



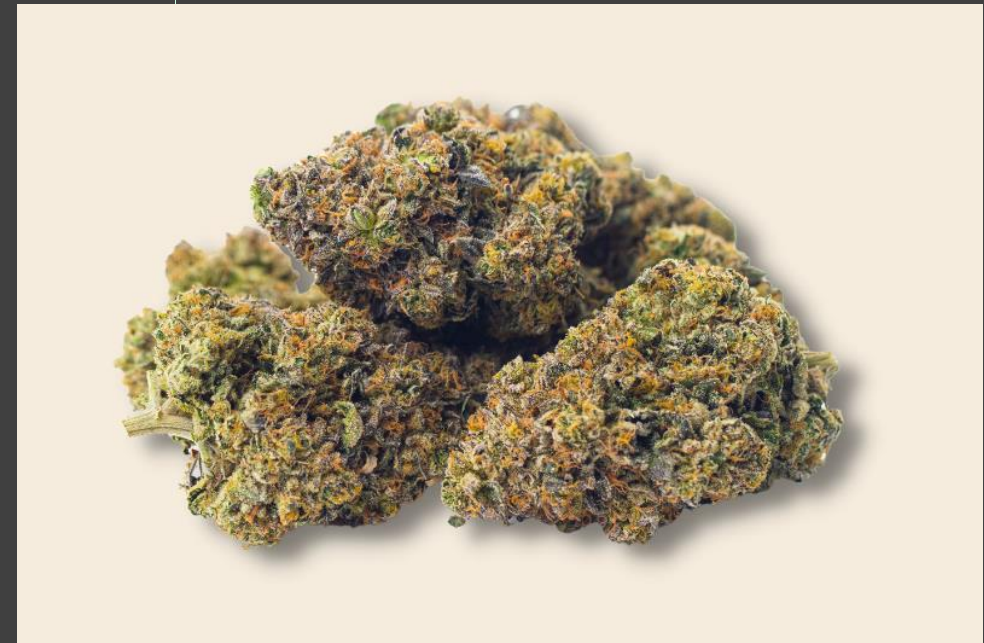
National Institute
on Drug Abuse

PAVING THE WAY FOR IMPROVED DATA COLLECTION ON CANNABIS USE



LISBON
ADDICTIONS
2022

Susan R.B. Weiss
Director
Division of Extramural Research
National Institute on Drug Abuse



Disclaimer:

The views and opinions expressed in this presentation are those of the author only and do not necessarily represent the views, official policy, or position of the U.S. Department of Health and Human Services or any of its affiliated institutions or agencies.

National Institute on Drug Abuse

RECOMMENDATIONS FOR
NIDA'S CANNABIS POLICY
RESEARCH AGENDA

REPORT FROM THE
CANNABIS POLICY RESEARCH WORKGROUP

February 6, 2018



PAVING THE WAY TO BETTER RESEARCH

- Explore the possibility of constructing a standardized dose similar to that for alcohol (the standard drink), tobacco (a cigarette), or opioids (morphine milligram equivalents) for researchers to employ in analyzing use and for users to understand their consumption.
- Establish standards for measuring cannabis intoxication and impairment.

PAVING THE WAY TO BETTER RESEARCH...

'Standard THC units': a proposal to standardize dose across all cannabis products and methods of administration

Tom P. Freeman^{1,2,3} & Valentina Lorenzetti⁴

Addiction and Mental Health Group (AIM), Department of Psychology, University of Bath, Bath, UK¹; National Addiction Centre, King's College London, London, UK²; Clinical Psychopharmacology Unit, University College London, London, UK³; and School of Behavioural and Health Sciences, Australian Catholic University, Fitzroy, VIC, Australia⁴

ABSTRACT

Background and Aims Cannabis products are becoming increasingly available in various forms of 9-tetrahydrocannabinol (THC) and cannabidiol (CBD). High-dose CBD may partially offset some of these effects. Lower THC doses based on quantity of use, and could be improved by implementing how units should be measured or standardized among products. **Argument** Existing proposals for standard cannabis units (e.g. joints) and these may not capture other methods, including edibles and liquids. Other proposals (e.g. grams of cannabis) cannot account for differences in potency between cannabis products. Similar to alcohol units, we argue that active pharmacological constituents (dose of THC). On the basis of existing policy, we propose that a 'standard THC unit' be used for all cannabis products, regardless of method of administration. If supported by sufficient evidence, this would facilitate research, and this was a key recommendation from NIDA's Cannabis Policy Research Council Workgroup 2. However, as discussed by Freeman & Lorenzetti, the development of such a measure has been challenging, due to concerns that the effects of any standardized dose would differ on the basis of mode of consumption or, possibly, how it is combined with other cannabinoids such as cannabidiol (CBD). These complexities hardly negate the value of having a standardized measure of THC, irrespective of product type. In fact, having and using such a standard is a prerequisite for comparing the effects of various cannabis products on THC bioavailability, pharmacokinetics and pharmacological effects, which is knowledge fundamental to studies pertaining to medical use of cannabis. A standardized measure will also be essential for advancing our understanding of some of the major concerns related to cannabis use, especially its influence on brain development, and the risk for cannabis use disorders and psychoses. Current and past studies evaluating the effects of cannabis on brain development and cognition, whether focused prenatally or during childhood or adolescence, are limited to rough estimates on the basis of

Keywords CBD, cannabis, harm reduction, safety guidelines

Correspondence to: Tom Freeman, Addiction and Mental Health Group (AIM), 11, freeman@bath.ac.uk
Submitted 29 January 2019; initial review completed 18 March 2019; final

Commentary | Open Access | © | | |

Importance of a standard unit dose for cannabis research

Nora D. Volkow & Susan R.B. Weiss

First published: 21 February 2020 | <https://doi.org/10.1111/add.14984> | Citations: 18

SECTIONS PDF TOOLS SHARE

“A standardized measure for 9-tetrahydrocannabinol (THC) content in cannabis products is necessary to advance research both on the adverse effects of cannabis (e.g. risks for brain development, mental illness and addiction) and on the drug's potential medical uses”

Recognizing the increasing diversity of cannabis products and their expanded use, Freeman & Lorenzetti propose a standard unit dose of 5 mg 9-tetrahydrocannabinol (THC) to be used for all cannabis products, regardless of method of administration 1. They argue that a standard dose would help to guide consumers towards safer patterns of cannabis use. The National Institute on Drug Abuse (NIDA) strongly supports the need for a standardized measure to facilitate research, and this was a key recommendation from NIDA's Cannabis Policy Research Council Workgroup 2.

