Marijuana Laws on Marijuana Use: The Devil is in the Details. *J Policy Anal Manage*, 34(1), pp.7–31.
- Stolzenberg, L., D'Alessio, S.J. & Dariano, D., 2015. The effect of medical cannabis laws on juvenile cannabis use. *International Journal of Drug Policy*, 27(Supplement C), pp.82–88.
- Wall, M.M. et al., 2011. Adolescent marijuana use from 2002 to 2008: higher in states with medical marijuana laws, cause still unclear. *Ann Epidemiol*, 21(9), pp.714–716.
- Wall, M.M. et al., 2016. Prevalence of marijuana use does not differentially increase among youth after states pass medical marijuana laws: Commentary on Stolzenberg et al. (2015) and reanalysis of US National Survey on Drug Use in Households data 2002–2011. *Int J Drug Policy*, 29, pp.9–13.
- Wen, H., Hockenberry, J.M. & Cummings, J.R., 2015. The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. *Journal of Health Economics*, 42, pp.64–80.
- Williams, A.R. et al., 2017. Loose regulation of medical marijuana programs associated with higher rates of adult marijuana use but not cannabis use disorder.

References

Slides 27-28:

- Substance Abuse and Mental Health Services Administration (SAMHSA), 2017. *National Survey on Drug Use and Health (NSDUH)*, USA: SAMHSA.

Slides 29, 73:

- Borodovsky, J.T. et al., 2015. Smoking, vaping, eating: Is legalization impacting the way people use cannabis? *International Journal of Drug Policy*, 36(Supplement C), pp.141–147.
- Wen, H., Hockenberry, J.M. & Cummings, J.R., 2015. The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. *Journal of Health Economics*, 42, pp.64–80.
- Williams, A.R. et al., 2017. Loose regulation of medical marijuana programs associated with higher rates of adult marijuana use but not cannabis use disorder.

Slide 30:

- Watson, T.M. & Mann, R.E., 2015. International approaches to driving under the influence of cannabis: A review of evidence on impact. *Drug and Alcohol Dependence*, 169(Supplement C), pp.148–155.
- Romano, E. et al., 2016. Marijuana and the Risk of Fatal Car Crashes: What Can We Learn from FARS and NRS Data? *The Journal of Primary Prevention*, 38(3), pp.315–328.

References

Slide 31:

- National Highway Traffic Safety Administration (NHTSA), 2010. *Drug Involvement of Fatally Injured Drivers*, Washington, DC: National Highway Traffic Safety Administration (NHTSA).
- National Highway Traffic Safety Administration (NHTSA), 2017. Fatality Analysis Reporting System (FARS).

Slide 32:

- Aydelotte, J.D. et al., 2017. Crash Fatality Rates After Recreational Marijuana Legalization in Washington and Colorado. *American Journal of Public Health*, 107(8), pp.1329–1331.
- Insurance Institute for Highway Safety (IIHS) & Highway Loss Data Institute, 2017. *High claims*, USA: IIHS.
- Masten, S.V. & Guenzburger, G.V., 2013. Changes in driver cannabinoid prevalence in 12 U.S. states after implementing medical marijuana laws. *Journal of Safety Research*, 50(Supplement C), pp.35–52.
- Pollini, R.A. et al., The impact of marijuana decriminalization on California drivers. *Drug & Alcohol Dependence*, 150, pp.135–140.
- Salomonsen-Sautel, S. et al., 2014. Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado(). *Drug Alcohol Depend*, 140, pp.137–144.
- Santaella-Tenorio, J. et al., 2016. US Traffic Fatalities, 1985–2014, and Their Relationship to Medical Marijuana Laws. *American Journal of Public Health*, 107(2), pp.336–342.

References

Slide 33:

- National Organization for the Reform of Marijuana Laws (NORML), 2017. State Laws.

Slide 34:

- Home Office, 2014. *Drugs: International Comparators*, UK: Government of the United Kingdom.

Slide 35:

- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017a. *Cannabis legislation in Europe: an overview*, Luxembourg: Publications Office of the European Union.
- Home Office, 2014. *Drugs: International Comparators*, UK: Government of the United Kingdom.
- Mansson, J., 2017. *Cannabis discourses in contemporary Sweden*, Sweden: Stockholm University.

References

Slide 51:

- Pacula, R.L. & Smart, R., 2017. Medical Marijuana and Marijuana Legalization. *Annual Review of Clinical Psychology*, 13(1), pp.397–419.

Slide 54:

- National Conference of State Legislatures (NSCL), 2017. State Medical Marijuana Laws.

Slide 65:

- Colorado Department of Public Health and Environment (CDPHE), 2016. *Monitoring Health Concerns Related to Marijuana in Colorado: 2016*, Colorado, USA: CDPHE.
- National Academies of Sciences, Engineering and Medicine, 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, Washington, DC: The National Academies Press.