However, as discussed by Freeman & Lorenzetti, the development of such a measure has been challenging, due to concerns that the effects of any standardized dose would differ on the basis of mode of consumption or, possibly, how it is combined with other cannabinoids such as cannabidiol (CBD).

These complexities hardly negate the value of having a standardized measure of THC, irrespective of product type. In fact, having and using such a standard is a prerequisite for comparing the effects of various cannabis products on THC bioavailability, pharmacokinetics and pharmacological effects, which is knowledge fundamental to studies pertaining to medical use of cannabis.

A standardized measure will also be essential for advancing our understanding of some of the major concerns related to cannabis use, especially its influence on brain development, and the risk for cannabis use disorders and psychoses 4, 5. Current and past studies evaluating the effects of cannabis on brain development and cognition, whether focused prenatally or during childhood or adolescence, are limited to rough estimates on the basis of

“As States **legalize** medical and adult-use marijuana and dispensaries create **greater access** to cannabis, there is increased urgency to study its effects—both adverse and potentially therapeutic—in a systematic fashion. This is especially needed with the widening **variety** of cannabis products, such as edibles and extracts, as well as the increasing **potency** of cannabis available on the street and in dispensaries. One hindrance to conducting such research is the **lack of a standardized measure** of the THC in various cannabis products, making it hard to compare the results of different studies.”

<https://nida.nih.gov/about-nida/noras-blog/2020/03/request-information-standard-unit-dose-thc>

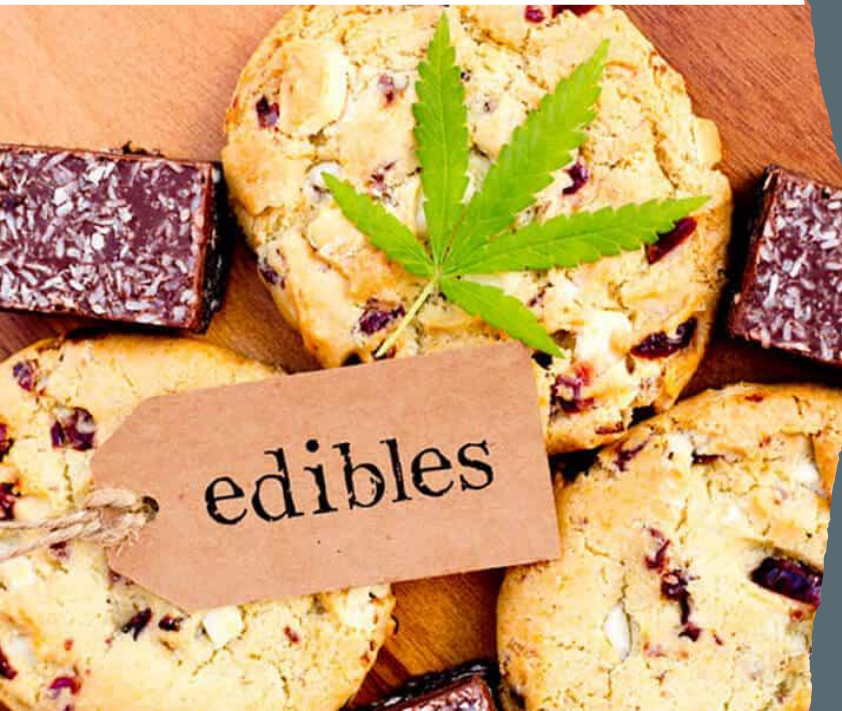


STANDARD UNIT OF MEASURE FOR CANNABIS RESEARCH: RATIONALE AND CAVEATS

- Inconsistency in measurement has been a major limitation across studies and over time (frequency of use/potency...)
- Delta-9 THC is the main component in cannabis responsible for its psychoactive effects
- MME (morphine milligram equivalent) has been useful for comparing opioid doses/exposures, as have alcohol standard drink sizes
- If adopted more broadly, would improve the quality of measurement in epidemiology/observational studies and inform consumer choice

BUT...

- Route of administration is highly variable and can determine how much THC is consumed (especially if smoked or vaporized)
- Products vary substantially in constituents (cannabinoids and others)
- STU of 5 mg may be too small (daily users may be consuming > 100 mg/day)
- Delta-8 THC (and others) emerging in the marketplace
- Pharmacokinetics/pharmacodynamics of cannabis are complex



Standard Unit of Measure for Cannabis Research

NIDA Follow Up

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

ADDICTION OPINION AND DEBATE

doi:10.1111/add.14842

'Standard THC units': a proposal to standardize dose across all cannabis products and methods of administration

Tom P. Freeman^{1,2,3}  & Valentina Lorenzetti⁴ 

Addiction and Mental Health Group (AIM), Department of Psychology, University of Bath, Bath, UK¹ National Addiction Centre, King's College London, London, UK² Clinical Psychopharmacology Unit, University College London, London, UK³ and School of Behavioural and Health Sciences, Australian Catholic University, Fitzroy, VIC, Australia⁴

ABSTRACT

Background and Aims Cannabis products are becoming increasingly diverse, and vary considerably in concentrations of Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD). Higher doses of THC can increase the risk of harm from cannabis, while CBD may partially offset some of these effects. Lower Risk Cannabis Use Guidelines currently lack recommendations based on quantity of use, and could be improved by implementing standard units. However, there is currently no consensus on how units should be measured or standardized among different cannabis products or methods of administration. **Argument** Existing proposals for standard cannabis units have been based on specific methods of administration (e.g. joints) and these may not capture other methods, including pipes, bongs, blunts, dabbing, vaporizers, vape pens, edibles and liquids. Other proposals (e.g. grams of cannabis) cannot account for heterogeneity in THC concentrations among different cannabis products. Similar to alcohol units, we argue that standard cannabis units should reflect the quantity of primary active pharmacological constituents (dose of THC). On the basis of experimental and ecological data, public health considerations and existing policy, we propose that a 'standard THC unit' should be fixed at 5 mg THC for all cannabis products and methods of administration. If supported by sufficient evidence in future, consumption of standard CBD units might offer an additional strategy for harm reduction. **Conclusions** Standard Δ^9 -tetrahydrocannabinol (THC) units can potentially be applied among all cannabis products and methods of administration to guide consumers and promote safer patterns of use.

Keywords CBD, cannabis, harm reduction, safety guidelines, standard unit, THC.

Correspondence to: Tom Freeman, Addiction and Mental Health Group (AIM), Department of Psychology, 10 West, University of Bath, BA2 7AY, UK. E-mail: L.p.freeman@bath.ac.uk

Submitted 29 January 2019; initial review completed 18 March 2019; final version accepted 27 September 2019

- Public Request for Information: 37 responses, largely supportive
- Follow up discussions with experts
- Presentation/discussion with NIDA Advisory Council
- Issued a Notice **requiring** the use of a standard THC unit (STU) of 5 mg for **applicable** human studies (NIDA, NCI, NHLBI, NIMH).
- Followed up with a funding opportunity to study the pharmacokinetics and pharmacodynamics of delta-9 THC

U.S. FEDERAL POLICY

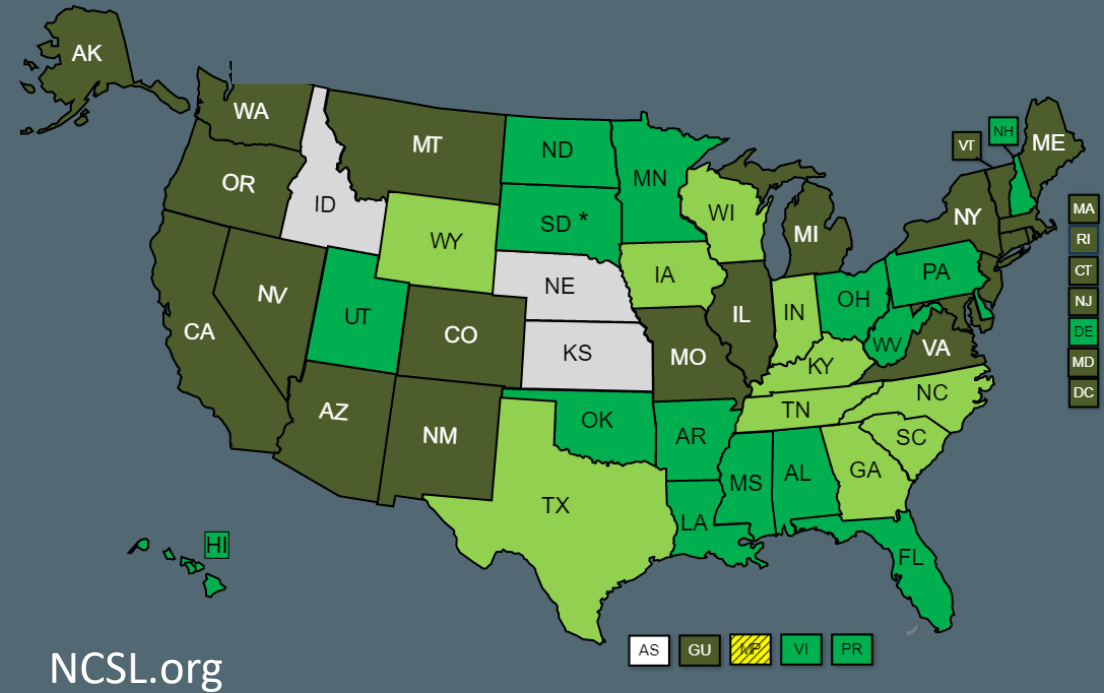
Marijuana (cannabis >0.3% delta-9 THC) is Schedule I under Controlled Substances Act: high risk for abuse; no accepted medical use.

- Illegal to grow, possess, or distribute
- Per International Treaty (single convention on narcotic drugs) each nation can designate a single source of marijuana for research purposes
- Until recently, DEA only licensed a single grower (University of Mississippi, since 1968), under a NIDA – supported contract.
- *Based on a change in treaty interpretation, several additional growers have now been approved.*

Hemp (not more than 0.3% delta-9 THC dry weight) is not controlled.

- Regulation of growing: Dept. of Agriculture
- Regulation of product quality and labeling: FDA

STATE POLICIES (Nov 2022)

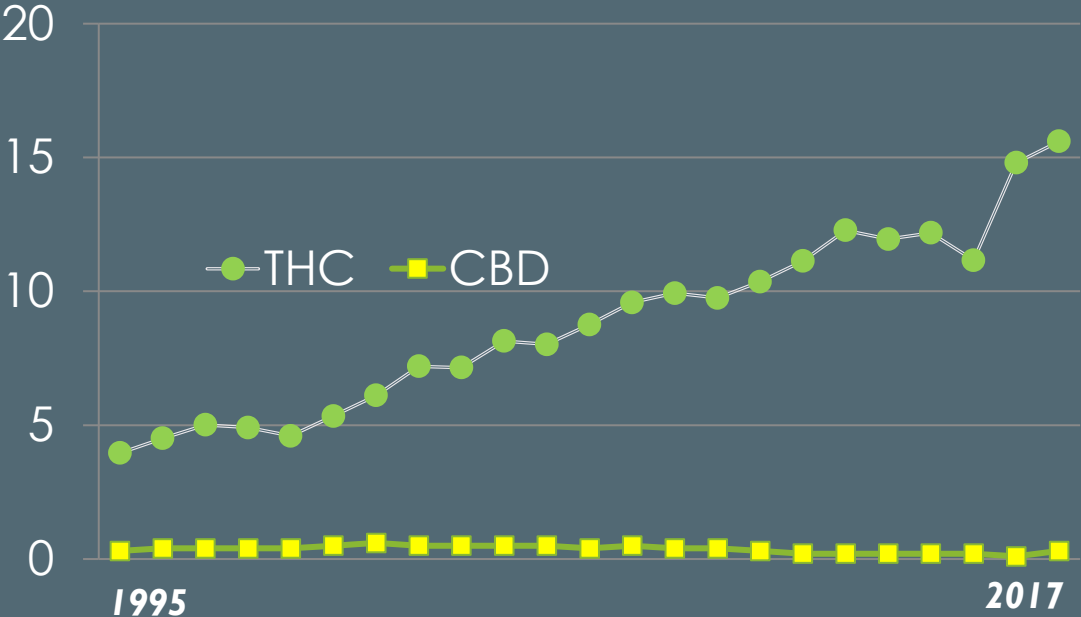


State Laws vary on:

- Marketing, product labeling, distribution
- Product testing
- Public consumption
- Taxation
- Licensing
- Expungement and Equity

CHANGING LANDSCAPE: INCREASING POTENCY (%THC), NEW ROUTES OF ADMINISTRATION, CBD PRODUCTS

Cannabis Potency Increasing



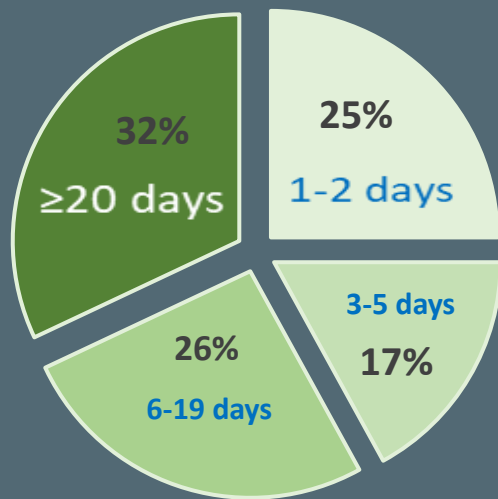
Source: U Miss, Potency Monitoring Project



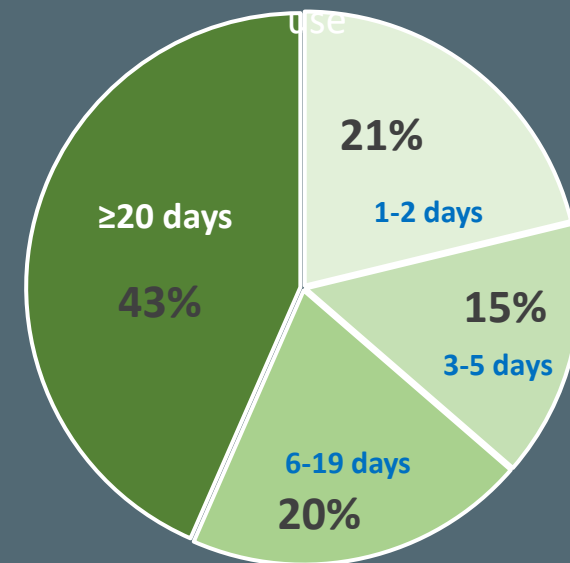
PATTERNS OF USE ARE CHANGING: MORE THAN TWO IN FIVE PAST MONTH USERS WERE DAILY OR ALMOST DAILY USERS IN 2019

Frequency of use	2002	2019	<i>P</i> value for the difference between 2002 and 2019
1-2 days	24.55%	20.99%	.015
3-5 days	17.46%	15.09%	.041
6-19 days	25.70%	20.44%	<.001
20+ days	32.29%	43.48%	<.001
Estimated no. past-month users	14.6 Million	31.6 Million	<.001