Slide 70:

- Borodovsky, J.T. et al., 2015. Smoking, vaping, eating: Is legalization impacting the way people use cannabis? *International Journal of Drug Policy*, 36(Supplement C), pp.141–147.

Slide 71:

- Borodovsky, J.T. et al., 2015. Smoking, vaping, eating: Is legalization impacting the way people use cannabis? *International Journal of Drug Policy*, 36(Supplement C), pp.141–147.
- Colorado Department of Public Health and Environment (CDPHE), 2016. *Monitoring Health Concerns Related to Marijuana in Colorado: 2016*, Colorado, USA: CDPHE.
- Northwest High Intensity Drug Traffificking Area, 2016. *Washington State Marijuana Impact Report*, Seattle, USA: NWHIDTA.
- Pacula, R.L. & Smart, R., 2017. Medical Marijuana and Marijuana Legalization. *Annual Review of Clinical Psychology*, 13(1), pp.397–419.

References

Slide 72:

- Bachhuber, M.A. et al., 2014. Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010. *JAMA Intern Med*, 174(10), pp.1668–1673.
- Bradford, A.C. & Bradford, W.D., 2017. Medical Marijuana Laws May Be Associated With A Decline In The Number Of Prescriptions For Medicaid Enrollees. *Health Affairs*, 36(5), pp.945–951.
- Bradford, A.C. & Bradford, W.D., 2016. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. *Health Affairs*, 35(7), pp.1230–1236.
- Kim, J.H. et al., 2016. State Medical Marijuana Laws and the Prevalence of Opioids Detected Among Fatally Injured Drivers. *Am J Public Health*, 106(11), pp.2032–2037.
- Mair, C. et al., 2015. The impacts of marijuana dispensary density and neighborhood ecology on marijuana abuse and dependence. *Drug Alcohol Depend*, 154, pp.111–116.
- Onders, B. et al., 2015. Marijuana Exposure Among Children Younger Than Six Years in the United States. *Clinical Pediatrics*, 55(5), pp.428–436.
- Shi, Y., Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever. *Drug & Alcohol Dependence*, 173, pp.144–150.
- Wang, G., Roosevelt, G. & Heard, K., 2013. Pediatric marijuana exposures in a medical marijuana state. *JAMA Pediatrics*, 167(7), pp.630–633.
- Wang, G.S. et al., 2014. Association of Unintentional Pediatric Exposures With Decriminalization of Marijuana in the United States. *Annals of Emergency Medicine*, 63(6), pp.684–689.
- Wang, G.S., 2016. Pediatric Concerns Due to Expanded Cannabis Use: Unintended Consequences of Legalization. *Journal of Medical Toxicology*, 13(1), pp.99–105.

References

Slide 74:

- Brady, J.E. & Li, G., 2014. Trends in Alcohol and Other Drugs Detected in Fatally Injured Drivers in the United States, 1999–2010. *Am J Epidemiol*, 179(6), pp.692–699.
- National Highway Traffic Safety Administration (NHTSA), 2010. *Drug Involvement of Fatally Injured Drivers*, Washington, DC: National Highway Traffic Safety Administration (NHTSA).
- Office of National Drug Control Policy, 2011. *Drug Testing and Drug-Involved Driving of Fatally Injured Drivers in the United States: 2005–2009*, Washington, DC: ONDCP.

Slides 75-76:

- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017a. *Cannabis legislation in Europe: an overview*, Luxembourg: Publications Office of the European Union.
- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017c. Statistical Bulletin 2017 — overdose deaths.
- Home Office, 2014. *Drugs: International Comparators*, UK: Government of the United Kingdom.
- Mansson, J., 2017. *Cannabis discourses in contemporary Sweden*, Sweden: Stockholm University.

References

Slide 77:

- Mitchell, O. et al., 2012. Drug Courts' Effects on Criminal Offending for Juveniles and Adults. *Campbell Systematic Reviews*, 4.
- National Drug Court Institute, 2011. *Best Practices in Drug Courts*, Alexandria, VA.
- Taylor, L.R., 2015. General Responsivity Adherence in Juvenile Drug Treatment Court. *Journal of Drug Issues*, 46(1), pp.24–40.
- Washington State Institute for Public Policy (WSIPP), 2012. *Chemical Dependency Treatment for Offendors: A Review of the Evidence and Benefit-Cost Findings*, Washington, USA: WSIPP.

Slide 78:

- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017d. Statistical Bulletin 2017 - Prevalence of Drug Use.

Slide 79:

- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017b. Penalties for drug law offences in Europe at a glance.

Slide 80:

- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2017a. *Cannabis legislation in Europe: an overview*, Luxembourg: Publications Office of the European Union.