among 14.6 M people in 2002 reporting past-month use

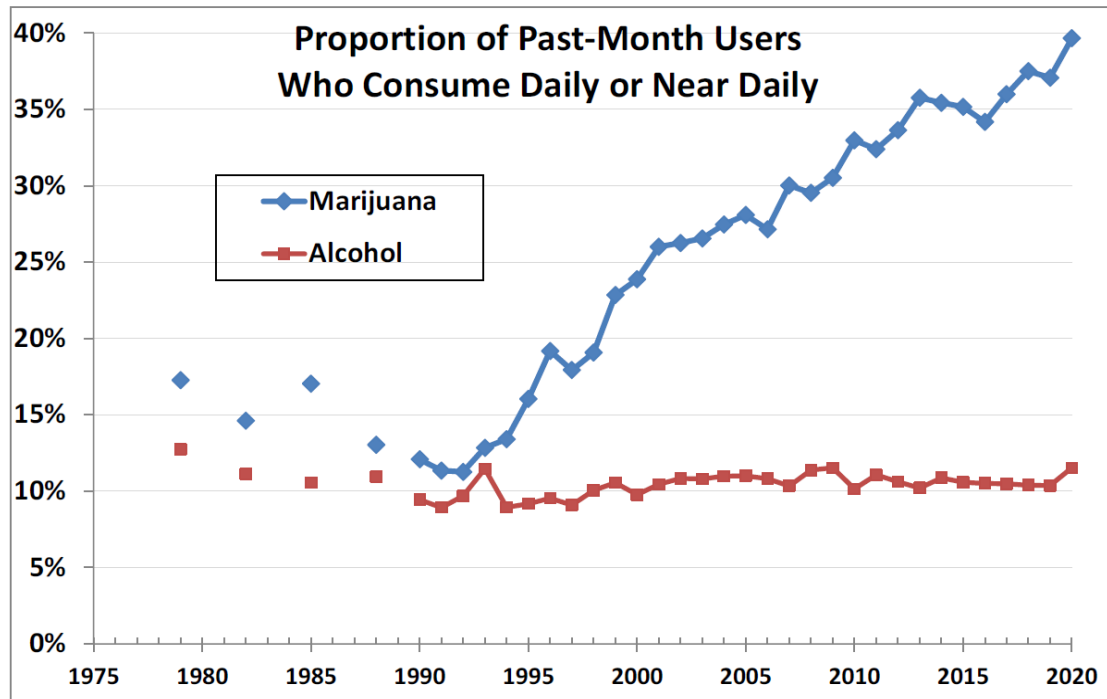


among 31.6 M people in 2019 reporting past-month use



PATTERNS OF CANNABIS USE ARE CHANGING

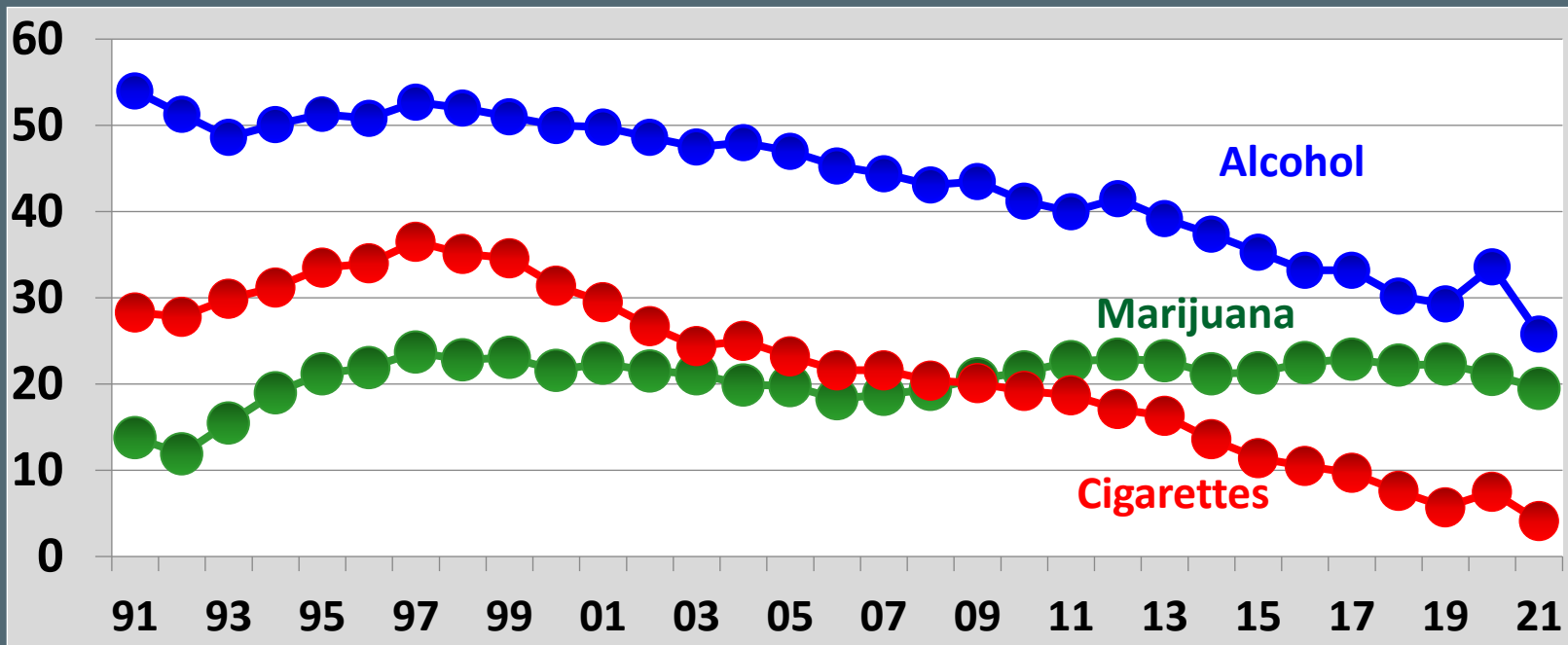
DND Cannabis Use is Relatively New



Contrast THC Consumption of Two Types of Users

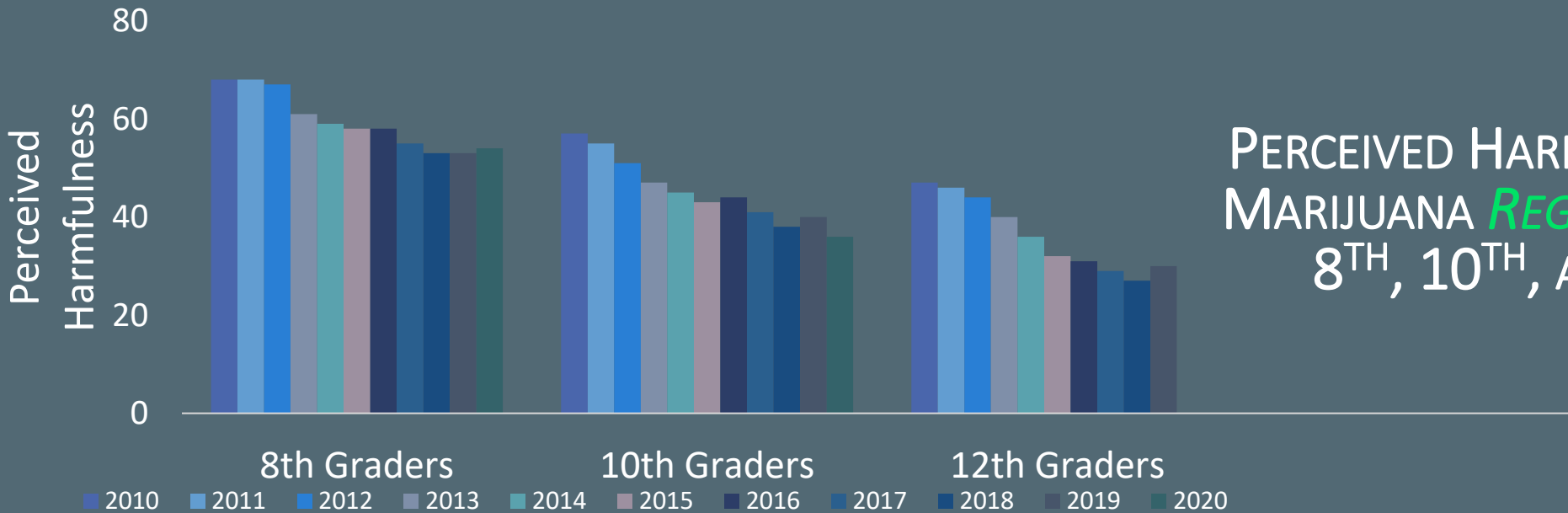
- 1 joint each weekend night, pre-2000
 - Assuming 0.4 gms/joint, 4% THC
 - $(2/7) * 0.4 * 4\% = 4.6$ milligrams/day
- Average daily user in today
 - Assuming 1.6 gms/day, 20% THC
 - $1.6 * 20\% = 320$ milligrams/day
- **That's ~70 times as much THC**

Slides Courtesy of Jonathan Caulkins



PAST MONTH DRUG USE
IN 12TH GRADERS

5.8 % report daily or near daily use of marijuana in 2021

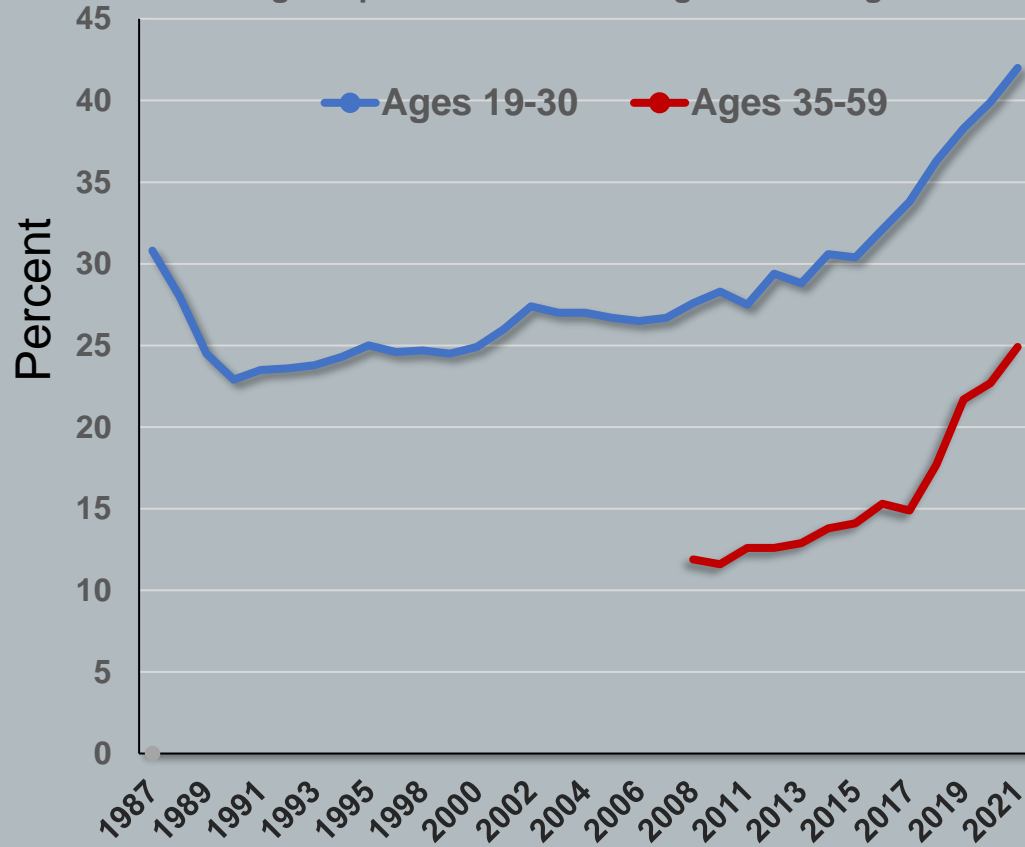


PERCEIVED HARMFULNESS OF SMOKING MARIJUANA *REGULARLY* IS DECLINING IN 8TH, 10TH, AND 12TH GRADERS

PAST YEAR SUBSTANCE USE AMONG ADULTS AGES 19-59, 1976-2021

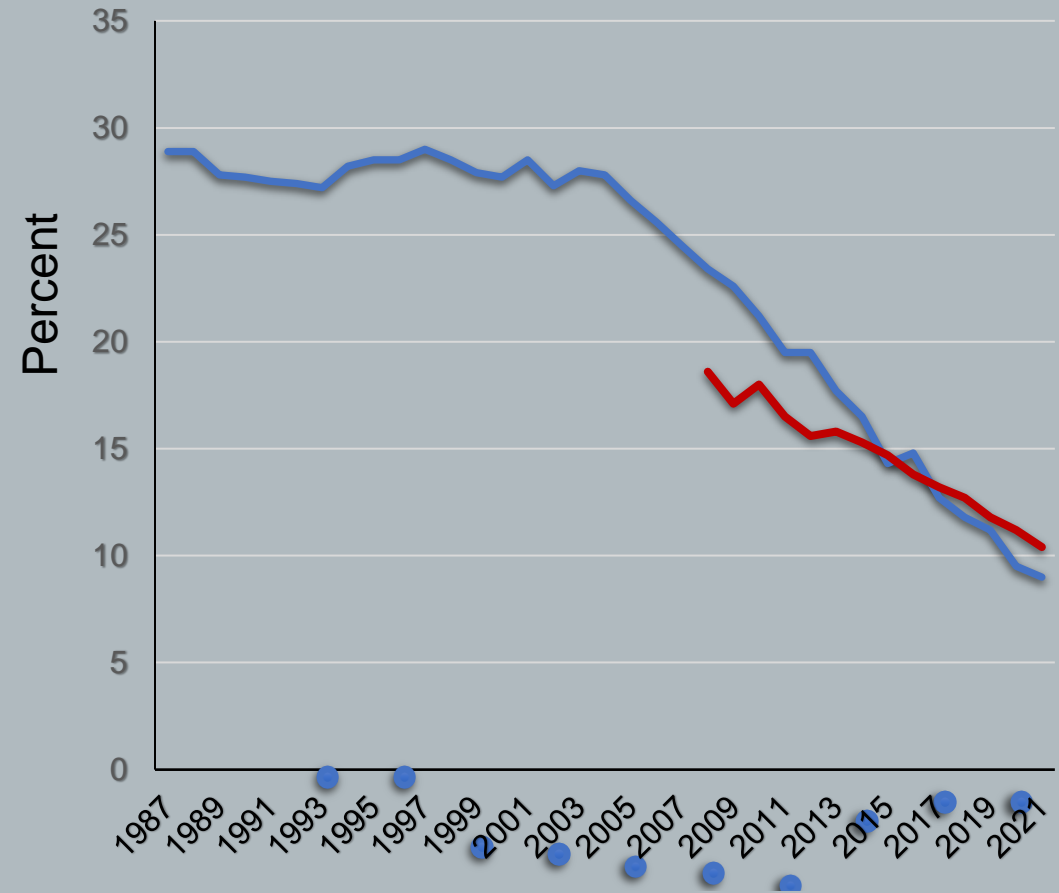
MARIJUANA

Trends in 12 Month Prevalence
Among Respondents of Modal Ages 19 through 59



CIGARETTES

Trends in 12 Month Prevalence
Among Respondents of Modal Ages 19 through 59





RESEARCH GAPS : PRENATAL AND ADOLESCENT EXPOSURE

Findings are often modest, results are inconsistent,
and may be confounded by other variables



- Better measures of cannabis exposure (biological and self report)
 - Frequency of use
 - Timing of exposure
 - Products used (CBD vs. THC)
 - Quantification of exposures
- Concurrent measures of other variables that could affect outcomes
 - Other substance use
 - Risk and protective factors (prenatal care, food/housing insecurity, stress, family support, lead exposure, socioeconomic resources...)
- Perinatal
 - Timing of exposure (1st, 2nd, 3rd trimester); post natal; pre-conception
 - Data from recent cohorts, esp. longitudinal studies
 - Post-natal parenting behaviors
- Adolescents
 - Timing of exposure/reasons for use
 - Other risk factors, especially in those who start young and use frequently
 - Polysubstance use (esp. alcohol and tobacco)
 - Persistence of effects if cannabis use is stopped
 - Relation to onset/severity of mental illness

WHAT CANNABIS
MEASURES ARE
NEEDED OUTSIDE OF
LABORATORY SETTINGS
TO PROVIDE
GRANULARITY AND
SPECIFICITY NOT
ACHIEVABLE IN
CURRENT POPULATION
SURVEYS?

Frequency: if daily, or near daily; how frequently over the course of the day

Quantities: how much delta-9 THC is consumed?

Patterns of use: weekends, daily, variability in patterns of use

Routes of administration: for smoked/inhaled products, estimates for variability in smoking behavior (?)

Products used: flower, vapes, concentrates, edibles, tinctures—*combinations*

Constituents other than THC (especially CBD)

Delta-8 products: less potent than delta-9, but widely available in some US states (can be derived from hemp)

Biological Measures: plasma, urine, hair

Reasons for use: medical, recreational, both

WHAT COULD WE DO WITH A STANDARD UNIT OF MEASUREMENT?



- Achieve comparability across research studies, including epidemiological and observational studies (ABCD/HBCD)
- Determine whether there are “safer” levels of exposure*, i.e., less likely to lead to serious adverse outcomes
- Determine what levels of exposure cause or contribute to adverse outcomes, including cannabis use disorder (CUD), mental illness, psychosocial impairments, hyperemesis....
- Identify meaningful CUD treatment outcomes—e.g., reduction-based endpoints vs. abstinence
- Determine appropriate doses/formulations for *medical* vs. *adult use*
 - Train physicians, patients, budtenders and others involved with cannabis distribution

*would not apply to women who are pregnant, children/adolescents, or those at high risk for mental illness

FAQs for Registry of Medical Cannabis Use and Health Outcomes: RFA-DA-23-011

Purpose of this FOA

The National Institute on Drug Abuse (NIDA) seeks applications to develop and maintain a medicinal cannabis use registry to assess the medical conditions reported as reasons for using medicinal cannabis, how and what products are being used, and the associated medical outcomes. The goal of this registry is to inform research, policy, and clinical recommendation practices on medicinal cannabis, associated conditions, and outcomes.

[RFA-DA-23-011: Registry of Medical Cannabis Use and Health Outcomes \(UM1 - Clinical Trial Optional\)](#)

Frequently Asked Questions

1. What is the UM1 mechanism?

This is a cooperative agreement grant mechanism that supports a Research Project with Complex Structure. The goal is to: support cooperative agreements involving large-scale research activities with complicated structures that cannot be appropriately categorized into an available single component activity code, e.g. clinical networks, research programs or consortium. The components represent a variety of supporting functions and are not independent of each component.

Substantial federal programmatic staff involvement is intended to assist investigators during performance of the research activities, as defined in the terms and conditions of the award. In practice, substantial involvement means that, after award, Federal scientific or program staff from the funding programs will assist, guide, coordinate, or participate in project activities. Under the cooperative agreement, the purpose of Federal staff is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role without assuming prime responsibility in the activities. The prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and Federal staff. Federal partners also will have access to project data and may participate in publications, if warranted.

2. What is the role of NIH staff in this project?

NIH staff provide oversight, coordination, or facilitation that goes substantially beyond what would normally be needed for a R-series grant. Working jointly with U awardees, NIH staff act as partners to support and stimulate the research. However, NIH staff are not meant to play a dominant role nor assume direction or primary responsibility for awardee activities.

3. Who will the program official and project scientist for this grant award be?

That has not yet been determined. Dr. Kimmel, the Scientific/Research Contact, will have a significant role in the award.

Registry of Medical Cannabis Use and Health Outcomes (UM1 - Clinical Trial Optional)

The National Institute on Drug Abuse (NIDA) seeks applications to develop and maintain a medicinal cannabis use registry to assess the medical conditions reported as reasons for using medicinal cannabis, how and what products are being used, and the associated medical outcomes. The goal of this registry is to inform research, policy, and clinical recommendation practices on medicinal cannabis, associated conditions, and outcomes.

MEASURES IN CURRENT ABCD PROTOCOL

Smoked or Vaped MJ Flower:

During the past year, what brand or strain of marijuana flower or bud do you smoke or vape? If you do not know, just say "I don't know." Interviewer: enter name, say "home grown," if unknown click on "don't know, below"

During the past year, what brand or strain of marijuana flower or bud do you smoke or vape? If you do not know, just say "I don't know." Interviewer: enter name, say "home grown," if unknown click on "don't know" Don't know reset

How strong or potent do you think your smoked or vaped marijuana flower or bud was that you used during the past year? Try to estimate the potency:

- 1, Low (around < 5% THC)
- 2, Medium (10%)
- 3, High (15%)
- 4, Very high (20%)
- 5, Don't know

Of the times you smoked or vaped marijuana flower or bud during the past year, how often did you smoke highly potent marijuana (such as "skunk", or MJ that is 15% THC or higher)? It is okay if you don't know.

- Never
- Almost never
- Sometimes
- Most of the time
- Almost always
- Always
- Don't know

Marijuana Concentrates Follow-Up Questions (Vaped or Smoked):

What was the typical type of MJ concentrate or oil that you used during the past year?

- 1, Hash oil
- 2, Kief
- 3, Water hash
- 4, Co2 oil extracted oil or wax
- 5, BHO solvent extracted oil or wax
- 6, Don't know

During the past year, what was the way you smoked marijuana concentrates or oils?

- 1, Pipe or bong
- 2, Dab rig
- 3, Joint or rolled paper
- 4, Other
- 5, Don't know

How strong or potent do you think your typical marijuana concentrate or oil was during the past year? Try to estimate the potency:

- 1, Low is around 20% THC
- 2, Medium (40%)
- 3, High (60%)
- 4, Very high (80%+)
- 5, Don't know

Event Details

Substance: Smoked MJ flower MJ Blunts Vaped MJ flower Vaped MJ oil Smoked MJ oil

Amount: grams

Start Time:

End Time:

Approximations for missed visits

limit range by days of the week

How often did you use marijuana concentrates or oils during the past year, how high did you typically get when you smoked or vaped marijuana concentrate or oil (concentrate that is 80% THC or more potent than flower, if you do not know, that is ok too.)

- Never
- Almost never
- Sometimes
- Most of the time
- Almost always
- Always
- Don't know

0 1 2 3 4 5 6 7 8 9 10

Buzzed High Very High Going, Going... Gone

During the past year, how high did you typically get when you smoked or vaped marijuana flower or bud?

0 1 2 3 4 5 6

Sober Buzzed High Very High

0 1 2 3

Marijuana Edibles Follow-Up Questions

Was your marijuana edible made with:

- 1, Only THC
- 2, Both THC and CBD
- 3, I don't know

How much THC was typically in your marijuana edible? Answer in THC milligrams (mg)

[measure in mg; 1 gram of ground MJ with 10% THC=100mg; typical serving size is 10mg]

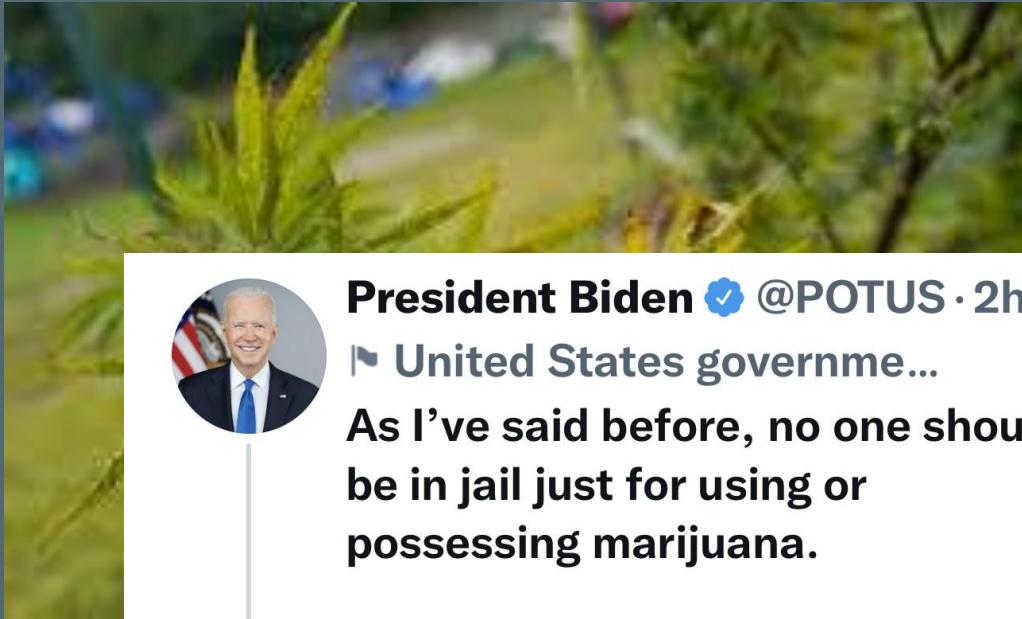
How often did you use marijuana concentrates or oils during the past year, how high did you typically get when you smoked or vaped marijuana concentrate or oil (concentrate that is 80% THC or more potent than flower, if you do not know, that is ok too.)

- Never
- Almost never
- Sometimes
- Most of the time
- Almost always
- Always
- Don't know

0 1 2 3 4 5 6 7 8 9 10

Sober Buzzed High Very High Going, Going... Gone

ARE THERE NEW OPPORTUNITIES FOR IMPLEMENTATION?



President Biden  @POTUS · 2h ...

🇺🇸 **United States governme...**

As I've said before, no one should be in jail just for using or possessing marijuana.

Today, I'm taking steps to end our failed approach. Allow me to lay them out.

 8,361  59.8K  246K 

- **Political Environment:**

- Re-consideration of Marijuana's Schedule I status (Biden, 10/6/2022)
- Multiple bills in Congress to facilitate research or decriminalize marijuana

- **Research Strategies:**

- Social media surveys
 - Detailed surveillance of product types, doses/servings consumed, routes of administration, user characteristics
- Observational studies using zoom (Cutler, 2021)
- Mobile Laboratory settings to measure subjective and biological outcomes (Hutchison, 2021)
- Patient Registries
- Marketing Research

- **Public and Consumer Education:**

- Standardized product labeling to inform consumers may promote safer consumption of cannabis products.
- Product testing standards would benefit legal market in States
- Training for cannabis providers, budtenders

- **Information sharing and dissemination:**

- researchers/regulators/consumers/healthcare community



THANK YOU!

FEDERAL REGULATION OF CANNABIS: IS THERE A MODEL?

- Modified Risk Products: Electronic Nicotine Devices (ENDS); Heat not Burn; Smokeless Tobacco
- Flavorings
- Nicotine levels
- Warning labels, Packaging
- Advertising
- Minimum age limits
- BUT: Bumpy road has slowed progress
 - multiple legal challenges have limited the effectiveness of this legislation

10 TOBACCO
CONTROL
ACT
YEARS
FOR TOBACCO PRO

